

28TH
INTERNATIONAL AUSTRALASIAN
WINTER CONFERENCE ON BRAIN RESEARCH



2010
Programme and Abstracts

28 August - 1 September 2010
Edgewater Resort Hotel, Wanaka, New Zealand
www.awcbr.org

Supported by the
Neurological Foundation of New Zealand



Neurological Foundation of New Zealand

3.00-6.00 PM	REGISTRATION, EDGEWATER RESORT HOTEL, WANAKA
5.30-6.00 PM	STUDENT MEET AND GREET
6.00 PM	OPENING RECEPTION, CASH BAR
7.00 PM	OPENING REMARKS

1. BEHAVIOURAL PHARMACOLOGY

CHAIR: NEIL McNAUGHTON

7.15 pm	1.1	INVITED SPEAKER Andrew Lawrence, <i>University of Melbourne, Australia</i> Animal models of drug-seeking: genetics and pharmacology
8.00 pm		Tea/Coffee break
8.15 pm	1.2	Aashish Morani, <i>Victoria University of Wellington, New Zealand</i> Anti-addiction and side effects profile of novel kappa opioid receptor agonists -Salvinorin A and DS1
8.30 pm	1.3	Bridget Simonson, <i>Victoria University of Wellington, New Zealand</i> The effect of novel kappa opioid receptor agonists on dopamine transporter function
8.45 pm	1.4	Kirsty Danielson, <i>Victoria University of Wellington, New Zealand</i> The effects of nicotine and total particulate matter of cigarette smoke on dopamine transporter expression and function
9.00 pm	1.5	Dave Harper, <i>Victoria University of Wellington, New Zealand</i> A comparison of MDMA and amphetamine in the drug discrimination paradigm





SUNDAY 29 AUGUST MORNING SESSION

7.30 AM

LIGHT BREAKFAST AVAILABLE

Posters to be set up at this time

2. DEVELOPMENT AND PLASTICITY

CHAIR: PING LIU

8.00 am	2.1	Miaomiao Mao, <i>University of Auckland, New Zealand</i> Structural development of the mouse dorsal cochlear nucleus
8.15 am	2.2	Bill Connelly, <i>University of Otago, New Zealand</i> Differential short term plasticity at convergent inhibitory synapses to the substantia nigra pars reticulata
8.30 am	2.3	Desiree Dickerson, <i>University of Otago, New Zealand</i> Abnormal neural synchrony in a maternal immune activation animal model of schizophrenia
8.45 am	2.4	Chris Thompson, <i>University of Auckland, New Zealand</i> Brain-derived neurotrophic factor val ⁶⁶ met polymorphism influences the magnitude of human long-term potentiation which predicts memory performance
9.00 am	2.5	Sarah Hulme, <i>University of Otago, New Zealand</i> Heterosynaptic metaplasticity in the hippocampus

SUNDAY 29 AUGUST AFTERNOON SESSION



3.30 pm

TEA AND COFFEE AVAILABLE

3. PLASTICITY MECHANISMS

CHAIR: CLIFF ABRAHAM

4.00 pm	3.1	INVITED SPEAKER Pankaj Sah, <i>University of Queensland, Australia</i> NMDA receptors in the basolateral and central amygdala: subunit composition and function
4.45 pm	3.2	Bruce Mockett, <i>University of Otago, New Zealand</i> Both synaptically- and chemically-induced Group I mGluR-mediated LTD are regulated by CaMKII in rat hippocampus
5.00 pm	3.3	Melissa Barry, <i>University of Otago, New Zealand</i> Effects of intermittent theta burst stimulation on interhemispheric inhibition recorded in pyramidal neurons of the motor cortex <i>in vivo</i>
5.15 pm	3.4	John Reynolds, <i>University of Otago, New Zealand</i> Visual stimuli induce firing pauses in striatal cholinergic interneurons <i>in vivo</i>
5.30 pm		Tea/Coffee break

4. EVENING POSTER SESSIONS

5.45 -7.45 pm

Presenters will be in attendance during this time

Posters available for viewing from 5.45 pm

Tea, coffee, finger food and cash bar available during poster viewing session

The poster session will be followed by a postgraduate dinner to be held at the Lone Star; details to be provided.

- 4.1 - A **Meghan Murphy, *University of Auckland, New Zealand***
Cognitive impairment in treatment resistant schizophrenia: A consequence of illness or medication used in treatment?
- 4.2 - B **Petra Makela, *Hutt Hospital, New Zealand***
Confabulation: A single deficit or multiple?
- 4.3 - A **Charlotte Haigh, *University of Auckland, New Zealand***
Reading with the right hemisphere: Investigating the neurological basis of developmental dyslexia
- 4.4 - B **Nicola Starkey, *University of Waikato, New Zealand***
Examining the incidence and outcome of paediatric traumatic brain injury in New Zealand
- 4.5 - A **Suzanne Barker-Collo, *University of Auckland, New Zealand***
Examining the incidence and outcomes of traumatic brain injury in New Zealand, design and rationale of the BIONIC study (2009-2012)
- 4.6 - B **Tessa Cowley, *Van der Veer Institute, New Zealand***
Prevalence and characteristics of acute headaches and dizziness in people with mild head trauma
- 4.7 - A **Sangeeta Balabhadrapatruni, *University of Otago, New Zealand***
Long-term effects of bilateral vestibular deafferentation on the total number of neurons in the subregions of the hippocampus estimated using the optical fractionator
- 4.8 - B **Yu Jing, *University of Otago, New Zealand***
Altered arginine metabolism in the hippocampus and prefrontal cortex in maternal immune activation rat offspring
- 4.9 - A **Yeri Kim, *University of Otago, New Zealand***
Synapse distribution in the cerebellar cortex of a mouse model of ataxia
- 4.10 - B **Caleb Carati, *Victoria University of Wellington, New Zealand***
Back off the wagon: Dopaminergic mechanisms of methamphetamine reinstatement in a rat model of relapse
- 4.11 - A **Peter Bosch, *Victoria University of Wellington, New Zealand***
MDMA internalises the serotonin transporter in a cell model without activating phospho-p38-mitogen activated protein kinase

- 4.12 - B **Reem Jan, *University of Auckland, New Zealand***
The effect of a single oral dose of Methylphenidate (MPD) on executive function and cognition in methamphetamine-dependent human participants using functional magnetic resonance imaging (fMRI)
- 4.13 - A **Ehson Negahbani, *University of Waikato, New Zealand***
Spectral analysis of epileptic activity in rodent brain slices
- 4.14 - B **Maher Elbohouty, *University of Waikato, New Zealand***
Measuring electrical conductivity of mouse brain slices
- 4.15 - A **Fernanda Gravina, *University of Newcastle, Australia***
Ketamine anesthesia helps preserve neuronal viability
- 4.16 - B **Ramatis de Oliveira, *University of Newcastle, Australia***
Pacemaker calcium currents: Difference in locus coeruleus neurons of mice and rats
- 4.17 - A **Kaier Wang, *University of Waikato, New Zealand***
Nonlinear dynamics-based continuum cortical modelling and its simulation of interacting Turing and Hopf instabilities
- 4.18 - B **Marcus Wilson, *University of Waikato, New Zealand***
A hybrid model of action potentials and network oscillations
- 4.19 - A **Victoria Martin, *University of Auckland, New Zealand***
Remembering the future: Hippocampal contributions to encoding future simulations
- 4.20 - B **Frances Brett, *University of Canterbury, New Zealand***
Spatial memory: Anterior thalamic nuclei versus laterodorsal thalamic nuclei
- 4.21 - A **Katharina Ulrich, *University of Otago, New Zealand***
Spatial working memory learning can be repeatedly tested and challenged with anterior thalamic lesions
- 4.22 - B **Saskia Campbell, *University of Otago, New Zealand***
Behavioural effects of a single bilateral intracerebroventricular infusion of preaggregated A β ₂₅₋₃₅ in rats

- 4.23 - A **Bruce Harland, *University of Canterbury, New Zealand***
 Hippocampus, neuronal morphology and memory: Brief review and some recommendations
- 4.24 - B **Steve Seo, *University of Otago, New Zealand***
 Co-localization of L-glutamate and agmatine in the hippocampal CA1 synaptic terminals in rats.
- 4.25 - A **Malinda Tantirigama, *University of Otago, New Zealand***
 GFP expression in Fezf2-GFP adult mouse brain
- 4.26 - B **Yassar Alamri, *Van der Veer Institute, New Zealand***
 Blackcurrant antioxidants and Parkinson's disease: Are metabolites present in the cerebrospinal fluid?

Presenters for Posters A will be in attendance from 5.45 to 6.45pm

Presenters for Posters B will be in attendance from 6.45 to 7.45pm

8.00 pm

Posters to be removed at this time

MONDAY 30 AUGUST MORNING SESSION



7.30 AM

LIGHT BREAKFAST AVAILABLE

5. COGNITIVE NEUROSCIENCE

CHAIR: IAN KIRK

8.00 am	5.1	<i>Amy Walsh, Victoria University of Wellington, New Zealand</i> Impaired inhibition of negative words in women with relative right hemisphere frontal asymmetry
8.15 am	5.2	<i>Karen Waldie, University of Auckland, New Zealand</i> Brain activity during word rhyming: Are two disorders better than one?
8.30 am	5.3	<i>Anna Wilson, University of Auckland, New Zealand</i> Neurological bases of developmental dyscalculia in adults, and influence of comorbid dyslexia
8.45 am	5.4	<i>Sarina Iwabuchi, University of Auckland, New Zealand</i> Distinctly lateralised networks for verbal and spatial working memory
9.00 am		Tea/Coffee break
9.15 am	5.5	<i>Bradley Patten, University of Auckland, New Zealand</i> A time to remember, A time to forget: Item dependent temporal priming in recognition memory for forgotten words
9.30 am	5.6	<i>Matt Gers, Victoria University of Wellington, New Zealand</i> The cultural causes of cognition
9.45 am	5.7	<i>Gary Bird, Victoria University of Wellington, New Zealand</i> The role of eye gaze in valuation

4.00 PM

AFTERNOON TEA AVAILABLE

6. DRUGS AND THE CNS

CHAIR: YIWEN ZHENG

4.30 pm	6.1	Joanne Lin, <i>University of Auckland, New Zealand</i> Investigating changes in fractional anisotropy in white matter in the brain due to methamphetamine addiction using diffusion tensor imaging
4.45 pm	6.2	HeeSung Lee, <i>University of Auckland, New Zealand</i> Using interhemispheric transfer time to investigate the effects of benzylphenylpiperazine and trifluoromethylphenylpiperazine and dexamphetamine on human brains
5.00 pm	6.3	Louise Curley, <i>University of Auckland, New Zealand</i> Determining the acute effects of the combination Benzylpiperazine (BZP) and Trifluoromethylphenylpiperazine (TFMPP) on cognition and executive functioning using functional Magnetic Resonance Imaging (fMRI) and the Stroop paradigm
5.15 pm	6.4	Andrew Yee, <i>University of Auckland, New Zealand</i> Non-conventional effects of L-DOPA on nigral dopaminergic neurons – Electrophysiological study in brain slices
5.30 pm	6.5	Raghavendra Nagaraja, <i>University of Otago, New Zealand</i> Sustained drug release to the cerebellum using ELVAX polymer implants
5.45 pm	6.6	Alistair Steyn-Ross, <i>University of Waikato, New Zealand</i> Hysteresis effects in general anaesthesia: Biophysical reality or measurement artifact?

MONDAY 30 AUGUST



Conference Dinner

7.30 pm

Edgewater Function Room

Tickets must be purchased in advance.
The function room at Edgewater will be open from 7.00 pm,
with dinner commencing at 7.30 pm

Musical entertainment will be provided.



TUESDAY 31 AUGUST

MORNING SESSION

8.30 AM

LIGHT BREAKFAST AVAILABLE

7. BRAIN DYSFUNCTION I

CHAIR: BRUCE RUSSELL

9.00 am	7.1	Yiwen Zheng, <i>University of Otago, New Zealand</i> Inducing and assessing chronic tinnitus in rats using unilateral acoustic trauma and a frequency-specific shift in discrimination function with a conditioned lick suppression paradigm
9.15 am	7.2	Emma Hamilton, <i>University of Otago, New Zealand</i> Effects of chronic tinnitus on attention and impulsive behavior in rats
9.30 am	7.3	Shweta Vagal, <i>University of Otago, New Zealand</i> Effects of baclofen on chronic tinnitus induced by acoustic trauma
9.45 am	7.4	Lucy Stiles, <i>University of Otago, New Zealand</i> Effects of the synthetic cannabinoid receptor agonists, WIN55,212-2 and CP55,940, on salicylate-induced tinnitus in rats
10.00am	7.5	Logan Voss, <i>University of Auckland, New Zealand</i> GABAergic compensation in connexin36 knock-out mice evident during low-magnesium seizure-like event activity
10.15 am	7.6	Chelsea Goulton, <i>University of Otago, New Zealand</i> Pharmacological preconditioning by GYKI 52466 against kainate induced seizures: An electrocorticographic study
10.30 am		Tea/Coffee break
10.45 am		ANNUAL GENERAL MEETING All conference participants are invited to attend

TUESDAY 31 AUGUST AFTERNOON SESSION



4.15 pm

TEA AND COFFEE AVAILABLE

8. BRAIN DYSFUNCTION II

CHAIR: KAREN WALDIE

4.30 pm	8.1	Madiah Rushaidhi, <i>University of Otago, New Zealand</i> Effects of aging on agmatine levels in the rat hippocampus and prefrontal cortex
4.45 pm	8.2	Dave Bergin, <i>University of Otago, Dunedin, New Zealand</i> Agmatine prevents against beta-amyloid (25-35)-induced spatial and object recognition memory deficits in the rat
5.00 pm	8.3	Sarah Wright, <i>Van der Veer Institute, New Zealand</i> Functional MRI of saccades in Alzheimer's disease: the reflexive and predictive tasks
5.15 pm	8.4	Andrew Clarkson, <i>UCLA, USA</i> Dampening tonic inhibition promotes post-stroke functional recovery in young and aged
5.30 pm	8.5	Suzanne Barker-Collo, <i>University of Auckland, New Zealand</i> The ASTRO study: Cognition and functional outcomes in 5-year stroke survivors

5.45 pm

AFTERNOON TEA

9. PARKINSON'S DISEASE

CHAIR: BEULAH LEITCH

6.15 pm	9.1	Charlotte Graham, <i>Van der Veer Institute, New Zealand</i> Does cognitive and motor status affect memory-guided saccades in Parkinson's disease?
6.30 pm	9.2	William Ha, <i>Van der Veer Institute, New Zealand</i> Voluntary tremor suppression in Parkinson's disease
6.45 pm	9.3	Leslie Livingston, <i>Van der Veer Institute, New Zealand</i> Rey complex figure test –Copy and planning in Parkinson's disease
7.00 pm	9.4	Simon Feng, <i>Van der Veer Institute, New Zealand</i> Correlations between ASL blood flow MRI and eye movement abnormalities in Parkinson's disease
7.15 pm	9.5	Tracy Melzer, <i>Van der Veer Institute, New Zealand</i> Reduced cerebral perfusion in cognitively impaired Parkinson's disease
7.30 pm	9.6	Hannah Farr, <i>University of Canterbury, New Zealand</i> Models of neurovascular coupling



WEDNESDAY 1 SEPTEMBER

MORNING SESSION I



8.30 am

LIGHT BREAKFAST AVAILABLE

10. SENSORY/MOTOR DISORDERS

CHAIR: BRUCE MOCKETT

9.00 am	10.1	Nadia Borlase, <i>University of Canterbury, New Zealand</i> Diffusion tensor imaging and fibre tracking applied to the thalamus – A new approach to understanding Parkinson's disease
9.15 am	10.2	Rebekah Scott, <i>University of Otago, New Zealand</i> Feigned paresis affects behaviour but not neuromotor preparatory activity
9.30 am	10.3	Chloe Stanley-Cary, <i>Monash University, Australia</i> An ocularmotor exploration of autism and Asperger's disorder: Evidence for dissociation of motor deficits?
9.45 am	10.4	Max Major, <i>University of Otago, New Zealand</i> The neural correlates of motor inhibition in autism
10.00 am	10.5	Hannah Pickering, <i>University of New South Wales, Australia</i> Sensory and perceptual disturbances evoked by an experimental model of CRPS
10.15 am		Tea/Coffee break

11. LIMBIC SYSTEM ACTIVITY AND BEHAVIOUR

CHAIR: STEVE KERR

10.40 am	11.1	<p>Neil McNaughton, <i>University of Otago, New Zealand</i> A comparison of ambulation- and spin-elicited theta rhythms in the regions of the hippocampus, posterior hypothalamus and periaqueductal gray in the rat</p>
10.55 am	11.2	<p>Ian Kirk, <i>University of Auckland, New Zealand</i> Age effects on theta-range EEG in spatial working memory task</p>
11.10 am	11.3	<p>Donna Addis, <i>University of Auckland, New Zealand</i> Age-related neural changes associated with remembering and imagining autobiographical events</p>
11.25 am	11.4	<p>Kristin Hillman, <i>University of Otago, New Zealand</i> Cost-benefit encoding in the anterior cingulate cortex</p>
11.40 am	11.5	<p>Valerie van Mulukom, <i>University of Auckland, New Zealand</i> Medial temporal responses to the novelty of future simulations</p>
11.55 am		<p>Closing Remarks</p> <p>Presentation of the Goddard Prize for the best student oral presentation and the prize for best student poster presentation</p>
12.00 noon		<p>Light lunch provided</p>

Acknowledgements

We are deeply indebted to Ms Norma Bartlett, Mrs Margaret McMurtrie, Department of Psychology, and Ms Ana Claasen, Department of Anatomy and Structural Biology, University of Otago for their help with the conference organisation and secretarial assistance. We are very grateful to the Neurological Foundation of New Zealand for its generous financial assistance toward student travel and registration.

Goddard Prize and Poster Prize Winners

- 1990 **Steven Morrison**, University of Otago, New Zealand
- 1991 **Oliver Davidson**, University of Otago, New Zealand
- 1992 **Nadia Solowij**, University of New South Wales, Australia
- 1993 **Kjesten Wiig**, University of Otago, New Zealand
- 1994 **Niki Butterworth**, University of Auckland, New Zealand
- 1995 **Gerald Ahern**, John Curtin School of Medical Research, Australia
- 1996 **Judy Swanson**, University of Otago, New Zealand
- 1997 **Donna Briggs**, University of Otago, New Zealand
- 1998 **Johanna Montgomery**, University of Otago, New Zealand
Suzanne Habjan, University of Sydney, Australia
- 1999 **Wendy Brooks**, University of Otago, New Zealand
- 2000 **John Lin**, University of Auckland, New Zealand
- 2001 **Tina Hinton**, University of Sydney, Australia
Michael Christie, University of Canterbury, New Zealand (Poster)
- 2002 **Gemma Irvine**, University of Otago, New Zealand
- 2003 **Evangelene Daniela**, Victoria University of Wellington, New Zealand
- 2004 **Bronwen Kelly**, University of Canterbury, New Zealand
- 2005 **Adam Errington**, University of Otago, New Zealand
Wendy Imlach, AgResearch, New Zealand (Poster)
- 2006 **David Cumin**, University of Auckland, New Zealand
Andrew Tattersfield, University of Auckland, New Zealand (Poster)
- 2007 **Carthur Wan**, University of Auckland, New Zealand
Suzanne Ackerley, University of Auckland, New Zealand (Poster)
- 2008 **Thomas Park**, University of Auckland, New Zealand
Joan Liu, University of Auckland, New Zealand (Poster)
- 2009 **Bill Connolly**, University of Otago, New Zealand
Bridget Simonson, Victoria University of Wellington, New Zealand (Poster)

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Abstracts in Presentation Order

Abstracts will be published on the AWCBBR website:

www.awcbr.org

They can be referenced as:

Proceedings of the International Australasian Winter Conference on Brain Research, 2010, 28, abstract # [URL for each abstract can be found at the above website].

1.1

Animal Models of Drug-seeking: Genetics and Pharmacology

A. J. LAWRENCE

*Addiction Neuroscience Laboratory, Florey Neuroscience Institutes,
Centre for Neuroscience, University of Melbourne, Victoria, Australia*

We have utilised neuropharmacological and genetic approaches to examine systems implicated in drug-seeking behaviour and/or drug induced plasticity. Acute treatment of multiple strains of alcohol-preferring rats with the selective mGlu5 receptor antagonist, MTEP, resulted in dose-related reductions in operant responding for alcohol. In C57/Bl6J mice, MTEP dose-dependently reduced appetitive and consummatory phases of alcohol self-administration. In mGlu5 receptor knockout mice on a C57BL/6J background, consumption and preference for alcohol was reduced compared to wildtypes, whereas consumption and preference for saccharin was normal. Combination treatment of rats with individually sub-threshold doses of MTEP and an adenosine A2a receptor antagonist reduced alcohol self-administration and relapse, suggestive of functional interactions and/or synergy between mGlu5 and adenosine A2a receptors. We have also investigated the impact of adenosine A2a receptor deletion on behavioral responses to morphine in a number of reward related paradigms. Decreased morphine self-administration and breakpoint in A2a knockout mice was observed. These data support a decrease in motivation to consume the drug, perhaps reflecting diminished rewarding effects of morphine in A2a knockout mice. In support, a place preference to morphine was not observed in A2a knockout mice but was present in wildtypes. In wildtype mice, MTEP can prevent a conditioned place preference to cocaine. In contrast, in mice lacking the adenosine A2a receptor, MTEP does not prevent a place preference to cocaine. In both genotypes, MTEP attenuates the acute cocaine-induced locomotor activation. These data suggest that a functional A2a receptor is implicated in the ability of MTEP (an mGlu5 antagonist) to dampen the conditioned reinforcement of cocaine, at least in CD1 mice. Overall, these studies suggest that mGlu5 and adenosine A2a receptors can interact to regulate drug and alcohol-seeking.

1.2

Anti-Addiction and Side Effects Profile of Novel Kappa Opioid Receptor Agonists Salvinorin A and DS1A. S. MORANI¹, S. SCHENK², T. E. PRISINZANO³, and B. KIVELL¹¹*School of Biological Science, Victoria University of Wellington, Wellington, New Zealand*²*School of Psychology, Victoria University of Wellington, Wellington, New Zealand*³*Department of Medicinal Chemistry, University of Kansas, USA*

Kappa opioid receptor (KOPr) activation by traditional agonists reduces drug-seeking behaviour. However, side effects such as sedation and depression limit their clinical utility. Recently, Salvinorin A (SalA), the active ingredient of the plant *Salvia divinorum* has been shown to be a potent and selective KOPr agonist with a novel structure. We have recently shown that SalA also has anti-addiction properties. However, its short duration of action is likely to limit its therapeutic development. We hypothesise that synthesis of compounds based on the unique structure of SalA with a longer duration of action may provide more effective anti-addiction pharmacotherapies. Our lab has recently shown that a structural analogue of SalA called DS1, with a longer duration of action, attenuates cocaine induced drug-seeking in rats. In this study, we tested the effect of the novel KOPr agonists on cocaine induced locomotion. To test the potential undesirable side-effects such as sedation and aversion we measured open field activity (motor function), conditioned taste aversion (CTA; aversion) and the forced swim test (FST; depression) behaviours in rats. A single injection of SalA had no effect on cocaine induced hyperactivity, whereas, DS1 significantly decreased hyperactivity compared to vehicle control ($p < 0.05$). Both, SalA and DS1 significantly attenuated cocaine sensitization ($p < 0.05$). Acute treatment with Sal A and DS1 (0.3 mg/kg), at a dose which attenuated cocaine reinstatement had no effect on open field activity and CTA ($p > 0.05$). However, SalA decreased swimming time ($p < 0.001$) and increased immobility time ($p < 0.01$) in the FST. These findings indicate that acute treatment with novel KOPr agonists attenuated the expression of cocaine induced behaviours without affecting motor function and inducing taste aversion but produces depression like behaviours in rats.

1.3

The Effect of Novel Kappa Opioid Receptor Agonists on Dopamine Transporter FunctionB. SIMONSON¹, J. H. MILLER¹, T. PRISINZANO², and B. KIVELL¹¹*School of Biological Sciences, Victoria University of Wellington, Wellington, New Zealand*²*Department of Medicinal Chemistry, University of Kansas, Kansas, USA*

Drug abuse and addiction is a major social and economic burden world-wide. Currently there are limited therapeutics available to combat drug addiction, with none available to treat psychostimulant abuse. The dopamine transporter (DAT) is involved in the process of addiction and the kappa opioid receptor (KOPr) has been shown to modulate DAT function. Therefore the design of novel KOPr agonists may lead to potential anti-addiction therapies through modulation of DAT. This study investigates the unique KOPr agonist Salvinorin A (SalA) and novel analogues based on SalA's structure. SalA, and novel analogues DS-1 and DS-3 were investigated for their ability to modulate DAT function in isolated rat brain tissue and in cells expressing KOPr and DAT proteins. Using rotating disk electrode voltammetry and confocal microscopy techniques we found that SalA, DS-1 and DS-3 increase DAT function in isolated brain tissue and cells ($p < 0.05$ to < 0.001). The effects were reversed by KOPr antagonist nor-binaltorphimine ($p < 0.001$) and were pertussis toxin sensitive ($p < 0.01$ to < 0.001). These compounds also caused a rapid, short lived increase in p-ERK, corresponding to the increase in DAT function ($p < 0.01$). Inhibition of p-ERK signaling prevented KOPr activation of DAT. SalA showed increased cell surface expression of DAT after 30 min ($p < 0.01$), whereas DS-1 and DS-3 did not cause significant increases. These studies may help elucidate the cellular mechanism by which these compounds work, leading to improved drug design for drug addiction treatment.

1.4

The Effects of Nicotine and Total Particulate Matter of Cigarette Smoke on Dopamine Transporter Expression and FunctionK. DANIELSON^{1,2}, P. TRUMAN², and B. KIVELL¹¹*School of Biological Sciences, Victoria University of Wellington, Wellington, New Zealand*²*ESR Kenepuru Science Centre, Wellington, New Zealand*

Cigarette smoke causes 5000 deaths per year in New Zealand and is the leading cause of preventable illness worldwide. The majority of smoking addiction research focuses on nicotine treatment alone, however, there are over 4000 compounds present in cigarette smoke, some of which are neurologically active. The dopamine transporter (DAT) is an important protein in the natural reward system of the brain and has been shown to be regulated by nicotine. This study has investigated the effects of nicotine (0.35 and 3 mg/kg i.p.) and total particulate matter (TPM) from cigarette smoke on the expression and function of DAT, with a focus on differences between nicotine and TPM treatment. Rotating disk electrode voltammetry (RDEV) experiments have shown that in the nucleus accumbens of *in vivo* treated rats TPM causes a significantly greater increase in dopamine (DA) uptake by DAT than nicotine alone ($p < 0.01$). Furthermore, there is no increase in DA uptake in tissue treated with nicotine and TPM *in vitro*, indicating that the observed changes are dependent on whole brain circuitry. There has been no significant increase in DA uptake observed in the striatum of *in vivo* treated rats with nicotine or TPM. This work will increase our understanding of the non nicotinic effects of cigarette smoke and may in future lead to the development of novel smoking cessation therapies.

1.5

A Comparison of MDMA and Amphetamine in the Drug Discrimination Paradigm

D. N. HARPER, A. CROWTHER, and S. SCHENK

School of Psychology, Victoria University of Wellington, Wellington, New Zealand

The goal of the current study was to compare the subjective experience of two commonly used stimulants that share overlapping neurochemical properties: 3,4-Methylenedioxymethamphetamine (MDMA) and d-amphetamine (AMPH). The Drug Discrimination paradigm was used to assess the relative subjective experience of acutely administered MDMA and AMPH. In this paradigm rats were required to respond on one lever if they have been given a specific drug (AMPH for one group of rats or MDMA for another group) vs. an alternate lever if they have been administered saline prior to a session. Generalisation and substitution testing was used to establish the extent to which rats previously trained to discriminate saline vs. MDMA responded to novel exposure of AMPH. Likewise, we examined the extent to which rats previously trained to discriminate saline vs. AMPH responded to novel exposure to MDMA. Higher doses of MDMA partially substituted for AMPH however no dose of AMPH substituted for MDMA. This suggests that MDMA induces some of the primary subjective experiences elicited by AMPH, but that the primary subjective experience of MDMA is markedly different from that of AMPH. The partial substitution on MDMA for AMPH, as well as the relatively greater impact of the D2 antagonist on the AMPH trained group, suggests that the DA-agonist properties of both drugs may underlie this partial overlap in the subjective experience of both drugs.

2.1

Structural Development of the Mouse Dorsal Cochlear Nucleus

M. MAO¹, J. M. MONTGOMERY¹, M. F. KUBKE² and P. R. THORNE^{1,3}*¹Department of Physiology, ²Department of Anatomy, ³Radiology and Section of Audiology,
University of Auckland, Auckland, New Zealand*

The cochlear nucleus (CN) in the medulla is the first auditory nucleus in the central auditory system and receives input from the cochlea via the 8th nerve. The CN is composed of three major subdivisions: anterior ventral (AVCN), posterior ventral (PVCN) and dorsal cochlear nucleus (DCN). The development of the VCN has been studied extensively, however, little is known about the development and maturation of the neuronal circuitry in the DCN. We investigated the organisational development of the DCN in the mouse (P0 to P21). Lipophilic dyes (NeuroVue® Red and NeuroVue® Jade) were applied to different regions of the cochlea to identify the afferent projections to the DCN. Histology (cresyl violet and fluorescent Nissl staining) and immunohistochemistry (MAP2 and synaptophysin) was used to provide more detail of the neuropil and synaptic organisation in the developing DCN. This study shows that the tonotopic projections to the DCN were established early in development (by P0), however, the DCN was poorly organised at this stage. There were significant increases in DCN volume and changes in the cellular organization from P3 and the three distinct layers of the mature DCN were identifiable by P6. This organisational development was accompanied by a dramatic decrease in cell density (between P3 to P12) and changes in the morphology of dendrites and distribution of synapses. There was relatively little change in the organisation of the DCN between P12 and P21. This study demonstrates that the DCN assumes an adult-like organisation by P12 and provides a platform for further investigations of the development of the neuronal circuitry in the DCN.

2.2

Differential Short Term Plasticity at Convergent Inhibitory Synapses to the Substantia Nigra Pars ReticulataW. M. CONNELLY^{1,2}, J. M. SCHULZ¹, J. N. J. REYNOLDS¹, and G. LEES²¹*Department of Anatomy and Structural Biology, Brain Health and Repair Research Centre*²*Department of Pharmacology and Toxicology, University of Otago, Dunedin, New Zealand*

Inhibitory projections from the striatum and globus pallidus converge onto GABAergic projection neurons of the substantia nigra pars reticulata (SNr). Based on existing structural and functional evidence, these pathways are likely to differentially regulate the firing of SNr neurons. Firstly, medium spiny neurons projecting from the striatum are largely silent, relative to the tonically active pallidal neurons. Secondly, pallidonigral terminals are formed on the soma of SNr neurons, while striatonigral neurons terminate mainly on the dendrites. Using whole-cell voltage clamp in brain slices with these pathways intact, we sought to investigate the functional differences in the inhibitory traffic supplied by these pathways. We found that striatonigral IPSCs had slow kinetics, but most strikingly, they showed a large degree of paired pulse facilitation. We tracked this facilitation over development, and found it reached an adult phenotype at P17, with a average paired pulse ratio of 2. We also found that the recovery from facilitation accelerated over development, again, reaching an adult phenotype by P17. When we investigated the pallidonigral pathway, we found that these synapses show paired pulse depression, and that this depression could be explained by solely presynaptic changes. The paired pulse ratio had a mean of 0.67, and did not change over development, however, the recovery from depression slowed over development. Pallidonigral IPSCs were significantly faster than striatonigral IPSCs. Finally, we investigated the functional consequences of inhibitory conductances on the pacemaker activity on SNr neurons. These findings highlight the importance of differential dynamics of neurotransmitter release in regulating the circuit behaviour of the basal ganglia.

2.3

Abnormal Neural Synchrony in a Maternal Immune Activation Animal Model of Schizophrenia

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The temporal synchronisation of neural firing has been proposed to bind and integrate diverse neural processes within the brain. Evidence suggests that disruption in neural synchronisation within and between brain regions may underlie a range of the deficits observed in schizophrenia. To explore this hypothesis, we examined synchronised neural activity between the medial prefrontal cortex (mPFC) and the hippocampus (HPC), two brain regions implicated in schizophrenia pathophysiology, using the Maternal Immune Activation (MIA) animal model in rats. This neurodevelopmental model of schizophrenia is induced through a single injection of the synthetic immune system activator polyriboinosinic-polyribocytidylic acid (Poly I: C), a synthetic analog of double-stranded RNA, a molecular pattern associated with viral infection, in pregnant rat dams. It is based on epidemiological evidence of increased risk of schizophrenia in adulthood following prenatal exposure to infection. In the present study, EEG coherence and neuronal phase-locking to underlying EEG were measured in freely moving MIA and control offspring. The MIA intervention produced significant reductions in mPFC-HPC EEG coherence that correlated with decreased prepulse inhibition (PPI) of startle, a measure of sensory gating and a hallmark schizotypal behavioural measure. Furthermore, changes in the synchronisation of neuronal firing to the underlying EEG were evident in the theta and low-gamma frequencies. Firing within a putative population of theta modulated, gamma-entrained mPFC neurons was also reduced in MIA animals. Thus MIA in rats produces a fundamental disruption in long-range neuronal synchrony in the brains of the adult offspring that models the disruption of synchrony observed in schizophrenia. These data, therefore, link an isolated environmental risk factor to the disrupted synchronisation that may be a fundamental factor in the disease presentation.

2.4

Brain-Derived Neurotrophic Factor val⁶⁶met Polymorphism Influences the Magnitude of Human Long-Term Potentiation which Predicts Memory Performance

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Long term potentiation (LTP) is a long lasting enhancement of synaptic communication, and is the principal candidate for the mechanism of memory. LTP has been studied extensively at the cellular and molecular level in animals. Recently, models have been developed that allow *in vivo* induction and measurement of LTP in humans. LTP involves a complex cascade of events, with brain derived neurotrophic factor (BDNF) identified as an important modulator of synaptic plasticity in humans. A single nucleotide polymorphism in the *BDNF* gene resulting in a valine-to-methionine substitution at codon 66 (val⁶⁶met) has been shown to affect activity-dependent secretion of BDNF and is associated with lower performance in memory tasks. The present study tested whether the *BDNF* val⁶⁶met polymorphism was associated with induction of LTP-like changes in visual evoked potentials. We also tested whether LTP-like changes and *BDNF* val⁶⁶met polymorphism was predictive of memory. Individuals containing met variants of the polymorphism had significantly lower LTP, as indexed by amplitude changes in the late phase of the N1 component of visual-evoked potentials. Also, Val/Met and Met/Met individuals performed significantly worse than Val/Val individuals on measurements of visual memory as indexed by the Wechsler Memory Scale. The degree of LTP and performance on visual memory tasks were also significantly correlated. These results add further weight to the suggestion that the LTP-like phenomena that is induced and measured by visual stimuli is LTP, and provides further evidence for the suggestion that polymorphisms for BDNF act on human memory processes via effects on LTP.

2.5

Heterosynaptic Metaplasticity in the Hippocampus

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It has been suggested that for long-term potentiation (LTP) and long-term depression (LTD) to underlie information storage, overall synaptic strengths need to be kept within a dynamic range by metaplastic regulation of plasticity mechanisms. Here we tested key predictions of one prominent computational model of synaptic plasticity, the Bienenstock, Cooper and Munro model (BCM, 1982). Two key predictions of the BCM model are that 1) the history of cell firing regulates the ability to produce LTP and LTD in 2) a cell-wide manner. To test these predictions, field excitatory postsynaptic potentials (fEPSPs) or intracellular EPSPs were recorded following stimulation of the Schaffer collaterals in area CA1 of acute hippocampal slices from male Sprague-Dawley rats. In accordance with the BCM model, high-frequency priming stimulation delivered to afferents in either stratum oriens or stratum radiatum inhibited subsequent LTP and facilitated LTD in an independent stratum radiatum pathway. This confirms that activity can induce a heterosynaptic metaplastic state that spreads widely across the dendritic arbour. In contrast to one critical prediction of the BCM model, postsynaptic cell firing was neither necessary nor sufficient to induce the metaplastic state. However, in agreement with recent variants of the BCM model, the induction of the metaplastic state was mediated by a calcium signal, namely the release of calcium from intracellular stores during priming. Neither NMDAR, L-type VDCC nor mGluR activation was the trigger for this. These results indicate that synaptic plasticity in CA1 of the hippocampus can be homeostatically regulated by the cell-wide history of synaptic activity through a calcium signal generated from intracellular stores of calcium.

Supported by a grant from the NZ Marsden Fund.

3.1

**NMDA Receptors in the Basolateral and Central Amygdala:
Subunit Composition and Function**

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The amygdala is a part of the limbic system that is involved in emotional processing. It is critically involved in a simple Pavlovian learning paradigm of fear conditioning. Both fear conditioning and extinction of learnt fear are thought to result from NMDA-receptor mediated synaptic plasticity in the basolateral amygdala. Moreover, recent experiments suggest that NR2B subunits of the NMDA receptors play a key role in synaptic plasticity involved in fear learning. Sensory information is processed in the BLA and then sent to the central nucleus, the output of which results in the physiological actions typically seen in fear. In this talk I will discuss the subunit combination of NMDA receptors that are present at excitatory synapses to both interneurons and pyramidal neurons in the basolateral amygdala and on cell types in the central amygdala. I will discuss their possible roles in both these structures.

3.2

**Both Synaptically- and Chemically-Induced Group I mGluR-Mediated
LTD are Regulated by CaMKII in Rat Hippocampus**B. G. MOCKETT^{1,3}, S. R. HULME^{1,3}, D. GUÉVREMONT^{2,3}, J. M. WILLIAMS^{2,3}, and W. C. ABRAHAM^{1,3}*¹Department of Psychology, ²Department of Anatomy and Structural Biology, ³Brain Health and Repair Research Centre
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We have shown previously that group I mGluR-dependent LTD (mGluR-LTD) induced by the specific agonist DHPG is partially dependent on calcium/calmodulin-dependent protein kinase II (CaMKII)-mediated protein synthesis through regulation of translation. Previous studies suggest that different cellular mechanisms may underlie synaptically- and chemically-induced mGluR-LTD. The present study tested whether these two types of LTD have a similar dependence on CaMKII. To further investigate the role of translation we also examined the phosphorylation of translation factors. Hippocampal slices with CA3 removed were prepared from 6-7 wk male Sprague-Dawley rats. Field EPSPs were recorded in area CA1 in response to synaptic stimulation (1200 pulses, 1 Hz) in the presence of the NMDAR blocker APV (50 μ M) and the CaMKII inhibitor KN62 (10 μ M) and the initial slope was measured. EPSCs were recorded in response to DHPG (100 μ M, 10 min) following intracellular infusion of a second CaMKII blocker (AIP, 50 μ M, 40 min) via the patch electrode, and amplitudes measured. Phosphorylation of translation factors was determined by Western blot following incubation of hippocampal synaptoneurosome with DHPG (10 μ M, 10 min). Synaptically-induced mGluR-LTD was significantly reduced by KN62 75 min post-stimulation (DHPG, 77 \pm 5%, n=7; DHPG+KN62, 91 \pm 3%, n=8; p=0.028). Similarly, DHPG-induced mGluR-LTD was significantly reduced by AIP 30 min post-treatment (DHPG, -51 \pm 6%, n=8; DHPG+AIP, -31 \pm 5%, n=7; p=0.036). No change in phosphorylation of the translation factors eIF4 or eEF2 was observed. These findings suggest that CaMKII mediates both forms of group I mGluR-dependent LTD, but not via eIF4 or eEF2 initiated translation.

3.3

Effects of Intermittent Theta Burst Stimulation on Interhemispheric Inhibition Recorded in Pyramidal Neurons of the Motor Cortex *In Vivo*

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Intermittent theta burst stimulation (iTBS) is a physiologically-derived stimulus protocol which increases muscular evoked potentials in humans. An N-methyl-D-aspartic acid receptor antagonist blocks this effect, indicating the underlying mechanism involves synaptic plasticity. In rats we have found suggestive evidence that iTBS applied to the cortex differentially modulates a number of different pathways that converge onto pyramidal neurons in the opposite motor cortex. In the present experiments we used subthreshold conditioning stimuli to preferentially activate a pathway thought to innervate inhibitory interneurons, which in turn contact pyramidal neurons. Thus, we measured the effect of interhemispheric inhibition (IHI) on pyramidal neurons in the opposite motor cortex, and its modulation after iTBS. Using intracellular recordings in urethane-anaesthetised Wistar rats, we found that a subthreshold intensity conditioning stimulus applied to the contralateral cortex 4-10 ms before a test stimulus applied to the ipsilateral cortex decreased the slope of the test postsynaptic potential (PSP) ($-17 \pm 2\%$ of control, $P < 0.05$, paired t-test; $n = 49$). We then tested the effect of contralateral iTBS on IHI. When iTBS was applied at a level sufficient to evoke a PSP in the neuron, IHI was unchanged ($-12 \pm 2\%$ of control, $n = 7$). However, when iTBS intensity was set below threshold for evoking a PSP, the IHI effect was abolished ($+6 \pm 6\%$ at +20 min, $n = 7$; $P < 0.05$, unpaired t-test). Finally, IHI remained largely intact if iTBS was given in the presence of the endocannabinoid antagonist AM251, indicating that synaptic plasticity mechanisms underlie the modulation of IHI by iTBS.

Funded by W & B Miller Scholarship from the Neurological Foundation of NZ and the Marsden Fund of the Royal Society of NZ.

3.4

Visual Stimuli Induce Firing Pauses in Striatal Cholinergic Interneurons *In Vivo*

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Tonically active neurons (TANs, assumed to be cholinergic interneurons) in the striatum of behaving monkeys acquire pause responses to visual stimuli during reward-related learning. Few TANs exhibit this response initially, whereas the majority will respond following repeated pairings between the stimulus and a reward. We made intracellular records from cholinergic interneurons (CINs) in urethane-anaesthetised rats, in order to investigate the effect of visual stimuli on tonic firing. All recorded neurons demonstrated characteristic electrophysiological properties of CINs ($n = 11$). During a baseline period of tonic firing (range 1 to 11 Hz), no neuron exhibited firing-rate modulation or subthreshold responsiveness to an LED flashed into the contralateral eye. However, after disinhibition of the deep layers of the superior colliculus (SC, $n = 7$) by local bicuculline injection, the majority of CINs ($n = 5$) exhibited spike rate modulations in response to visual stimulation ($p < 0.001$). Typically, this consisted of a period of excitation of markedly variable duration followed by inhibition of spike firing. All neurons exhibited a depolarisation-hyperpolarisation sequence underlying any spike-rate modulation, consistent with an excitatory post-synaptic potential (EPSP) followed by an afterhyperpolarisation (AHP). In one recording where action potential firing was absent, hyperpolarisation area and length were correlated both to the amplitude of the EPSP and the simultaneously-recorded visual-evoked potential in the SC. This suggests that the visual-evoked input drove the initial depolarisation via thalamic and cortical pathways, which in turn induced an intrinsic AHP. These data demonstrate that a visual stimulus, rendered 'salient' by disinhibition of the deep layers of the SC, induces an EPSP/AHP sequence which underlies a firing pause response in CINs.

Poster 4.1

**Cognitive Impairment in Treatment Resistant Schizophrenia:
A Consequence of Illness or Medication Used in Treatment?**M. E. MURPHY¹, R. R. KYDD², and B. R. RUSSELL¹*¹School of Pharmacy, ²Department of Psychological Medicine, University of Auckland, Auckland, New Zealand*

A characteristic feature of schizophrenia is the presence of neurocognitive deficits. Cognitive dysfunction predicts functional outcomes for patients with schizophrenia more consistently than positive symptoms. Interestingly, clozapine has been found to have less effect than other antipsychotics in improving cognition despite its significant role in treatment resistant schizophrenia. The reasons for this are unclear but may relate to clozapine's unique receptor binding profile, specifically anticholinergic effects. Antagonists at the cholinergic M₁ receptor, such as clozapine, have been shown to cause learning and memory deficits in animal and human studies. This study set out to examine the effects of clozapine on neurocognitive function in order to test the hypothesis that residual neurocognitive deficits in schizophrenia patients taking clozapine are due to the anticholinergic effects of clozapine rather than the illness itself. Twelve clinically stable patients receiving clozapine were recruited from a forensic psychiatric unit for cognitive assessment using the IntegNeuro test battery (Brain Resource Company). Participants' scores were compared to data from over 2000 control subjects. A significant correlation was found between high clozapine levels and diminished overall cognitive performance ($R=0.775$, $R^2=0.601$, $p=0.002$). Conversely, duration of untreated psychosis and duration of illness, clinical variables reported to influence neurocognitive performance in schizophrenia, showed no such association. Greater than half the study sample showed deficits in tests of verbal memory and switching of attention. Correlational analysis of key markers on these tasks revealed a trend towards poor cognitive performance with increasing clozapine levels. The findings of this study are supportive of the hypothesis that high clozapine levels would be associated with impaired neurocognitive performance in schizophrenia.

Poster 4.2

Confabulation: A Single Deficit or Multiple?

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The key cognitive mechanism in confabulation has not been established. The three main theories currently debated are: strategic retrieval, reality monitoring, and temporal-context confusion. Identification of dissociable sub-components of confabulation would facilitate investigation into underlying processes. Part 1 of this study investigated confabulatory tendencies in 30 normal subjects on confabulation battery questions, a semantic narratives task, a novel gist recall task and in free recall of single items. Executive and memory control processes were measured using tasks of cognitive estimation, initiation and inhibition of responses, impulsiveness, reality monitoring and temporal monitoring. Part 2 of the study investigated two patients who were confabulating following brain damage, compared with five matched controls. Principal components analysis of results from measures of confabulation in Part 1 produced a three-factor solution. Factor 1 comprised general confusions of information and was significantly correlated with a self-reported measure of impulsiveness, as well as WTAR-estimated FSIQ. Factor 2 emphasised intrusions into recall and was associated with reduced suppression of inappropriate responses. Factor 3 reflected false recognition and external details in incorrect contexts, and was associated with poorer reality- and temporal-monitoring. Part 2 gave support for this model in the confabulating patients. This study suggests that confabulation fractionates into more than one component and that these are associated with different executive and memory control failures. Further exploration would facilitate development of a standardised measure of confabulatory deficits, to assist future research into underlying processes and enable comprehensive clinical assessment in confabulating patients.

Poster 4.3

**Reading with the Right Hemisphere:
Investigating the Neurological Basis of Developmental Dyslexia**

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Previous imaging studies of developmental dyslexia have provided evidence of decreased activation of the left posterior language system during single word reading in dyslexia relative to non-impaired readers. Considerably less attention has focused on areas of hyperactivation and the role of the right hemisphere in dyslexic reading. The aim of the current study is to understand the neural basis of developmental dyslexia, and how this differs to brain organization underlying normal reading. Functional Magnetic Resonance Imaging (fMRI) was used to compare performance and brain activation patterns of 12 phonological dyslexic and 16 non-impaired readers in four experimental conditions: letter case decision, regular word reading, irregular word reading, and pseudo-homophone reading. The experimental conditions used a 'go/no-go' response interspersed with fixation. Functional data was analysed in a factorial ANOVA and a laterality index was used to compare hemispheric lateralisation. Dyslexic readers showed hypo-activation in the left occipital areas for regular reading and right occipital areas for pseudo-homophone reading. They also showed areas of hyperactivation in several right hemisphere regions, including the insula lobe and precentral gyrus. The laterality indices for the temporal lobe demonstrated that, in the regular and irregular comparisons, both groups were left lateralised. In the sublexical comparison, a significant difference was observed whereby dyslexic participants showed right lateralised activation whereas controls showed left lateralisation ($t_{(26)} = -2.24, p = 0.034$). These results, which may be interpreted within a dual route framework of reading, support the hypothesis that dyslexics are reading words that would require the use of the sublexical route in typical readers, with their right hemisphere.

Poster 4.4

Examining the Incidence and Outcome of Paediatric Traumatic Brain Injury in New Zealand

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Paediatric Traumatic Brain Injury (TBI) impacts previously acquired skills, the learning of new skills and attainment of developmental milestones. It is the single most common cause of death and disability in children in the US. Self reports suggest 31% of children experience a head injury before the age of 18, whilst 44% of 14-15 year olds reported a head injury in the previous 3 years. In NZ, head injury rates during childhood are highest for those under 4 yrs and the 15-19 year age groups, with males being at greater risk than females. However, the true incidence of head injury is likely to be significantly higher as many with mild TBI do not seek medical treatment, or are not admitted to hospital. This study aims to determine TBI incidence, case fatality and 1-year outcome of TBI. Assessments will take place at baseline, 1 month, 6 months and 12 months post injury covering a variety of areas including cognitive and behavioural functioning, mood disorders, quality of life, service utilisation and family burden. Findings from the study will describe the aetiology, incidence and outcome of TBI in children and help to identify barriers to treatment and gaps in existing service provision. Initial case registrations suggest that the incidence of TBI is significantly higher than expected (385 registered cases in ten weeks, a third of which are children), indicating that the long term burden and impact of TBI may be greater and more widespread than previously estimated.

This study is supported by funding from the Health Research Council of New Zealand.

On behalf of the Bionic Research Team (Brain injury Incidence and Outcomes in the Community).

Poster 4.5

**Examining the Incidence and Outcomes of Traumatic Brain Injury in New Zealand,
Design and Rationale of the BIONIC Study (2009-2012)**

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Traumatic brain injury (TBI) is a leading cause of disability and death in young adults and has a significant impact on person, family/whanau, friends, and society. The exact burden of TBI in NZ has yet to be quantified. This study will determine TBI incidence, case fatality and 1-year outcomes in the New Zealand population. Factors to be examined include disability, quality of life, employment status, and cognitive and behavioural/emotional consequences. This prospective population-based TBI register and of Hamilton and Waikato districts began in March 2010. All new TBI cases (all ages and all severity levels) will be ascertained over a 12 month period. Survivors who consent will be followed up for 1 year. Outcome data will be collected at 1, 6 and 12 months post-injury. This study is the only epidemiological investigation of incidence, case fatality, disability, costs, and the health care requirements for TBI subjects in a large and well-defined population. Accurate and nationally representative estimates of the incidence and burden of TBI and inequalities in these, risk factors for incidence, natural course of recovery, and factors influencing early and late outcomes are essential for evidence-informed policy, resource allocation, planning of relevant services, and evaluation of sector and service performance in our country.

Poster 4.6

**Prevalence and Characteristics of Acute Headaches and
Dizziness in People with Mild Head Trauma**T. K. COWLEY^{1,2}, M. THAN³, M. R. MACASKILL^{1,2}, and T. J. ANDERSON^{1,2,4}¹*Van der Veer Institute for Parkinson's and Brain Research, Christchurch, New Zealand*²*Department of Medicine, University of Otago, Christchurch, New Zealand*³*Emergency Department, ⁴Neurology Department, Christchurch Public Hospital, Christchurch, New Zealand*

Of head injury admissions, 80% are classified as mild, with a loss of consciousness no greater than 30 minutes, a Glasgow Coma Scale of 13-15, and post-traumatic amnesia of less than 48 hours. Headaches are the most common symptom after head injury, followed by dizziness, which includes vague symptoms of disorientation, lightheadedness and imbalance, as well as vertigo. Little research has been undertaken into the prevalence and characteristics of the acute symptoms following mild head injury, especially within the first month. We will recruit of 100 mild head injury patients identified by the Christchurch Hospital Emergency Department, followed up at 1 week, 1 month and 3 months via questionnaire over the phone. Participants describe their symptoms in their own words before being asked more specific questions by the researcher. With 19 week 1 follow up interviews completed, 15 participants had headaches, 6 had dizziness and 4 had nausea. Of these, only 3 had both headaches and dizziness at 1 week. The major causes of these mild head injuries were physical altercation (9), and sports injury (6), with the remainder due to household accidents (2) and falls (2). Of those asked to participate in the study so far the response rate has been 63%. We will also attempt to identify candidate risk factors for frequency and severity of symptoms, which in turn may assist in better management of people with mild head injury.

Poster 4.7

Long-Term Effects of Bilateral Vestibular Deafferentation on the Total Number of Neurons in the Subregions of the Hippocampus Estimated using the Optical FractionatorS. BALABHADRAPATRUNI¹, Y. ZHENG¹, C. L. DARLINGTON¹, R. NAPPER², and P. F. SMITH¹*¹Department of Pharmacology and Toxicology, ²Department of Anatomy and Structural Biology, University of Otago, Dunedin, New Zealand*

It has been suggested that vestibular information is important for spatial learning and memory. Neurochemical and electrophysiological changes in the hippocampus, part of the brain involved in learning and memory, were also reported following the vestibular damage. Moreover, hippocampal atrophy was observed in patients at 8-10 years following bilateral vestibular damage. However, it is not clear whether this atrophy is associated with neuronal loss in the hippocampus. In the present study, the total number of neurons in different subregions of the hippocampus was estimated in rats at 14 months following either sham (n = 4) or bilateral vestibular deafferentation (BVD) (n = 4) surgery. The animals were perfused with 4% paraformaldehyde and the brains were dissected and cryoprotected with 30% sucrose. Serial sagittal frozen sections, 40µm thick, were collected throughout the hippocampus using a random, systematic design. The sections were stained with Cresyl Violet and the number of neurons in the CA1, CA3, dentate gyrus (DG), hilus and subiculum of the hippocampus was counted using the optical disector method. The total number of neurons in each subregion was determined using the optical fractionator method. The preliminary results showed that the total number of neurons was approximately 8.75×10^4 in DG, 6.95×10^4 in CA1 and 1.99×10^4 in CA3 in sham animals, while 4.5×10^4 , 2.6×10^4 and 1.4×10^4 in BVD animals. This suggests that BVD may have differential effects on the total number of neurons in subregions of the hippocampus.

Poster 4.8

Altered Arginine Metabolism in the Hippocampus and Prefrontal Cortex in Maternal Immune Activation Rat OffspringY. JING¹, H. ZHANG², A. WOLFF³, D.K. BILKEY³, and P. LIU¹*¹Department of Anatomy and Structural Biology, ²School of Pharmacy, ³Department of Psychology, Brain Health and Repair Research Centre, University of Otago, Dunedin, New Zealand*

Maternal immune activation (MIA) is a newly developed animal model of schizophrenia, which uses a single systemic administration of the synthetic cytokine inducer polyinosinic-polycytidilic acid during mid-gestation to induce MIA in pregnant animals. A number of behavioural features of schizophrenia are evident in the adult MIA offspring. The present study measured the levels of arginine and its metabolites in the CA1, CA2/3 and dentate gyrus sub-regions of the hippocampus and prefrontal cortex in 4 months old MIA rat offspring (n = 6) and age-matched controls (n = 5) using liquid chromatography/mass spectrometry and high performance liquid chromatography. Significantly increased arginine, ornithine and putrescine levels and decreased agmatine level were found in MIA rat offspring relative to controls in a region-specific manner. There were no marked differences in spermidine and spermine levels between the two groups in any brain region examined. These results, for the first time, demonstrate that maternal immune activation leads to altered arginine metabolism in the hippocampus and prefrontal cortex in the adult offspring. The functional significance remains to be determined in the future.

Poster 4.9

Synapse Distribution in the Cerebellar Cortex of a Mouse Model of Ataxia

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Mice that lack the gene for PMCA2, the plasma membrane Ca^{2+} ATPase, a calcium transporter protein, exhibit cerebellar ataxia. The phenotype is consistent with the absence of the normally-enriched expression of PMCA2 in the cerebellar cortex. Recent evidence indicates that PMCA2 is expressed at cerebellar pre- and post-synaptic sites where it makes molecular interactions with other synaptic proteins. Using immunohistochemistry, we provide evidence that the distribution of excitatory synapses within the cerebellar cortex is disrupted in PMCA2^{-/-} mice. 30 micron sagittal cerebellar sections were prepared from PMCA2^{+/+}, PMCA2^{-/-} and PMCA2^{+/-} mice (21-28 days old) and incubated with primary antibodies specific for PSD-95 (Abcam) (post-synaptic protein) and VGLUT1 (Synaptic Systems) pre-synaptic protein. Secondary detection used Alexa 488 coupled antibodies and confocal microscopy followed by particle analysis of PSD-95 and VGLUT1-positive punctae. Initial results showed that the distribution of PSD-95 and VGLUT1-positive punctae was similar in PMCA2^{-/-} cerebellar cortex compared with wild type, even though the PMCA2^{-/-} cerebellar tissue expressed only half wild-type PMCA2 levels. Instead the median size of VGLUT1 and PSD95-positive punctae was increased from $0.21 \pm 0.06 \mu\text{m}^2$ to $0.45 \pm 0.06 \mu\text{m}^2$ and from $0.11 \pm 0.04 \mu\text{m}^2$ to $0.17 \pm 0.02 \mu\text{m}^2$ in PMCA2^{-/-} cerebellar cortex ($p < 0.05$, t-test). Our results indicate that complete loss of PMCA2 leads to permanent alterations in the distribution of excitatory synapses in the cerebellar cortex.

We acknowledge the support of the New Zealand Neurological Foundation, the Department of Physiology (HH) and an OSMS Summer Scholarship (YK).

Poster 4.10

Back off the Wagon: Dopaminergic Mechanisms of Methamphetamine Reinstatement in a Rat Model of Relapse

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Dopaminergic mechanisms have been proposed to mediate relapse to drug-seeking behaviour. Research primarily in the area of cocaine abuse has implicated D1 and D2 receptor mechanisms, specifically. The present study used an animal model of drug-seeking to determine the role of D1- and D2-like receptor mechanisms in relapse to methamphetamine (MA) abuse. Rats were trained to self-administer MA and then responding was extinguished by replacing the MA solution with saline. Experimenter-administered injections of MA (0-2.0 mg/kg) reinstated extinguished responding in a dose-dependent manner. Pretreatment with the D1-like antagonist, SCH 23390 (0-0.04 mg/kg) attenuated drug-seeking but pre-treatment with the D2-like antagonist, eticlopride (0-0.05 mg/kg) was ineffective. Drug-seeking was produced by experimenter-administered injections of the dopamine uptake inhibitor GBR 12909 (0-10.0 mg/kg), but not the D2-like agonist, quinpirole (0-1.0 mg/kg), or the D1-like agonist, SKF 81297 (0-4.0 mg/kg). The results suggest that MA-seeking is produced by non-selective agonists that increase synaptic DA, but not by selective activation of either D1- or D2-like receptors. These findings are in contrast to the literature on drug-seeking following self-administration of other drugs, and suggest that relapse to different drugs of abuse may rely upon different DA receptor mechanisms.

Poster 4.11

MDMA Internalises the Serotonin Transporter in a Cell Model Without Activating Phospho-p38- Mitogen Activated Protein KinaseP. BOSCH¹, J. H. MILLER¹, D. DAY¹, S. SCHENK², and B. KIVELL¹*¹School of Biological Sciences, ²School of Psychology, Victoria University of Wellington, Wellington, New Zealand*

3,4-methylenedioxymethamphetamine (MDMA) causes serotonin depletion and reduced serotonin transporter (SERT) function within the brain's natural reward pathway. This study aimed to further investigate the effects of MDMA on short-term changes in SERT in an isolated cell model. Mouse neuroblastoma (N₂A) cells were transiently transfected with green-fluorescent-protein tagged human SERT (pEGFP-hSERT) and exposed to MDMA. Total internal reflection fluorescence (TIRF) and live-cell confocal microscopy showed a rapid redistribution of SERT from the cell surface to intracellular vesicles within 5 min of MDMA administration. Cell surface biotinylation confirmed a dose-dependent change that persisted for at least 90 min following MDMA (1 µg/mL and 10 µg/mL). Following this, we investigated the mechanism of internalization by using Western Blotting with antibodies against phospho-p38-MAPK, a known signaling modulator of SERT localization, and found no significant change 60 min after MDMA administration (10 µg/mL). The redistribution of SERT may account for the loss of function seen in animals following long-term MDMA exposure, indicating that MDMA may be neuroadaptive, rather than neurotoxic.

Poster 4.12

The Effect of a Single Oral Dose of Methylphenidate (MPD) on Executive Function and Cognition in Methamphetamine-Dependent Human Participants Using Functional Magnetic Resonance Imaging (fMRI)R. K. JAN¹, J. C. LIN¹, N. A. MCNAIR¹, I. J. KIRK², R. R. KYDD³, and B. R. RUSSELL¹*¹School of Pharmacy, ²Department of Psychology, ³Department for Psychological Medicine, University of Auckland, Auckland, New Zealand*

Methamphetamine (MA) abuse has become a global epidemic in recent years with a corresponding increase in violent crime and hospitalisations. Studies using the Stroop task have reported attentional deficits in this group which may be attributed to an inability to suppress irrelevant information and decreased cognitive inhibition. This study was a randomised placebo-controlled double-blind trial designed to determine the acute effects of MPD on neurocognition in MA-dependent and control participants using fMRI. 15 MA-dependent and 19 healthy control participants aged 18-46 years were randomly assigned to receive a single oral dose of MPD (18mg) or placebo and 50 minutes later scanned using fMRI (Siemens Magnetom Avanto 1.5T). Echo-planar images were collected, while participants performed an overt Stroop paradigm, and analysed using SPM8. During the Stroop Interference task, MA-dependent participants on placebo activated the left superior and medial frontal gyri (BA10), whereas MA-dependent participants on MPD activated the left anterior cingulate (BA24,32) and the left inferior frontal gyrus (BA47). Control participants exhibited a different and more pronounced pattern of activation. Controls on placebo activated the right cingulate gyrus (BA32) and left superior (BA8), middle (BA10) and inferior (BA47) frontal gyri as well as the right precentral frontal gyrus (BA6). Controls on MPD only activated the left precentral gyrus (BA4,6) ($p < 0.001$). This study demonstrates that each group exhibits significant differences in regional activation during the Stroop interference task following an oral dose of MPD in comparison to placebo.

Poster 4.13

Spectral Analysis of Epileptic Activity in Rodent Brain SlicesE. NEGAHBANI¹, D. A. STEYN-ROSS¹, M. L. STEYN-ROSS¹, L. VOSS², J. W. SLEIGH², and M. T. WILSON¹¹*School of Engineering, University of Waikato, Hamilton, New Zealand*²*Waikato Clinical School, University of Auckland, Waikato Hospital, Hamilton, New Zealand*

Generation of epileptiform activity in a rodent brain slice bathed with carbogenated no-magnesium artificial cerebrospinal fluid makes it possible to have an in vitro model of epileptogenesis, and to study its characteristics. As a biological signal, the frequency content of a recorded epileptiform event is one of the conventional and important descriptors of its behaviour, and our work has focused on the spectral analysis of this event. Neocortical brain slices of mice have been perfused with zero-magnesium solution in a recording chamber. Following emergence of spontaneous seizure-like events, the population voltage response of the tissue has been measured using a single 50-um teflon-coated tungsten wire, amplified, digitized, and stored in a computer. Proper considerations were carried out to minimize external sources of interference such as induced noise from power lines. The database consists of continuous recordings containing seizure-like events interspersed with periods of silence. Two groups of data were extracted from this database: a group of seizure-like events, and a group containing only inter-event background activity. A comparison of the averaged power spectral densities for the active and silent epochs showed significant differences between the frequency contents of tissue. During seizure-like events, the tissue shows stronger spectral components in both low (1-5 Hz), and high (60-120 Hz) frequencies. The buildup in the amplitude of these frequencies may have biological relevance, and may help in determining the different underlying processes.

Poster 4.14

Measuring Electrical Conductivity of Mouse Brain Slices

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We present an experimental methodology for measuring the electrical conductivity of slices of mouse brain. Brain slices are placed on a chip containing an array of protruding platinum electrodes. A standard four-point measurement is used to find the conductivity using an Agilent E4980A LCR meter, over frequencies of order 10 to 100 Hz. This is achieved by measuring the potential difference between two electrodes while a known current is passed between the other two electrodes. The resulting impedance measurement can be mapped to conductivity of the system using an expression derived theoretically for point-electrodes. This calculation has been supported with a comprehensive modelling exercise using COMSOL Multiphysics, in which the electric field patterns between the electrodes of the array have been established. The methodology has been checked by measuring a salt-solution of known concentration for which conductivity can be calculated. To distinguish the conductivity of the slice from that of the artificial cerebrospinal fluid in which it is bathed, measurements need to be made on both slice/fluid and fluid-only combinations. The slice has lower conductivity than the fluid. Electrical conductivity is a useful quantity to measure since it gives an indication of the nature of long-range connectivity in the brain. For example, we will use it as a measure of the extent of gap-junction connections within the cortex, and potentially to pick up changes in this form of connectivity due to different chemical environments.

Poster 4.15

Ketamine Anesthesia Helps Preserve Neuronal Viability

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The dissociative anesthetic ketamine that acts as an N-methyl-D-aspartate (NMDA) antagonist has been reported to improve neurological damage after experimental ischemic challenges. Here we show that deep anesthesia with ketamine before euthanasia by decapitation improves the quality of neonatal mouse neuronal brain slice preparations. All animal-associated procedures were approved by the University of Newcastle Animal Care and Ethics Committee. Swiss mice (P7-12) were either deeply anesthetized with ketamine (100 mg/kg i.p.) and decapitated, or decapitated without anesthesia. Brain slices containing *locus coeruleus* (LC) and hypoglossal motor neurons were then prepared. Electrophysiological parameters were recorded using the whole-cell patch clamp procedure. It was found that LC neurons from ketamine-anaesthetized mice exhibited significantly higher input resistances (~30%, $p < 0.001$) compared to control (no ketamine). Depolarizing voltage ramp experiments (40 mV/s; holding potential of -58 mV) demonstrated that ketamine improved the rate of success in voltage clamping LC neurons during the voltage ramp protocol from 42% to 73% ($p < 0.05$). These results suggest that ketamine anesthesia before euthanasia improves cell viability. This effect probably arises through the well-established antagonist action of ketamine, which is known to inhibit NMDA receptors and Na^+ and K^+ channels. This would decrease metabolic demand caused by the otherwise markedly increased neuronal firing and resultant Ca^{2+} loading that occurs during slice preparation. The resultant damage is likely to be reflected electrophysiologically as a decreased R_{IN} this in turn compromising the voltage clamp. In summary, we found that ketamine anesthesia before animal sacrifice reduced the conductance (i.e. leakiness) and hence improved whole cell voltage control.

Poster 4.16

Pacemaker Calcium Currents: Difference in Locus Coeruleus Neurons of Mice and Rats

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Pacemaker currents acting during the interspike interval of spontaneously firing neurons depolarize the membrane potential to reach threshold for activation of fast voltage-dependent channels. Calcium currents play an important role in the pacemaker process of Locus coeruleus (LC) neurons, as they activate Ca^{2+} -activated potassium channels and shape action potentials and hence modulate firing rates. Most studies of calcium currents in LC neurons have been performed using rats. The aim of the present study is to compare the activation of voltage-dependent calcium channels during the interspike interval between mice and rats. All animal-based procedures were approved by the University of Newcastle Animal Care and Ethics Committee. Swiss mice were deeply anesthetized with ketamine and euthanized with brain stem slices containing LC neurons then prepared. LC neuronal calcium currents were recorded in artificial cerebro-spinal fluid containing 1 μM TTX by whole-cell patch clamp recording using a Cs^+ -filled internal pipette solution and holding neurons at -85mV. Although calcium currents could be identified at membrane potentials more depolarized than -40 mV, we found that mouse LC neurons lack a persistent calcium current within the interspike interval, a current previously described to be present in rats. The lack of a "persistent" Ca^{2+} current in mice may therefore affect Ca^{2+} -dependent mechanisms during normal pacemaking, generating important differences in pacemaking in the two species. In summary, our results show that in terms of activation of calcium channels rats and mice are not alike, and direct comparison of studies using different animal species should be performed with caution.

Poster 4.17

Nonlinear Dynamics-based Continuum Cortical Modelling and its Simulation of Interacting Turing and Hopf Instabilities

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An explicit analytic model for the electrical activity generated by the brain would be of great value. To enable computer simulation of a simplified model cortex, we have developed coupled sets of nonlinear partial differential equations to predict the mean activities of densely interconnected neuronal aggregates, in which neuron groups communicate via **chemical** (neurotransmitter controlled) and **electrical** (gap-junction) synapses simultaneously. Our model reproduces default and cognitive states referring to two contrasting philosophies of information transmission: a slow-soma limit when the soma responds slowly to dendritic inputs, and a fast-soma limit when the soma response is prompt. Through running a series of numerical simulations of the cortical sheet, we find that the fast-soma neurons support gamma oscillations (~30-Hz), which is consistent with EEG observations of high-cognitive activity during attention tasks and accessing of working memory. The slow-soma case is of particular research interest as our linear stability analysis predicts that a spatially-organized firing behaviour, also known as a **Turing** pattern, can be spontaneously generated when there is a sufficient density of gap-junction connections. In addition, our numerical simulations show that if the rate-constant for the inhibitory post-synaptic potential is sufficiently small, we observe interactions between a low-frequency (~1-Hz) **Hopf** oscillation and a stationary Turing instability. Such interactions between Turing and Hopf instabilities may be of direct relevance to brain pathologies such as schizophrenia and epileptic seizure. A better understanding of the role of gap-junctions in mode-dynamics may assist our understanding of schizophrenia, epileptogenesis and their prevention.

Poster 4.18

A Hybrid Model of Action Potentials and Network Oscillations

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Models of neural activity in the brain have typically focused on two extremes. First, there are neuron-by-neuron models, where the membrane potentials and intrinsic currents of large numbers of neurons, and the connections between them, are modelled explicitly. Secondly, there are the mean-field models, where a population of neurons is modelled, and activity is represented by a locally-averaged firing rate. Both extremes can shed light on measurable phenomena such as the rhythms of the electroencephalogram, but they exclude the interplay between activity of individual neurons and large-scale modes of oscillation. We present a model that combines these two extremes. Specifically, it consists of a chain of neurons, each explicitly modelled; these are coupled by a decaying connectivity function that also facilitates a population-based analysis. This model demonstrates various regimes of activity – for example, non-synchronized firings, total synchronization of neurons, and waves of activity propagating across the chain. Of particular interest is where a resonance in network activity (*e.g.* corresponding to a travelling wave of activity) corresponds with the firing rate of a neuron. In this case the two effects support each other leading to a very strong oscillation at this frequency. Conversely, where a neuron's firing rate is well away from any network resonance, there is little organizational effect and the firing patterns are less synchronous. This model may help the understanding of the interplay between individual neural firings and network oscillations in phenomena such as alpha and spindle resonances in the electroencephalogram.

Poster 4.19

Remembering the Future: Hippocampal Contributions to Encoding Future SimulationsV. C. MARTIN¹, D. L. SCHACTER², M. C. CORBALLIS¹, and D. R. ADDIS¹¹*Department of Psychology, University of Auckland, Auckland, New Zealand*²*Department of Psychology, Harvard University, Cambridge, Massachusetts, USA*

Neuroimaging evidence has shown that both remembering past experiences and imagining future experiences engage a core network that includes the medial prefrontal cortex, medial parietal cortex, and medial temporal lobes. However, some regions within this network, including the anterior hippocampus, are preferentially engaged by imagining future events. The present fMRI study investigated whether increased anterior hippocampal activity during the imagining of future events is related to the integration of details into a coherent scenario or the encoding of the newly constructed event representation. In the scanning session, participants imagined hypothetical future events, rated their imaginings in terms of detail, and completed a mental imagery control task. A post-scan cued-recall test probing memory for each imagined scenario determined which future events were successfully encoded (later-remembered) and which were not (later-forgotten). Results showed that the core network, including medial prefrontal and parietal cortices, and bilateral hippocampus and parahippocampal gyrus, was engaged by imagining future events relative to the control task, replicating the findings of previous studies. Additional analyses revealed two distinct adjacent clusters in the anterior hippocampus, one in which activity was significantly higher for later-remembered events than later-forgotten ones (i.e. encoding, with detail ratings entered as a covariate), and the other in which activity was linearly related to participant detail ratings (i.e. detail, controlling for encoding success by only analyzing later-remembered events). These findings indicate that anterior hippocampal activity evident when simulating the future can be attributed to two distinct processes: the generation and recombination of vivid details into the future scenario; and encoding this new scenario into memory.

Poster 4.20

Spatial Memory: Anterior Thalamic Nuclei versus Laterodorsal Thalamic Nuclei

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It is widely accepted that the anterior thalamic nuclei (AT) are part of an extended hippocampal system that processes episodic memory (Aggleton and Brown, 1999). However, the relative influence of the adjacent laterodorsal thalamic nuclei (LD), which have additional connections with the parietal cortex, is less clear. The effects of AT (n=9), LD (n=10) and SHAM lesions (n=13) in rats were examined on two Morris water-maze tasks. The first task used a pool surrounded by a curtain and five proximal cues above the water; the cue-platform configuration rotated across trials to minimise remaining room cues. The groups learned this proximal cue task equally well (Block, $F(11,297)=29.05$, $p<0.001$; Group and Group x Block, $F_s<1.0$). When subsequently tested on the standard distal-cue Morris task, all three groups differed; AT rats now showed impaired acquisition relative to SHAMs, while LD rats showed intermediate performance (Group, $F(2,29)=14.10$, $p<0.001$; Session x Group, $F(16,232)=1.75$, $p<0.05$). Latency differences in the SHAM group between the two Morris tasks suggested the use of different strategies, such as egocentric versus allocentric strategies, across the two tasks. A follow-up experiment is assessing egocentric and allocentric strategies more explicitly on (dry) cheese-board tasks to assess the effects of AT, LD and SHAM lesions (each group, n=18) in proximal and distal cue conditions (order counterbalanced within group). Probe trials administered during acquisition will assess strategy use via manipulations of the start point and cues relative to the food location. We predict a double dissociation between the lesion effects on these tasks. LD rats may be more impaired in egocentric navigation compared to allocentric navigation due to parietal cortex connections and vice-versa for AT rats.

Poster 4.21

Spatial Working Memory Learning Can Be Repeatedly Tested and Challenged With Anterior Thalamic LesionsK. ULRICH^{1,2}, P. N. AITKEN^{1,2}, W.C. ABRAHAM^{1,2}, J. C. DALRYMPLE-ALFORD³, and N. MCNAUGHTON^{1,2}¹*Department of Psychology, ²Brain Health and Repair Research Centre, University of Otago, Dunedin, New Zealand*³*Department of Psychology, University of Canterbury, Christchurch, New Zealand*

Memory deficits occur in many brain disorders, including stroke and dementia. Anterior thalamic (ATN) damage produces dense amnesia in humans and loss of spatial and temporal order memory in rats. We tested Adult male Long Evans rats in a T-maze (with varying start arm positions) on spatial non-matching to sample before and after ATN lesions and then, in separate groups, after either a 1-week or 4-month break. Lesions were made by 3 injections of N-methyl-D-aspartic acid into the ATN on each side. Sham controls received the same surgery without fluid injection. All rats reached ~85% correct initially. Rats with ATN lesions dropped to chance levels throughout post-operative testing. Interestingly, sham rats performed at lesion levels at the start of both post-operative tests with both break lengths but relearned to 85%. Thus a delay as short as one week produces forgetting of the task, when 24 hours does not. This shows that the effects of lesions on learning (and not just memory) can be repeatedly tested with brief periods of testing provided a break of at least a week is inserted between tests. This confirms and extends a previous report of partial relearning by shams against a background of no learning in ATN lesion damage in the same task.

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Poster 4.22

Behavioural Effects of a Single Bilateral Intracerebroventricular Infusion of Preaggregated A β ₂₅₋₃₅ in Rats

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It has been proposed that amyloid beta peptides (A β) play a central and causative role in the development of Alzheimer's disease. A β ₂₅₋₃₅, an 11-amino acid fragment, is the toxic domain of the full-length A β . The present study investigated the effects of a single bilateral intracerebroventricular (i.c.v.) infusion of preaggregated A β ₂₅₋₃₅ (30 nmol/rat) on animals' performance in the Y-maze, elevated plus maze, open field, object recognition memory and water maze tasks at the time point of 11-16 days post-A β infusion. A β ₂₅₋₃₅ rats displayed normal spontaneous alternation in Y-maze, and were not significantly impaired in the open field, object recognition memory task (reaction to novel object) and simplified water maze test as compared to the A β ₃₅₋₂₅ (30 nmol/rat) control rats. In the elevated plus maze, however, A β ₂₅₋₃₅ rats spent significantly less time in the open arms and more time in the enclosed arms relative to the controls (all $p < 0.05$). These findings demonstrate that a single bilateral i.c.v. infusion of preaggregated A β ₂₅₋₃₅ alters animals' anxiety level with no marked effects on spontaneous alternation, exploratory and locomotor activity, object recognition memory and spatial memory at about the 2-week time point post-A β infusion.

Poster 4.23

Hippocampus, Neuronal Morphology and Memory: Brief Review and Some Recommendations

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There is considerable support for the view that changes in neuronal morphology, including spine morphology and density, reflect experience-dependent changes in the brain. Much of the evidence supporting the relationship between learning and hippocampal neuronal morphology, however, includes (1) tasks that are weakly associated with hippocampal dependency, and (2) lacks sufficient controls for sensorimotor and nonspecific stimulation. In a widely cited study, for example, Moser et al. (1994) tested the association between CA1 spine density and spatial learning experience in rats trained in a complex cage, but these were compared to home cage controls only. More recently, both Knafo et al. (2004) and Restivo et al (2006) employed pseudotrained groups and found relatively increased CA1 spine density in trained animals, but both studies examined simple olfactory discrimination, which is arguably not dependent on hippocampal integrity. It is possible that the relationships between neuronal structure and function vary with behavioural task and across brain regions, perhaps even across different neurons. It will be suggested that stronger evidence in favour of the proposed relationship between memory and hippocampal dendritic and spine morphology requires (1) tasks known to be strongly dependent on hippocampal function, (2) inclusion of a suitable control group that experiences matching housing environment, sensorimotor and reward-related experience, and (3) evidence from animals that either acquire or fail to acquire the task, such as those that show poor performance due to a disruption to hippocampal system function, those that show recovery of function, and intact animals that fail to learn the task because of old age or genetic strain.

Poster 4.24

Co-localization of L-glutamate and Agmatine in the Hippocampal CA1 Synaptic Terminals in Rats

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Agmatine is a metabolite of L-arginine and is considered a novel putative neurotransmitter. Recent evidences support its roles in learning and spatial working memory. Agmatine-like immunoreactivity has been found in CA1 terminals in the hippocampus and is associated with axonal synaptic vesicles of asymmetric excitatory synapses. This has raised the possibility that agmatine may be co-localized and co-released with L-glutamate, the primary excitatory neurotransmitter in hippocampal pyramidal neurons. The aim of the current study was to determine if agmatine is co-localized with glutamate in the hippocampal CA1 terminals. Quantitative immunogold double-labelling and transmission electron microscopy were used to investigate co-localization of glutamate and agmatine in CA1 terminals (n=300) of male Sprague-Dawley rats (n=4). All experimental procedures were conducted in accordance with the regulations of the University of Otago Committee on Ethics in the Care and Use of Laboratory Animals, and EM image analysis was performed in a blind-controlled manner. Agmatine was found to be co-localized with glutamate in 98% of glutamatergic neurons identified. As a previous study demonstrated increase in agmatine levels in CA1 terminals in water maze trained rats (WM) compared to rats forced to swim in the pool without an escape platform (SW), we then investigated changes in glutamate levels following the water maze task. The WM rats showed significant increases in both agmatine and glutamate levels in CA1 terminals (~65% increase in agmatine, p<0.001; ~30% increase in glutamate, p<0.05), compared to the SW rats terminals (n=200). Collectively, our results suggest that agmatine is co-localized with glutamate in CA1 terminals, and together may play a role in learning and memory processing.

Poster 4.25

GFP Expression in Fezf2-GFP Adult Mouse BrainM. L. S. TANTIRIGAMA¹, S. M. HUGHES², and R. M. EMPSON¹¹*Department of Physiology, ²Department of Biochemistry, University of Otago, Dunedin, New Zealand*

Agmatine is a metabolite of L-arginine and is considered a novel putative neurotransmitter. Recent evidences support its roles in learning and spatial working memory. Agmatine-like immunoreactivity (LI) has been found in CA1 terminals in the hippocampus and is associated with axonal synaptic vesicles of asymmetric excitatory synapses. This has raised the possibility that agmatine may be co-localized and co-released with L-glutamate, the primary excitatory neurotransmitter in hippocampal pyramidal neurons. The aim of the current study was to determine if agmatine is co-localized with glutamate in the hippocampal CA1 terminals. Quantitative immunogold double-labelling and transmission electron microscopy were used to investigate co-localization of glutamate and agmatine in CA1 terminals (n=300) of male Sprague-Dawley rats (n=6). All experimental procedures were conducted in accordance with the regulations of the University of Otago Committee on Ethics in the Care and Use of Laboratory Animals, and EM image analysis was performed in a blind-controlled manner. Agmatine was found to be co-localized with glutamate in 97% of glutamatergic neurons identified. As a previous study demonstrated increase in agmatine levels in CA1 terminals in water maze trained rats (WM) compared to rats forced to swim in the pool without an escape platform (SW), we then investigated changes in glutamate levels following the water maze task. The WM rats showed significant increases in both agmatine and glutamate levels in CA1 terminals (~80% increase in agmatine, p<0.01; ~40% increase in glutamate, p<0.05), compared to the SW rats terminals (n=300). Collectively, our results suggest that agmatine is co-localized with glutamate in CA1 terminals, and together may play a role in learning and memory processing.

Poster 4.26

**Blackcurrant Antioxidants and Parkinson's Disease:
Are Metabolites Present in the Cerebrospinal Fluid?**Y. A. ALAMRI^{1,2}, M. R. MACASKILL^{1,2}, and T. J. ANDERSON^{1,2,3}¹*Van der Veer Institute for Parkinson's and Brain Research, Christchurch, New Zealand*²*Christchurch School of Medicine, University of Otago, Christchurch, New Zealand*³*Neurology Department, Christchurch Public Hospital, Christchurch; New Zealand*

Blackcurrant anthocyanins are pigmented compounds found in blackcurrants (*Ribes nigrum* L.), and have been shown to possess potent antioxidant activity. Since increased oxidative stress in neural cells has been implicated in neurodegenerative disorders, especially Parkinson's disease (PD), a number of studies have suggested the use of blackcurrant-derived anthocyanins as a neuroprotective agent. In order for such an agent to be able to exert its putative effects on the brain, it needs to be able to access it. Several animal studies have detected anthocyanins in brain extracts of berry fruit-fed rats and pigs. However, there is no study, to date, that has examined the presence of anthocyanins in human brains post-ingestion of berry fruit. This project will involve the recruitment of a group of PD patients (n = 10) who will take blackcurrant supplement capsules daily for four weeks. Evaluation of anthocyanin content in the cerebrospinal fluid, via lumbar puncture, and in the blood will be made before and after (day 28) daily blackcurrant capsule therapy. In order to assess any symptomatic effects of blackcurrant anthocyanins, standard PD evaluations (UPDRS, PDQ-39, MMSE, HADS, MoCA) will be undertaken by patients before and after blackcurrant treatment. Data will be presented showing whether blackcurrant anthocyanins are able to cross the human blood-brain barrier and be present in the cerebrospinal fluid of PD patients.

5.1

Impaired Inhibition of Negative Words in Women With Relative Right Hemisphere Frontal Asymmetry

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Vulnerability to depression is associated with both greater relative right hemisphere frontal activity (measured using EEG recordings of alpha power), and with a constellation of cognitive impairments and negative processing biases. However, research linking this hemispheric asymmetry with the cognitive characteristics of depression is lacking. It may be that greater relative RH frontal asymmetry reflects underlying frontal serotonergic asymmetries that affect cognitive and emotional responses to emotional stimuli. One cognitive deficit in depression is the inability to inhibit and disengage from negative information. This leads to extensive elaboration of negative stimuli, increasing emotional responsiveness, and contributing to the downward cycle into depression. In the current study, resting EEG alpha asymmetry was recorded for healthy, never depressed participants, followed by administration of an event-related potential (ERP) emotional Stroop task. Participants identified the colour of neutral and negative words (of high and low arousal); the meaning of the words was irrelevant to the task. As predicted, people with relatively more right hemisphere frontal activity showed interference (that is, they were slower for negative words than for neutral words), whereas people with relatively more left hemisphere frontal activity did not. Neural responses to the emotional word stimuli were further examined using an ERP paradigm. Differences in the ERP signal between those with leftward and rightward frontal asymmetry were found in late components, consistent with the hypothesis that frontal asymmetry is related to inhibition and disengagement. Interference from negative words was not related to current anxiety or depressive levels, indicating that it is specifically the rightward frontal asymmetry, and not current mood, that is related to interference from negative words.

5.2

Brain Activity During Word Rhyming: Are Two Disorders Better Than One?

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Reading is a complex process, drawing on a variety of brain functions in order to link symbols to words and concepts. The two major brain areas linked to reading and phonological analysis include the parietotemporal region and the inferior frontal gyrus. Numerous fMRI studies have shown that adults with dyslexia show reduced activity in the posterior reading system during phonological reading tasks but we know very little about individuals with both dyslexia and mathematical disabilities (MDRD), despite the fact that they coexist in approximately half of cases. As part of the Auckland Comorbidity Study, we sought to understand the aetiology of comorbid learning disabilities by assessing brain activity during a word rhyming task (block design 1.5 T fMRI with a line matching control task). Laterality indices were also computed in SPM 5 to describe the asymmetry of activation. In the temporal lobe only, the dyslexic group showed the least hemisphere lateralisation. Specifically, BOLD data revealed that both the dyslexic and MDRD groups showed significantly less activation than controls in the left supramarginal/angular gyrus. The single deficit dyslexic group showed more activation in the right angular gyrus than all other groups, suggesting compensatory activity. Dyslexics also showed more activity in the right middle temporal gyrus than the MDRD group and less activity in the left dorsolateral prefrontal gyrus. The single deficit MD group showed less activity than controls in the left fusiform gyrus (VWFA) and more left angular gyrus activation. In sum, the temporo-parietal hypoactive effect appears to characterise both groups that are reading disabled, whereas right hemisphere compensation appears to be specific to the single deficit dyslexic group. As right hemisphere compensation is now generally accepted to reduce reading proficiency, it may be that the addition of comorbid maths disability confers some neural benefits, at least in relation to phonological processing.

5.3

Neurological Bases of Developmental Dyscalculia in Adults, and Influence of Comorbid DyslexiaA. J. WILSON^{1,2}, S. ANDREWES¹, K. MASKELL¹, V. ROWE¹, J. KEIR¹, P. LIGHT¹, and K. E. WALDIE¹¹*Department of Psychology, University of Auckland, Auckland, New Zealand*²*School of Educational Studies and Human Development, University of Canterbury, Christchurch, New Zealand*

Developmental dyscalculia (mathematical learning disability) affects around 6% of the population, and has been the subject of relatively few brain imaging studies. It is comorbid with dyslexia around 20-60% of the time, although it is not known whether this is due to common cognitive and neural impairments. Dyscalculia has been proposed to be due to a 'core deficit' in number sense, caused by structural and/or functional impairment of the intra-parietal sulcus (IPS). An alternative hypothesis is that it is due to an 'access deficit' in efficiently linking nonsymbolic representation of number in the IPS to symbolic representation in perisylvian language areas. We used a block fMRI design to measure brain activity in four groups of adults: control, dyscalculia, dyslexia, and comorbid dyscalculia/dyslexia. Participants were scanned while performing a nonsymbolic numerosity matching task (vs. colour matching control) and a multiplication task (vs. digit matching control). Preliminary results support the access deficit account of dyscalculia; participants with dyscalculia showed less activation in perisylvian language areas (left inferior frontal gyrus, superior temporal gyrus and angular gyrus), even during nonsymbolic numerical tasks, suggesting that they may have a weaker connection between nonsymbolic and symbolic number representations. Comorbid learning disabilities were associated with increased activation of dorsolateral prefrontal cortex, possibly indicating working memory as a compensatory mechanism. We will discuss final results and their implications for our knowledge of the neural bases of dyscalculia and dyslexia, as well as the causes of learning disability comorbidity.

5.4

Distinctly Lateralised Networks for Verbal and Spatial Working Memory

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Working memory refers to the ability to temporarily maintain and manipulate information. Numerous functional imaging studies have reported a hemispheric organisation of the fronto-parietal working memory network that is dependent on the nature of the information (i.e. spatial or verbal stimuli). However, few studies have directly linked these functional asymmetries to structural asymmetries. Using both functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI), we investigated the connectivity between functionally defined regions involved in the processing of verbal and spatial working memory. Nine healthy right-handed participants completed a spatial and verbal 2-back task during fMRI and also underwent DTI. Participants were presented with 3-letter consonant-vowel-consonant words that could appear in one of eight locations, and instructed to memorise either the location or word. Both tasks showed regions of peak activation bilaterally in the frontal and parietal regions. These were used to create seed regions of interests (two in each hemisphere) in order to track probabilistic pathways within each hemisphere for both tasks. Pathways which were present in at least 30% of participants were masked onto each individual's fractional anisotropy (FA) maps to derive FA values. Results showed a greater FA in the right hemisphere than the left for the spatial working memory network only. However, laterality indices of FA significantly differed between spatial and verbal working memory, revealing a rightward asymmetry for spatial working memory and leftward asymmetry for verbal working memory, which is consistent with left-hemispheric language processes and right-hemispheric visuospatial functions. This may suggest that there are distinct fronto-parietal working memory networks for maintaining spatial and verbal information.

5.5

**A Time to Remember, A Time to Forget:
Item Dependent Temporal Priming in Recognition Memory for Forgotten Words**

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This study used an item-method directed forgetting task to determine if temporal aspects of the study events can operate as memory cues during the recognition test phase ($N=32$). During the study phase, words were presented 500, 800, 1100, or 1400ms after the onset of a fixation cross. Half of the words at each temporal interval were cued to be remembered, and half were cued to be forgotten. In the subsequent test phase, the entire list of words plus an equal number of new words, were presented under a similar range of temporal intervals. For studied words, this produced temporal differences between the interval employed during study and the interval employed during test. Temporal differences ranged from -900ms (test interval shorter than study fixation) to +900ms (test interval longer than study) in 300ms steps. Paralleling work with spatial locations (Hourihan, Goldberg, & Taylor, 2007) a quadratic trend appeared in the forget data showing a memory benefit when words were presented at, or near, the same temporal interval during test as they were presented during study, with poorer recognition for greater temporal distances between test and study. These findings are discussed in light of theories of time and memory processing.

5.6

The Cultural Causes of Cognition

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At least three distinct views on the relationship between cultural technologies and minds can be found in the literature. The most radical is Clark (2008), Menary (2007), & Rowlands' (2009) notion of an Extended Mind, where external objects in some cases form proper parts of cognitive systems. This approach denies Kim's (1981) claims that external states and relations cannot be part of the supervenience base for minds. Sterelny (forthcoming), however, argues that Extended Mind cases are limiting cases of environmental scaffolding. Though not false, Extended Mind complicates the picture, and Niche Construction Theory is a more helpful framework for understanding human action. Wilson (2010) emphasizes the effect that cultural technologies have in 're-tooling' the mind. She notes the reorganization of neural systems that occurs when we use cultural technologies and argues for the importance of culture in 're-engineering' cognition. None of these pictures is strictly false, but uniting them all is the basic notion of causation. In this paper I very briefly outline each approach. I then explain how genes clearly satisfy a weak criteria of causation with respect to cognitive phenotypes, whereas cultural technology at least in some cases, satisfies a stronger causal criteria. Cultural technologies are important causes of cognition.

5.7

The Role of Eye Gaze in Valuation

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Shimojo et al. (2003) provided preliminary evidence that gaze may have an active role in valuation formation, thus posing a problem for attention theories that view eye gaze as a simple reflection of conscious processing. As in Shimojo et al.'s experiment, the current study alternatively presented two faces (one for 900ms, one for 300ms) for six repetitions. One group was required to make eye movements to laterally presented faces and judge attractiveness (gaze-attractiveness condition), a second were not required to make eye movements to centrally presented faces and judge attractiveness (central-attractiveness condition). In addition to this replication, inter-stimuli interference was controlled for in the current study via a mask preceding stimuli presentation. In contradiction to the findings of Shimojo et al., subjects in the central-attractiveness condition were more likely to choose the longer presented face as being more attractive. Subjects in the gaze-attractiveness condition chose their preference at chance levels. The results suggest that a simple exposure effect is more likely to explain the gaze-duration effect in Shimojo et al.'s study. However, further investigation is required as to why there was an absence of this effect in the gaze-attractiveness condition of the present study, which is contrary to Shimojo et al.'s findings.

6.1

Investigating Changes in Fractional Anisotropy in White Matter in the Brain Due to Methamphetamine Addiction Using Diffusion Tensor ImagingJ. C LIN¹, R. K JAN¹, R. R KYDD², and B. R RUSSELL¹*¹School of Pharmacy, ²Department of Psychological Medicine, University of Auckland, Auckland, New Zealand*

Methamphetamine addiction is an epidemic of global proportion and its consequences have become a major international health problem. Drug-related harm was estimated to cost New Zealand a minimum of \$2 billion annually, which is reported to have the third highest usage of methamphetamine/capita worldwide. Diffusion tensor imaging (DTI) studies in dependent participants have found reductions in fractional anisotropy (FA) in white matter suggesting axonal injury or altered myelination due to methamphetamine use. This study aimed to investigate the effect of methamphetamine addiction on white matter in the brain using DTI. Diffusion-weighted echo-planar imaging sequence with $b=0$, 1000sec/mm² and 30 directions was acquired in 16 methamphetamine-dependent participants aged 22-46, and compared with 21 healthy controls. Imaging was undertaken at the Centre for Advanced MRI at the University of Auckland on a 1.5T Siemens Magnetom Avanto System. Results were analysed using the FDT and TBSS toolboxes within FSL. Statistical analysis – co-varied for age and gender – showed significantly higher FA in white matter of methamphetamine-dependent participants ($p<0.05$) compared to controls, specifically in the body of the corpus callosum. Contrary to findings made by previous research, higher FA values were seen in methamphetamine-dependent participants; however, unlike comparative trials the participants were not abstinent. Increased FA values may result from decreased crossing fibre populations or decreased radial diffusion with no change in longitudinal diffusion in currently using methamphetamine-dependent participants.

6.2

Using Interhemispheric Transfer Time to Investigate the Effects of Benzylphenylpiperazine and Trifluoromethylphenylpiperazine and Dexamphetamine on Human Brains

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Benzylphenylpiperazine (BZP) and trifluoromethylphenylpiperazine (TFMPP) are psychoactive drugs that were marketed as safe, legal alternatives to illicit drugs such as methylenedioxyamphetamine (MDMA) and methamphetamine. Clinical studies have reported that oral doses of BZP and TFMPP produce physiological and subjective effect changes similar to dexamphetamine. Despite their psychoactive properties in humans, no research has been undertaken to determine how BZP and TFMPP affect central information processing. Healthy, right-handed males (25 ± 5.6 years old) were given an oral dose of either placebo ($n = 23$), TFMPP (60mg, $n=15$), combined BZP and TFMPP (100/30mg, $n=15$) or dexamphetamine (20 mg), as a positive control ($n=15$). Subjects were tested pre- and 2 hr post-drug administration. The interhemispheric transfer time (IHTTs) were analysed by subtracting the N160 latency obtained in the contralateral hemisphere from the N160 latency obtained in the hemisphere ipsilateral to stimulus signal. IHTTs were then analysed using three-way repeated measures ANOVA. TFMPP ($F_{(1,36)} = 34.705$; $p < 0.001$), combination of BZP/TFMPP ($F_{(1,36)} = 11.059$; $p < 0.005$) and dexamphetamine ($F_{(1,36)} = 10.640$; $p < 0.005$) significantly reduced the IHTT. However placebo did not significantly affect the IHTT. This research demonstrates for the first time that TFMPP and the combination of BZP/TFMPP, have effects on neural transmission similar to that of the positive control dexamphetamine.

6.3

Determining the Acute Effects of the Combination Benzylpiperazine (BZP) and Trifluoromethylphenylpiperazine (TFMPP) on Cognition and Executive Functioning Using Functional Magnetic Resonance Imaging (fMRI) and the Stroop Paradigm

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A relatively new group of recreational drugs containing a combination of BZP and TFMPP were widely and legally available in NZ until recent legislative change. BZP is a stimulant with similar effects to dexamphetamine, while TFMPP is reported to have similar effects to 3,4-methylenedioxyamphetamine (MDMA). There is a paucity of information about the effects of BZP/TFMPP in humans. This study is a randomised double blind cross-over trial to determine the effects of BZP/TFMPP in comparison to placebo on cognition and executive function in humans using fMRI. 11 healthy participants aged 18-40 underwent fMRI at the Centre for Advanced MRI. Echo planar images (Siemens Magnetom Avanto 1.5T, Germany) were collected whilst participants completed a Stroop paradigm 90 minutes after an oral dose of BZP/TFMPP (100mg/30mg) or Placebo. Data was then pre-processed and analysed using SPM8 to identify areas of regional activation. BZP/TFMPP-induced changes in activation in the Prefrontal cortex (PFC) and Dorsolateral Prefrontal cortex (DLPFC) compared to Placebo during the Stroop (Congruent versus Incongruent) Condition ($p = 0.001$). Reaction Time was also significantly increased by BZP/TFMPP in comparison to placebo. This study is the first to investigate the effect of BZP/TFMPP using fMRI on cognition and executive function. Our results suggest changes in activation within the PFC and DLPFC following BZP/TFMPP administration may reflect the need for additional cognitive resources to be utilised to enable participants to perform the task to the same level of accuracy as those taking placebo.

6.4

Non-conventional Effects of L-DOPA on Nigral Dopaminergic Neurons – Electrophysiological Study in Brain Slices

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The symptomatic benefits of L-DOPA treatment in Parkinson's disease (PD) are undisputed. However, L-DOPA has been shown to induce oxidative stress and leads to neurotoxic effects on dopaminergic neurons in cell culture. These *in vitro* studies have raised concerns as to whether similar toxic mechanisms contribute to side effects and to the continued degeneration of nigrostriatal dopaminergic neurons in PD. To further investigate the possible detrimental effects of L-DOPA, conventional extracellular recordings were made from acute rat midbrain slices. As expected, L-DOPA (300 μ M) produced an inhibitory effect on the pacemaker-like firing of dopamine (30 μ M)-sensitive neurons. Sulpiride (D2 receptor antagonist; 2 μ M) reversed the inhibition produced by L-DOPA, and unmasked an excitatory effect. Excitation was potentiated by L-DOPA auto-oxidation (removal of ascorbic acid; 450 μ M), and attenuated by AMPA/kainate glutamate receptor antagonist CNQX (20 μ M). These findings are consistent with the involvement of TOPA quinone, an oxidative product of L-DOPA, previously shown to induce excitatory effects via AMPA/kainate receptors in non-dopaminergic neurons. L-DOPA evoked a distinct, early peak in excitation which was abolished by CNQX, although persistent excitation was still present. Excitatory effects were greatly enhanced by glutamate transporter blocker TBOA (15 μ M), suggesting that L-DOPA releases glutamate. The persistent excitatory effect of L-DOPA observed in the presence of both CNQX and NMDA receptor antagonist APV (50 μ M) suggested that L-DOPA-induced excitation involves not only activation of ionotropic glutamate receptors, but also other mechanisms that still need to be determined. Our results show for the first time that L-DOPA activates glutamate receptors in nigral dopaminergic neurons, and suggests that the effects are due to both the direct action of TOPA quinone on AMPA/kainate receptors, and to the release of glutamate.

6.5

Sustained Drug Release to the Cerebellum using ELVAX Polymer Implants

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Cerebellar ataxia is a poorly treated neurological disorder. Recent evidence suggests that cerebellar metabotropic glutamate receptor 1 (mGluR1) signalling activity may offer a therapeutic target, provided manipulations are targeted directly to the cerebellum without risk of effects outside the brain. Here we use polymer implants to deliver the mGluR1 agonist (DHPG) and antagonist (CPCCOEt) directly into the mouse cerebellum *in vivo*, as a potential therapeutic strategy. Mixtures of ELVAX 40W polymer, fluorescent dye and dichloromethane solvent \pm DHPG/CPCCOEt were prepared at -20°C. 2-3 weeks later 100 μ m thick polymer implants, first rinsed for 2 hours in sterile saline, were placed onto the surface of the cerebellum of 17-19 day old mice, under controlled anaesthesia and aseptic conditions. 7 days later, 250 μ m thick cerebellar slices were prepared and fluorescence observed in the tissue. We did not observe any adverse effects from the polymer implant procedure during this period. Using whole cell patch clamp recordings we evoked excitatory post synaptic currents (EPSCs) at the parallel fibre (PF) to Purkinje Neuron (PN) synapse and climbing fibre (CF) to PN synapse and measured Paired Pulse Facilitation (PPF) and Paired Pulse Depression (PPD) respectively, as an indicator of glutamate release probability. PPF was similar between wild type and sham treated PNs. In DHPG-treated PNs we observed an increase in PPF and conversely a decreased PPF in CPCCOEt-treated PNs. PPD was unchanged in all treatments. Our findings indicate that slow, sustained delivery of tools to manipulate mGluR1 signalling alters glutamate release probability at cerebellar synapses.

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6.6

Hysteresis Effects in General Anaesthesia: Biophysical Reality or Measurement Artifact?D. A. STEYN-ROSS¹, M. L. STEYN-ROSS¹, J. W. SLEIGH², and M. T. WILSON¹¹*School of Engineering, University of Waikato, Hamilton, New Zealand*²*Waikato Clinical School, University of Auckland, Waikato Hospital, Hamilton, New Zealand*

It is a well-established, yet paradoxical, observation that most general anaesthetic drugs have a “biphasic” effect on electrical activity in the brain: at low drug concentrations there is a surge in low-frequency EEG power that occurs around the time of loss of consciousness; at higher concentrations, brain activity diminishes, and eventually tends towards electrical silence. A second surge in EEG power appears during the return to consciousness, and this emergence peak typically occurs at a lower concentration than that recorded during the induction peak, suggesting a hysteresis separation between induction of, and recovery from, anaesthetic coma. However, for intravenous agents (such as propofol), drug concentration is measured in the arterial blood while drug effect occurs in the brain, so there needs to be a pharmacokinetic (PK) extrapolation for the ~2-min equilibration-time required for diffusive transport across the blood–brain barrier. Traditionally, modellers would tune their PK parameters in order to eliminate the hysteresis loop, the implicit assumption being that induction and emergence biphasic peaks occur at identical drug concentrations. We test this assumption in a propofol sheep model that has been instrumented to allow accurate estimation of brain concentration using an mass-balance paradigm. We find clear evidence of a true hysteresis separation between induction and emergence trajectories, and this finding is consistent with the phase-transition predictions of a mathematical model of the cortex. This suggests that progression into anaesthesia is a switch-like change of state rather than a smoothly graduated transition along a continuum of cortical states.

7.1

Inducing and Assessing Chronic Tinnitus in Rats Using Unilateral Acoustic Trauma and a Frequency-Specific Shift in Discrimination Function with a Conditioned Lick Suppression Paradigm

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Tinnitus is a phantom auditory perception affecting 10–15% of the population and in about 1–3%, tinnitus is severe enough to affect the quality of life. However, there is no curative treatment available. Drug development for tinnitus has been hugely limited by the lack of understanding of tinnitus pathology and the lack of validated animal models for in vivo drug testing. Although noise trauma is the second most common cause of tinnitus in humans, a rat model of noise-induced tinnitus has never been created in our laboratory. The aim of this study was to induce chronic tinnitus in rats using unilateral acoustic trauma and to assess the presence of tinnitus behaviourally. Sixteen male Wistar rats were subjected to either the unilateral noise exposure under anaesthesia (n = 8) for 1 hour or the sham exposure (anaesthesia only, n = 8). Following 2 weeks of recovery, the animals were trained to suppress their drinking activity during silence while challenged with brief periods of noise and tones of various intensities and frequencies. For sham animals, a test stimulus resembling tinnitus would have no effect on their drinking activity, but for animals with tinnitus, a test stimulus resembling tinnitus would serve as a signal for drinking suppression. The results clearly showed that noise exposure produced a significant downward shift in the frequency-response curve, which indicated the presence of tinnitus. To induce and assess chronic tinnitus in rats provides a useful tool to investigate the underlying mechanisms of tinnitus and to screen drugs for tinnitus treatment.

7.2

Effects of Chronic Tinnitus on Attention and Impulsive Behavior in Rats

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Although tinnitus is an auditory disorder, it is often associated anecdotally with attention deficits and emotional problems. Functional neuroimaging studies in humans have revealed that the hippocampus, amygdala and anterior cingulate, areas of the brain involved in emotion, attention and spatial processing, are also involved in auditory memory and tinnitus perception. However, tinnitus-evoked emotional and cognitive changes have never been studied in animal models of tinnitus. In the present study, we investigated whether chronic tinnitus induced by acoustic trauma would affect attention and impulsivity in a 5-choice serial reaction time task in rats. Eight male Wistar rats were exposed to unilateral acoustic trauma (105 dB, 16 kHz for 1 h under anesthesia) and 8 rats underwent the same anesthesia without acoustic trauma. The animals were then tested for the presence of tinnitus using a frequency-specific shift in discrimination function with a conditioned lick suppression paradigm at 2 weeks after the noise exposure. At 6 months after the confirmation of tinnitus, the rats were tested in a 5-choice serial reaction time task. The behavioural procedure involved training the rats to discriminate a brief visual stimulus presented randomly in one of five spatial locations and responding by poking its nose through the illuminated hole and collecting a food reward from the magazine. While all the animals performed equally well in making correct responses with a similar rate of errors of omission, the tinnitus animals made significantly more premature responses when tested with long, unpredictable inter-trial intervals or with short stimulus duration. These results suggest that rats with chronic tinnitus have impaired impulse control.

7.3

Effects of Baclofen on Chronic Tinnitus Induced by Acoustic Trauma

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It is estimated that 10% of the population experience tinnitus in a form severe enough to require medical attention. However, there is no effective treatment available due to the uncertain pathology underlying tinnitus. One hypothesis is that tinnitus is associated with neuronal hyperactivity in the central auditory system. Noise trauma, a common cause of tinnitus, has been shown to cause a decrease in inhibition in the cochlear nucleus. Therefore it is expected that drugs that increase GABAergic neurotransmission within the central nervous system, such as baclofen, could thereby decrease hyperactivity and alleviate tinnitus. Sixteen Wistar rats were divided into sham (n = 8) and tinnitus (n = 8) groups. Tinnitus was induced by unilateral exposure to acoustic trauma and the presence of tinnitus was assessed by a frequency-specific shift in the discrimination function with a conditioned lick suppression paradigm. The hearing threshold was also examined by acoustic brainstem-evoked responses (ABR). Once tinnitus was confirmed, the animals were injected (s.c) with either vehicle or baclofen at 1, 3 and 5 mg/kg while being tested for the presence or absence of tinnitus. Acoustic trauma significantly increased the ABR in the exposed ear and the frequency-response curve was significantly shifted downward in the noise-exposed animals, which indicated the presence of tinnitus. Preliminary results have shown that baclofen has no effect on tinnitus at a low dose (1 mg/kg). However, at a medium dose (3 mg/kg), baclofen significantly reduced the psychophysical behaviour associated with tinnitus. The results so far suggest that baclofen may be useful in the treatment of noise-induced tinnitus.

7.4

Effects of the Synthetic Cannabinoid Receptor Agonists, WIN55,212-2 and CP55,940, on Salicylate-Induced Tinnitus in Rats

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Previous studies in animals and humans have shown that, in some cases at least, anti-epileptic drugs can reduce the severity of tinnitus. Given that cannabinoid receptor agonists have been shown to exert anti-epileptic effects in some circumstances, we investigated whether two synthetic CB₁/CB₂ receptor agonists, WIN55,212-2, and CP55,940, could inhibit the behavioural manifestations of salicylate-induced tinnitus in rats in a conditioned suppression task. Acute tinnitus was induced by a single dose of sodium salicylate (350 mg/kg, s.c.) and the presence of tinnitus was assessed behaviourally by a conditioned lick suppression paradigm. WIN55,212-2 (3 mg/kg s.c.) or CP55,940 (0.1 or 0.3 mg/kg s.c.) were administered 30 min prior to the induction of tinnitus. We found that neither WIN55,212-2 nor CP55,940, significantly reduced conditioned behaviour associated with tinnitus. However, both 3 mg/kg WIN55,212-2 and 0.3 mg/kg CP55,940 did significantly increase tinnitus-related behaviour compared to the vehicle control groups. These results suggest that cannabinoid receptor agonists may not be useful in the treatment of salicylate-induced tinnitus and that at certain doses, they could actually exacerbate the condition.

7.5

GABAergic Compensation in Connexin36 Knock-Out Mice Evident During Low-Magnesium Seizure-Like Event Activity

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Gap junctions are transcellular channels that allow direct electrical and ionic coupling between adjacent cells. Cerebrocortical gap junctions may facilitate cortical seizure activity by their ability to synchronize electrical activity. One approach to investigate this is to compare wild-type (WT) animals with those lacking the gene for connexin36 (Cx36KO); the protein that forms neuronal gap junctions within the cerebral cortex. A concern with utilizing genetically modified knock-out animals is the possibility of compensatory effects; the risk is that differences between WT and Cx36KO animals could be erroneously attributed to Cx36 gap junction effects. We investigated the effect of GABA_A-receptor modulation (augmentation with etomidate (16µM) and blockade with picrotoxin (100µM)) in WT and Cx36KO mouse cortical slices made seizurogenic by exposure to low-magnesium. In WT slices, picrotoxin enhanced both the amplitude (49% increase) and frequency (26% increase) of seizure-like events (SLEs); etomidate also enhanced SLE amplitude (22% increase) but reduced event frequency (27% decrease). In Cx36KO slices, the frequency effects of the two drugs were similar to WT, but the amplitude responses were abolished. Importantly, pre-treatment with the gap junction blocker mefloquin in WT slices did not significantly alter the drug responses. These findings indicate that the reduction in amplitude effect seen in the Cx36KO mice was due to compensatory changes, not a direct effect of Cx36 gap junction blockade. In conclusion, results from studies comparing seizure characteristics between WT and the Cx36KO mouse must be viewed with a degree of caution because of the possible confounding effect of compensatory neurophysiological changes in the genetically modified animals.

7.6

**Pharmacological Preconditioning by GYKI 52466 Against Kainate Induced Seizures:
An Electrographic Study**

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Previous studies in our lab have shown that preconditioning with GYKI 52466 (GYKI), an AMPA receptor antagonist, protects against seizures induced by high dose kainic acid (KA). In those studies, administration of low-dose GYKI produced significant reductions seizure behaviours and hippocampal cFOS expression. These effects were seen using GYKI at doses far lower, and with preadministration times far exceeding any previously documented, and support the possibility of a metabotropic mechanism of action (Hesp et al., 2004). In the present study we employed electrocorticographic (ECoG) recording to further assess low-dose GYKI preconditioning protection. Male Sprague Dawley rats (300-400g) were surgically implanted with a digital telemetry transmitter and allowed 7-10 days to recover before experimentation. Either saline or low-dose GYKI (1 or 3 mg/kg) was administered 10, 90 or 180 minutes prior to seizure induction by KA (10mg/kg). GYKI (3mg/kg; 90 min) produced strong and consistent protective effects relative to saline preconditioned controls. Decreases in ECoG power spectral density were observed in the delta, theta, alpha and beta frequency bands ($p < 0.01$, each). High frequency, high amplitude electrographic spiking was also reduced ($p < 0.05$), and consistent with previous studies of low-dose GYKI preconditioning, we again observed significant reductions in cumulative seizure scores ($p < 0.05$) and the expression of level 4 seizure behaviours ($p = 0.001$). Taken together, these findings provide strong support for GYKI 52466 as an effective neuroprotective agent, and reinforces the potential of pharmacological preconditioning as a prophylactic strategy against excitotoxic brain damage.

8.1

Effects of Aging on Agmatine Levels in the Rat Hippocampus and Prefrontal CortexM. RUSHAIDHI¹, S. CHARY², Y JING¹, J. T. KENNARD¹, N. C. COLLIE¹,
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Agmatine, decarboxylated L-arginine, is a novel neurotransmitter. Recent evidence suggests that agmatine may participate directly in the processes of learning and memory. The present study measured agmatine levels in the CA1, CA2/3 and dentate gyrus (DG) sub-regions of the hippocampus and the prefrontal cortex (PFC) in aged (24-month-old, $n = 8$) and young (4-month-old, $n = 8$) male Sprague Dawley rats by liquid chromatography/mass spectrometry. There were significantly decreased agmatine levels with age in the tissue homogenates of the CA2/3 ($p < 0.01$), DG ($p < 0.05$) and PFC ($p < 0.05$). When agmatine levels in synaptoneurosomes (containing enriched synaptosomal material) were measured, a significant decrease in agmatine level was found in PFC ($p < 0.05$), but not in the CA1, CA2/3 or DG sub-region of the hippocampus, in aged rats. These results demonstrate age-related region-specific changes in agmatine in these memory-associated brain regions. As agmatine functions as a neurotransmitter, decreased agmatine level in prefrontal synaptoneurosomes may lead to impaired synaptic neurotransmission and contribute to age-related learning and memory deficits.

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8.2

Agmatine Prevents Against Beta-amyloid (25-35)-induced Spatial and Object Recognition Memory Deficits in the Rat

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Amyloid beta (A β) peptides have been proposed to play a central and causative role in the development of Alzheimer's disease. A β_{25-35} , an 11-amino acid fragment, has the critical neurotoxic properties of full-length A β and causes memory impairments in rodents. Recent research suggests a neuroprotective role of agmatine. The present study investigated the effects of agmatine treatment (40 mg/kg) administered intraperitoneally 30 min prior to a single bilateral intracerebroventricular (i.c.v.) infusion of aggregated A β_{25-35} (30 nmol) and then once daily for a further 9 consecutive days on A β_{25-35} -induced behavioural deficits tested from day 26 post-A β infusion in adult male Sprague-Dawley rats. Animals with A β_{25-35} infusion and saline (1 mg/kg, i.p.) treatment were mildly impaired in the reference memory version of the water maze task, but performed poorly in the working memory version of the task and in the object recognition memory task, relative to those that received the inactive control peptide A β_{35-25} i.c.v. infusion and saline treatment. By contrast, animals with A β_{25-35} i.c.v. infusion and agmatine treatment did not show performance impairments in the working memory version of the water maze task and the object recognition memory task. These results, for the first time, demonstrate that agmatine protects against A β_{25-35} -induced spatial working memory and object recognition memory deficits, and the underlying mechanisms of it will be explored in the future.

8.3

Functional MRI of Saccades in Alzheimer's Disease: The Reflexive and Predictive Tasks

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The fMRI of saccadic eye movements in Alzheimer's disease (AD) have been scarcely studied. The sole study showed right parietal lobe dominance during a reflexive paradigm suggesting visuospatial dysfunction. Saccades in AD are abnormal and may exhibit impaired reflexive saccade latency. The externally generated 'reflexive' task is more demanding of spatial attention, compared with the internally generated 'predictive' task that requires learning spatial and temporal target locations. Prediction is thought to involve the prefrontal cortex, lateral frontal eye fields (FEF), inferior parietal lobe and supplementary eye fields (SEF) whereas reflexive saccades are generated by the FEF and parietal eye fields (PEF). Twelve patients with mild-moderate AD and twelve age and sex-matched controls performed the reflexive and predictive tasks both in the laboratory and during fMRI. As a group, patients' latencies (mean 253ms) were significantly longer than controls (209ms, $p < 0.001$) in the reflexive task. There was not a significant group difference in the predictive task. The AD group demonstrated reduced BOLD signal changes in the FEF and the PEF for the reflexive task and reduced BOLD signal changes in the FEF and SEF during the predictive task ($p < 0.005$ uncorrected, 10 voxel extent). The AD group had reduced activity compared to the controls in the left FEF during the reflexive task relative to the predictive task. No regions were less active in the predictive task than the reflexive task. Our findings suggest that AD reflexive saccade deficits are associated with dysfunction of the fronto-parietal network responsible for the generation of reflexive saccades.

8.4

Dampening Tonic Inhibition Promotes Post-stroke Functional Recovery in Young and AgedA. N. CLARKSON^{1,2}, B. HUANG¹, I. MODY¹, and S. T. CARMICHAEL¹¹*Department of Neurology, UCLA, Los Angeles, USA*²*Department of Anatomy and Structural Biology, Department of Psychology, University of Otago, Dunedin, New Zealand*

Post-stroke neural repair and rehabilitation processes continue for weeks to months after the initial insult. These processes are mediated in part by activity dependent physiological changes. Extrasynaptic GABA_A receptors, GABA_ARs, consisting of alpha5 (α 5) or delta (δ) subunits, mediate tonic inhibitory currents that control baseline levels of excitability. The present study assessed the role of tonic inhibition on post-stroke recovery using pharmacogenetic manipulations to α 5 and δ -subunit containing GABA_ARs in young and aged mice. Electrophysiology recordings of layer II/III pyramidal neurons *ex vivo* revealed increased tonic inhibition within peri-infarct cortex that was blocked following application of L655,708, a α 5GABA_AR inverse agonist. Assessment of motor behaviors *in vivo* revealed significant ($P < 0.001$) forelimb deficits out to 6-weeks post-stroke. Treatment with L-655,708, starting 3-days after stroke, significantly decreased forelimb deficits on both cylinder and gridwalking tasks, with near maximal effects seen from 7-days post-stroke. Assessment of α 5-/- mice showed similar functional gains, whilst δ -/- mice only showed mild improvements. Assessment of motor function after stroke in aged mice revealed greater motor deficits compared to young. Treatment with L655,708 resulted in a significant decrease in forelimb deficits, with the functional gains comparable to those seen in the young. These results demonstrate that stroke produces a state of hypoexcitability in peri-infarct motor cortex through increased tonic GABA signalling. Suppression of tonic inhibitory currents results in an early and sustained reversal of forelimb motor deficits after experimental stroke that is comparable between young and aged.

8.5

The ASTRO Study: Cognition and Functional Outcomes in 5-year Stroke Survivors

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Studying long-term cognition post-stroke and its contribution to functional outcomes may improve stroke outcomes. However, existing data are not population-based, and restricted to limited, short-term outcomes. This population-based 5-year follow-up examined associations between neuropsychological deficits (verbal/visual memory, executive function, information processing speed (IPS), visuoperceptual/construction ability, language) and functional outcomes in 307 5-year stroke survivors. The greatest proportion of participants had average cognitive functioning; while 30-50% performed at lower levels on most measures. Few performed above the average range. Deficits were most common in the areas of executive functioning and information processing speed (IPS). In multiple regression IPS and visuoperceptual ability made significant independent contributions to functional outcomes above that of age, depression or current Barthel Index, suggesting these areas are a possible target for rehabilitative efforts.

9.1

Does Cognitive and Motor Status affect Memory-Guided Saccades in Parkinson's disease?

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Memory guided saccades are impaired in Parkinson's disease (PD), but the relative influence of cognitive and motor status is unknown. We examined the relationship between Montreal Cognitive Assessment (MoCA) scores and Unified Parkinson's Disease Rating Scale part III (UPDRS III) motor scores on latency and accuracy of memory-guided saccades in 74 PD patients and 26 controls using video oculography. A fixation stimulus was presented, followed 2s later by a peripheral target for 400ms while the fixation remained visible. The subject was required to maintain gaze on the fixation stimulus for an additional 2.5s when it was extinguished simultaneous to a tone, cueing the subjects to saccade as rapidly as possible to the remembered target location, which became the fixation location for the next trial. The 14 dementia patients (PDD) exhibited prolonged latencies ($F(3, 95) = 29.2, p < 0.001$) and reduced accuracy ($F(3, 97) = 7.91, p < 0.001$) compared to the 43 cognitively normal patients (PDN), the 17 patients with mild cognitive impairment (PD-MCI) and the controls, which did not differ significantly. Latency and accuracy correlated with MoCA ($r = -0.60$ and $0.44, p < 0.001$) and UPDRS ($r = 0.48$ and $r = -0.33, p < 0.005$). PD-MCI and PDD groups had more fixation errors than PDN and Controls ($F(3, 97) = 23.2, p < 0.001$). Fixation errors in the PD-MCI and PDD groups are consistent with disinhibition, perhaps arising from prefrontal cortex dysfunction. Longer latencies and reduced final saccade gain likely reflect cognitive slowing and short-term memory deficits in the PDD group. Thus, memory guided saccadic performance may be a useful overall objective measure of cognitive status in PD.

9.2

Voluntary Tremor Suppression in Parkinson's Disease

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Rest tremor is a cardinal symptom in Parkinson's disease, typically presenting as a rhythmic pill rolling finger movement with pronation/supination movements of the forearm. It has been observed that some patients with parkinsonian rest tremor are able to suppress their tremor voluntarily with mental concentration or by focussing attention on the affected limb; however this process is not well understood. This study will investigate voluntary tremor suppression in patients with Parkinson's disease both peripherally, with tremor and movement assessment tools, and centrally, with functional imaging to identify the brain regions activated in this process. Ten patients with isolated unilateral parkinsonian rest tremor in the upper limb and the ability to suppress this tremor voluntarily will be recruited. Each patient will undergo assessments comprising electromyography, electromagnetic movement tracking and the tremor components of the Unified Parkinson's Disease Rating Scale to record key tremor measurements such as frequency, severity, muscle burst duration, pattern of muscle activation, tremor activation conditions and how these measures change during voluntary tremor suppression. Each participant will also undergo fMRI in a 3.0 Tesla scanner with paradigms designed to assess brain involvement in tremor suppression. Preliminary results showed large reductions in tremor severity in one patient. Functional imaging with a standard fMRI block design paradigm involving blocks of tremor followed by tremor suppression suggests significant cortical activation in parts of the motor cortex during tremor suppression. We will determine whether this is a direct inhibitory suppression process or simply related to the activation of antagonistic muscle groups that oppose the tremor.

9.3

Parkinson's Disease and Cognition: Clarifying the Spectrum of Impairments

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Parkinson's disease (PD) is a multisystem brain disorder with 75-80% cumulative prevalence of dementia. Identification of "Parkinson's disease with mild cognitive impairment" (PD-MCI) may therefore help target patients at risk of future dementia and an ideal group for intervention studies. Unfortunately, seven different criteria have been used to establish PD-MCI. We examined a large sample of PD patients and their cognition using extensive neuropsychological testing covering the four cognitive domains identified by the recent Movement Disorders Society Task Force as relevant to PD-D. A global neuropsychological score was derived from these domains to assess the impact of different MCI criteria on individual PD patients without dementia (N=109) relative to PD-D patients (N=21) and 50 healthy controls. Some criteria (e.g., needing one score in one domain that fell $\geq 1.0SD$ below normative data) produced a high number of "MCI" in both the PD group (90%) and the controls (70%). By contrast, the more stringent criteria in current use at the Van der Veer (VDV) Institute for Parkinson's and Brain Research (2 scores within a single domain that are $\geq 1.5SD$ below normative data) identified 30 cases (28%), and a smaller proportion overlapping with the global scores obtained by healthy controls. This "VDV" PD-MCI group showed functional status that was more similar to other non-dementia PD patients, plus a 3-D ROC analysis of their Montreal Cognitive Assessment scores confirmed high diagnostic separation between the three PD groups.

9.4

Correlations Between ASL Blood Flow MRI and Eye Movement Abnormalities in Parkinson's Disease

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Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting the motor pathway. Eye movements provide useful information about the changes in the motor system in PD. As the eye is limited to three axes of rotation, it provides measurements that are precise and simple to interpret compared to a complex multi-joint limb. Another tool in mapping change in PD patients is ASL (arterial spin labelling) blood flow MRI. Using ASL, our group has identified a PD related cerebral perfusion networks with each individual having a network score indicating the extent of their expression of the pattern. The aim of this study is to explore correlations between the MRI imaging and eye movement abnormalities in Parkinson's patients. Network scores and saccadic eye movement measures in 61 PD patients and 30 controls were compared. Significant correlation ($r = 0.45$ $p = 0.00026$) between expression of network score and reflexive saccade latency was found and shows increased expression of the network score is associated with an increase in reflexive latency. We conclude that the combination of cerebral perfusion and saccadic eye movement parameters may provide novel markers of PD status and disease progression.

9.5

Reduced Cerebral Perfusion in Cognitively Impaired Parkinson's Disease

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Arterial Spin Labeling (ASL) is a non-invasive, *in vivo* magnetic resonance imaging (MRI) technique that quantitatively measures cerebral perfusion without the use of exogenous contrast agents. Parkinson's disease (PD) is associated with reduced cortical metabolism and perfusion. Previous radiotracer studies by others indicate that predominantly posterior reductions correlate with cognitive impairment. In this study we used a general linear model analysis of ASL MR images to characterize perfusion in healthy controls (n = 30) and PD participants with varying degrees of cognitive impairment, including those with normal cognition (PD-N; n = 32), mild cognitive impairment (PD-MCI; n = 17), and dementia (PD-D; n = 11). The PD group (as a whole) exhibited extensive cortical perfusion deficits, extending subcortically to include bilateral caudate, when compared to controls (corrected for multiple comparisons using false discovery rate; $p < 0.05$). There were no significant perfusion differences within normal cognition (controls vs PD-N) or between the impaired groups (PD-MCI vs PD-D). PD-MCI showed significant deficits compare to PD-N in extensive posterior, frontal, and temporal cortices with accompanying bilateral caudate and thalamic reductions. These findings suggest that cerebral hypoperfusion in PD is associated with cognitive decline and provides a potential physiological correlate of the progression of cognitive impairment in PD.

9.6

Models of Neurovascular Coupling

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Functional hyperaemia is an important metabolic autoregulation mechanism by which increased neuronal activity is matched by a rapid and regional increase in blood supply. This mechanism is facilitated by a process known as "neurovascular coupling"-the orchestrated intercellular communication between neurons, astrocytes and microvessels. An important step in this process is the movement of potassium in and out of extracellular space by two potassium channels, BK and KIR. Previous models of neurovascular coupling have not included the mechanisms involving these channels. Here we provide such a model, which successfully accounts for (1) the arteriolar dilation caused by the release of glutamate into the synaptic space between neurons, and (2) the removal of accumulating extracellular potassium by astrocytes that possess a distribution of varying electrophysiological properties. This model can achieve an approximate 20% vasodilation due to the physiological rise in extracellular potassium concentration from 3 to 6mM, as well as achieving extracellular potassium homeostasis.

10.1

**Diffusion Tensor imaging and Fibre Tracking Applied to the Thalamus –
A New Approach to Understanding Parkinson's Disease**

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Standard MRI techniques have shown that decreases in thalamic volume are linked with cognitive dysfunction in multiple sclerosis, dementia and schizophrenia. Different thalamic nuclei have also been associated with different cognitive domains, presumably through an association with their different cortical neural connections. New developments in diffusion tensor imaging (DTI) provide an opportunity to investigate cognition and thalamic integrity. We will present evidence using diffusion tensor imaging, as well as new fibre tracking techniques, to assess both overall volume and the integrity of individual thalamic nuclei in Parkinson's disease (17 dementia patients, 22 MCI patients and 59 patients with relatively normal cognition; and 25 healthy controls). Thalamic volume derived from the diffusion tensor and T1 images showed a small reduction in the dementia patients (post-hoc Newman-Keuls, $p < 0.05$, relative to controls and PD-N group), but there were no differences across the other groups. Volumetric and microstructural integrity data for individual nuclei will be presented, together with an analysis of their association with performance on cognitive tasks that assess executive function, attention and working memory, visuoperceptual function and episodic memory.

10.2

Feigned Paresis Affects Behaviour But Not Neuromotor Preparatory Activity

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A key feature of Conversion Disorder is the presence of neurological symptoms (without an organic origin) that are not consciously feigned. Diagnosis is challenging because conversion symptoms are difficult to dissociate from intentionally feigned symptoms. The purpose of this experiment was to investigate whether healthy participants instructed to feign movement impairment would demonstrate conversion-like behavioural and brain activity outcomes. The parameter precuing paradigm was used to manipulate the amount (partial or complete) and nature (hand or finger) of information presented to the participant before an imperative stimulus signalled initiation of a rapid finger flexion response. Measures included reaction time (RT), movement time (MT) and the amplitude of the contingent negative variation (CNV) over C3 and C4. Two groups of 12 healthy participants were instructed to imagine they had difficulty moving their left upper limb under one of two instruction methods: "move against an imaginary resistance" or "diminish the effort to move". Although type of instruction had no effect on RT, MT or CNV ($p > .05$), feigning overall had a strong effect on behaviour. RT and MT of the affected hand were slower ($p < .001$) than the unaffected hand. There was no difference in RT for precue conditions in which hand was unknown. As observed in controls, but not patients, CNV amplitudes were larger over the contralateral hemisphere when hand could be pre-specified ($p < .05$) regardless of which hand was to be moved. Feigning slowed the initiation and execution phases of voluntary movement resembling conversion-like paresis, but concomitant changes in motor cortex activity specific to preparing an impaired motor response were not present. These results indicate that measures of CNV have the potential to discriminate "true" Conversion Disorder from feigning in the absence of differences in behavioural outcomes.

10.3

An Oculomotor Exploration of Autism and Asperger's Disorder: Evidence for Dissociation of Motor Deficits?

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It remains unclear whether autism and Asperger's disorder exist on a symptom continuum or are separate disorders with discrete neurobiological underpinnings. In addition to impairments in communication and social cognition, motor deficits constitute a significant clinical feature in both disorders. Previous research by our group has suggested that motor deficits may dissociate the groups, with evidence that deficits in AD may reflect front-striatal dysfunction, whereas deficits in high-functioning individuals with autism (HFA, IQ > 70) may reflect both fronto-striatal and cerebellar deficits. We used a range of saccade tasks to profile oculomotor deficits in these groups to examine evidence of differentially disrupted motor circuitry. We tested three groups of adolescent males; nine with AD, eight with HFA and ten normally developing males as the comparison group. While reflexive saccades were preserved in both clinical groups, group differences emerged for both AD and HFA relative to the comparison group for volitional, predictive and self-pacing saccades. Deficits included increased variability in latency and timing, altered waveform dynamics, reduced consistency in velocity profile measures, and reduced inhibition of unwanted saccades. Although both the AD and HFA groups demonstrated a range of motor abnormalities suggestive of disrupted fronto-striatal and cerebellar motor control; the nature of these deficits relative to the comparison group was often different. The results suggest that while oculomotor deficits in AD and HFA are not dissociable in terms of cerebellar involvement being specific to HFA, the nature of cerebellar and striatal dysfunction and subsequent motor deficits may be different in the groups.

10.4

The Neural Correlates of Motor Inhibition in Autism

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The basal-ganglia-frontal-dopamine system has been identified as a main circuit involved in action selection and the inhibition of competing actions. Deficits in response inhibition have been observed in individuals with depleted dopamine. We examined evoked response potentials derived from EEG data in healthy controls and people with Autism using a Go/No-Go task with additional manipulations on subliminal priming. Our primary focus was on the N2 and P3 components overlying frontal regions of the brain. We hypothesised that when primed with a Go stimulus Autists will produce larger N2 amplitudes, indicating high pre-motor response inhibition. If Autists successfully inhibit a subliminally primed Go stimulus, we hypothesised that they would produce larger P3 amplitudes, indicating learning of motor inhibition on a subconscious level. Preliminary results revealed larger N2 on Go trials and No-Go trials in Autistic individuals compared to controls, which suggests higher pre-motor response inhibition; in our view, this demonstrates a possible conflict between subconscious and conscious motor programs. There was a gradual recovery to baseline of the P3 following its initial amplitude in Autists compared to a robust P3 in controls. This would suggest that Autists lacked successful learning of motor inhibition on a subconscious level. In addition, there was a significant difference in the amplitude of the N2 produced on primed trials compared to non-primed trials, suggesting that priming produces a tendency toward higher response readiness. Overall, these results suggest that deficits in the inhibitory systems underlying responses to Go and No-Go cues observed in Autistic individuals may be controlled by cortical regions influenced by basal ganglia dopaminergic signals.

10.5

Sensory and Perceptual Disturbances Evoked By an Experimental Model of CRPSH. PICKERING¹, P. MINEI¹, G. L. MOSELEY², C. S-Y. LIN^{1,2}, and M. LEE³¹*Faculty of Medicine, University of New South Wales, Sydney, Australia*²*Neuroscience Research Australia, Sydney, Australia*³*Department of Chiropractic, Macquaire University, Sydney, Australia*

Complex regional pain syndrome (CRPS) is a neuropathic pain disorder with unknown aetiology. Neurogenic inflammation commonly results after acute injury and subsequent immobilisation, factors consistently associated with the onset of this disorder. Sensory disturbances such as hyperalgesia and allodynia are key features of CRPS and sufferers report an increased size perception of their affected limb as well as difficulties with motor imagery. The purpose of this study is to investigate sensory changes subsequent to acute injury and forced limb immobilisation. Acute injury was induced experimentally via application of topical capsaicin over the first dorsal interosseous muscle. Capsaicin produced hyperalgesia and allodynia and mild burning pain after application. The hand was subsequently immobilised using a thermo-plastic splint for 24 hours. The Quantitative Sensory Testing (QST) system was used to examine the function of A-delta and C fibres. Motor imagery was assessed using a judgement task which required subjects to identify pictures as left or right hands and limb perception was assessed via a hand drawing task. Sensory functions were examined before and after capsaicin and/or immobilization. Capsaicin decreased heat pain thresholds, increased detection thresholds for warm and cold stimuli, increased perceived hand size and increased reaction time in the hand judgement task of the affected hand. Immobilisation subsequent to experimental injury, increased sensory deficits and produced greater body image distortion. Thus experimental acute pain and short-term immobilisation produced similar sensory impairments commonly reported by CRPS patients, suggesting that acute injury and immobilization are key features in the pathogenesis of CRPS.

11.1

A Comparison of Ambulation- and Spin-Elicited Theta Rhythms in the Regions of the Hippocampus, Posterior Hypothalamus and Periaqueductal Gray in the Rat

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Vestibular lesions have previously been reported to reduce hippocampal theta rhythm. Vestibular activation (in the absence of active movement) elicits theta. We carried out experiments to assess whether vestibular signals generated by passive spinning generated the same pattern of theta, across a range of structures, as active movement. Electrode arrays with 4 poles spaced at 0.5mm were inserted through 1) the cortex and into the CA1/2 areas of the hippocampus; 2) from above the hypothalamus, through the posterior hypothalamus to the supramammillary nucleus; and 3) from above, through and below the periaqueductal gray. Within the hippocampus there appeared to be slight differences between area CA1 and area CA2. The cortex above CA1 appeared to generate distinct theta but with similar properties to that of CA1. Move-spin differences in the frequency profile of theta power were similar for different sites within the hypothalamus, but distinct from the areas above it and these, in turn, appeared somewhat different from the hippocampus. Ventral periaqueductal gray and/or an area below it showed theta generation with a move-spin difference that was distinct from the other areas studied. These data suggest that vestibular input produces a distinct pattern of activation in the network of structures that show theta rhythm and provide further evidence that different structures are involved in theta under different conditions.

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11.2

Age Effects on Theta-Range EEG in Spatial Working Memory Task

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Although theta activity has been proposed as a potential biomarker for mild cognitive impairment (MCI) and Alzheimer's disease (AD), the degree to which theta-range electroencephalographic (EEG) activity changes in the process of healthy ageing is unclear. The aim of the present study was to compare the temporal and spatial characteristics of scalp-recorded theta activity in healthy older adults with that of younger adults during performance of a spatial recognition memory task. Ten healthy older participants and 10 younger adults were asked to remember the locations of eight representational drawings, each presented simultaneously with two landmarks (white squares) on a computer screen, while their scalp EEG was recorded. No significant difference was found in the behavioural performance (analyzed as percentage of correct responses) of the two age groups. Wavelet-based time-frequency analysis revealed that during encoding, retention and retrieval of spatial information the onset, peak periods and amplitude of theta-range oscillations in older individuals did not differ significantly from those of younger people. Consistent with previous reports, there was a trend towards lower peak frequency in older individuals. However, the topographic distributions were similar in younger and older individuals, suggesting that older individuals recruit the same underlying structures as younger adults in the performance of a spatial recognition memory task. These data suggest that if variations in peak frequency of theta are allowed for (and there is some individual variation in this parameter, regardless of age), other aspects of theta oscillations seem very similar in younger and older individuals.

11.3

Age-Related Neural Changes Associated with Remembering and Imagining Autobiographical EventsD. R. ADDIS¹, R. ROBERTS¹, and D. L. SCHACTER²¹*Department of Psychology, University of Auckland, Auckland, New Zealand*²*Department of Psychology, Harvard University, Massachusetts, USA*

When remembering the past or imagining the future, young adults tend to generate specific, unique events while older adults tend to generate more generic, routine events. This fMRI study investigated whether the age-related overproduction of generic autobiographical events is associated with changes in brain activity – specifically, decreased activation of regions mediating episodic detail (e.g., hippocampus, precuneus) and increased activation of regions mediating conceptual detail (e.g., lateral temporal regions). Fourteen young (M=20 years) and fourteen older (M=73 years) adults recalled past events or imagined future events in response to cue words (e.g. “car”) presented during scanning. A control task requiring semantic and visuospatial processing was also completed. The specificity of each past and future event generated during scanning was determined and, as expected, older adults generated significantly more generic events than young adults. Analysis of fMRI data using Spatiotemporal Partial Least Squares revealed that when generating autobiographical events, both age-groups activated a common network including medial prefrontal and parietal cortices, hippocampus, and lateral parietal and temporal regions. However, there was a significant task-by-group interaction. Young adults exhibited a greater autobiographical>control task effect than older adults in the hippocampus and medial parietal cortex. In contrast, older adults showed a greater autobiographical>control task effect than young in lateral temporal regions. These results demonstrate that older adults can activate many regions of the core network when remembering past events and imagining future events. Even so, older adults showed decreased recruitment of regions mediating episodic detail, but increased recruitment of lateral temporal regions supporting the generation of the increased conceptual detail that comprises a substantial number of their past and future events.

11.4

Cost-Benefit Encoding in the Anterior Cingulate Cortex

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Optimal decision-making often requires an assessment of the costs and benefits associated with each available course of action. Previous studies have shown that lesions to the anterior cingulate cortex (ACC) impair cost-benefit decision-making in laboratory animals, however the neural mechanisms underlying the deficit are not well understood. Here we recorded from ACC neurons in freely moving rats as they performed a spatial cost-benefit decision-making task. Over 124 recording sessions, 54 neurons were stably recorded for the full duration of the multi-day experiments. The apparatus used was a continuous T-maze baited with food reward. In the baseline configuration, “2:6B,” rats could pursue 2 or 6 food pellets, the latter obtained by climbing a barrier (high-cost, high-reward (HCHR)). In this configuration the mean percentage of HCHR choices was $69 \pm 4\%$, and a substantial portion of ACC neurons (63%) exhibited significantly higher firing for one goal trajectory versus the other; for 94% of these cells higher firing was associated with the HCHR option. This HCHR-bias was not simply attributable to the larger reward, the barrier, or behavioral preference. In inter- and intra-session manipulations involving at least one barrier (2:6B, 2B:6B, 2:2B), ACC activity rapidly adapted and was consistently biased towards the economically advantageous option relative to the configuration. Interestingly, when only a difference in reward magnitude was presented (2:6, no barrier, HCHR choices $84 \pm 4\%$), ACC activity was minimal and non-biased. One interpretation of our data is that the ACC encodes a relative, integrated cost-benefit representation of available choice options that is biased towards the “better” option in terms of effort-outcome ratio. This representation may be specifically recruited when an assessment of reward *and* effort is required to optimally perform a task.

11.5

Medial Temporal Responses to the Novelty of Future SimulationsV. VAN MULUKOM, D.L. SCHACTER², M.C. CORBALLIS¹, and D.R. ADDIS¹¹*Department of Psychology, University of Auckland, Auckland, New Zealand*²*Department of Psychology, Harvard University, Cambridge, Massachusetts, USA*

Recent neuroimaging research has shown that a common brain network is engaged both for remembering past events and imagining future events. This common network comprises medial temporal (including the hippocampus), parietal and prefrontal cortices. However, there is greater neural activity when imagining future events relative to remembering past events, particularly in the right anterior hippocampus. This fMRI study investigated whether increased anterior hippocampal activation is a response to the novelty inherent in future events, but not past events. Fourteen participants completed an adapted repetition-suppression paradigm that required them to generate novel future events and then simulate each event another two times across the duration of the scanning session. Thus, the novelty of future events was manipulated, with the “first simulation” being more novel than the “third simulation”. Consistent with repetition suppression studies, reaction times for event construction significantly decreased from the first to the third simulation. As predicted, right anterior hippocampus showed more activity for the first versus third simulation. Interestingly, bilateral amygdala also showed this first>third effect. These preliminary findings suggest that greater right anterior hippocampal activity for future versus past events may reflect, at least in part, the inherent novelty of imagined events. This result is consistent with recent findings that anterior hippocampus is particularly involved in the encoding of novel information. In the current study, bilateral amygdala also exhibited a novelty response, consistent with previous evidence that the amygdala acts as a novelty detector. Together, these findings suggest that the amygdala and anterior hippocampus work in concert to detect the inherent novelty of, and encode, future events.

