AWCBR

Australasian Winter Conference for Brain Research

2024 Programme

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SYMBIOTIC DEVICES

Programme at a Glance

SATURDAY 31ST AUGUST

AWCBR REGISTRATION (3:30-6:00PM)	AWCBR OPENING RECEPTION (6:00-7:00PM)	AWCBR CONFERENCE OPENING (7:00-7:05PM)	PLENARY: PROF DAVID CAPPER (7:05-8:05PM)	DISORDERS OF THE NERVOUS SYSTEM (8:05-9:05PM)

SUNDAY 1ST SEPTEMBER

COFFEE/ TEA (7:45-8:00AM)	NON-NEOPLASTIC SURGICAL NEUROPATH-OLOGY (8:00-9:00AM)	NEUROTRUMA (9:00-10:15AM)	MORNING TEA (10:15-10:45AM)	CTE (10:45 AM-11:30 PM)	SYMPOSIA: CTE (11:30 AM-12:30 PM)	LUNCH (12:30-1:30 PM)	PLENARY LECTURE: PROF ARIE PERRY (1:30-2:30PM)	DISORDERS OF THE NERVOUS SYSTEM (2:30-3:00PM)	AFTERNOON TEA (3:00-3:30PM)	PLENARY: PROF GLENDA HALLIDAY (3:30-4:15PM)	NEURODEGENERATION (4:15-5:30PM)	ANZSNP CLOSING REMARDS (5:30-6:00PM)	QRW: OPENING LECTURE (6:30-8:20PM)	AWCBR CONFERENCE DINNER (8:20-11:30PM)
							QRW PARALLEL SESSION: MĀORI AND PACIFIC RESEARCH IN AOTEAROA (1:30-3:30PM)							

MONDAY 2ND SEPTEMBER

COFFEE/TEA (8:45-9:00AM)	PLENARY: JANA VUKOVIC (9:00-9:45AM)	SYMPOSIA: GLIA & CNS INJURY (9:45-10:45AM)	MORNING TEA (10:45-11:15AM)	SOCIAL ACTIVITIES (11:15AM-5:30PM)	DEVELOPMENT (5:30-6:15PM)	BREAK (6:15-6:30PM)	NOVEL METHODS (6:30-7:30PM)	AWCBR STUDENT DINNER (8:00-10:00PM)

TUESDAY 3RD SEPTEMBER

COFFEE/TEA (8:00-8:15AM)	PLENARY: PROF TIM ANDERSON (8:15-9:00AM)	SYMPOSIA: BASAL GANGLIA (9:00-10:00AM)	MORNING TEA (10:00-10:30AM)	CELLULAR MECHANISMS (10:30-11:30AM)	BREAK (11:30-11:45AM)	COGNITION AND BEHAVIOUR (11:45AM-12:45PM)	AWCBR AGM (12:45-1:45PM)	AFTERNOON TEA (3:15-3:45PM)	FLASH TALKS (3:45-4:30PM)	POSTER SESSION (4:30-6:00PM)	SYMPIOTIC DEVICES STUDENT & ECR SESSION (6:00-7:30PM)

WEDNESDAY 4TH SEPTEMBER

COFFEE/TEA (9:00-9:15AM)	DISORDERS OF THE NERVOUS SYSTEM (9:15-10:00AM)	MORNING TEA (10:00-10:30AM)	COGNITION AND BEHAVIOUR (10:30-11:30AM)	BREAK (11:30-11:45AM)	SENSORY AND MOTOR SYSTEMS (11:45AM-12:30PM)	LUNCH & PRIZEGIVING (12:30-1:30PM)

Saturday 31 August 2024

3:30 pm-6:00 pm		Registration, Crowne Plaza Hotel
6:00 pm		Opening Reception, Cash Bar and Light Food, Atrium
7.00 pm		Chair's Opening Remarks

1. COMBINED LECTURE
CHAIR: FOUZIA ZIAD

7:05 pm	1.1	**David Capper,** ***Institute of Neuropathology, Charité Universitätsmedizin, Berlin, Germany*** DNA methylation profiling and its practical implications

2. DISORDERS OF THE NERVOUS SYSTEM
CHAIR: BLAKE HIGHET

8:05 pm	2.1	**Toni Pitcher,** ***University of Otago, Christchurch,, New Zealand*** The New Zealand Parkinson's Environment and Genes Study (NZPEGS)
8:20 pm	2.2	**Samantha Edwards,** ***The University of Adelaide, Adelaide, Australia*** Characterising chronic synergistic effects of traumatic brain injury and pesticide exposure on Parkinson's disease development and progression in a novel rat model
8:35 pm	2.3	**Angus McNamara,** ***The University of Adelaide, Adelaide, Australia*** More than a one-hit wonder: Exploring synergistic effects of genetic and environmental risk factors in the progression of Parkinson's disease
8:50 pm	2.4	**Eden Yin,** ***University of Auckland, Auckland, New Zealand*** Beyond rare: A meta-analysis of PINK1 Parkinson's disease prevalence, phenotypic diversity, and α-synuclein pathology

Sunday 1 September 2024

7:45 am		COFFEE/TEA BREAK

3. NON-NEOPLASTIC SURGICAL NEUROPATHOLOGY

CHAIR: THOMAS ROBERTSON

8:00 am	3.1	**Arie Perry,** ***University of California San Francisco Parnassus Campus, San Francisco, USA*** Non-neoplastic CNS lesions
8:45 am	3.2	**BN Nandheesh,** ***National Institute of Mental Health and Neuro Sciences, Bengaluru, India*** Non-neoplastic case presentation – 'Unusual cerebellar vermian lesions – a short case series'

4. NEUROTRAUMA

CHAIR: REIMAR JUNCKERSTORFF

9:00 am	4.1	**Michael Buckland,** ***The University of Sydney, Sydney, Australia*** Chronic traumatic encephalopathy (CTE) – Overview and Australian perspectives
9:45 am	4.2	**Michael Buckland,** ***The University of Sydney, Sydney, Australia*** Co-existing pathologies with CTE
10:15 am		MORNING TEA BREAK

5. CHRONIC TRAUMATIC ENCEPHALOPATHY

CHAIR: CLINTON TURNER

10:45 am	5.1	**Helen Murray,** ***University of Auckland, Auckland, New Zealand*** Neuropathological features that differentiate CTE and Alzheimer's disease: insights from a multiplex immunohistochemistry study of 50 proteins

6. SYMPOSIA: CHRONIC TRAUMATIC ENCEPHALOPATHY

CHAIR: HELEN MURRAY

11:30 am	6.1	**Catherine Suter,** ***Sydney Local Health District, Sydney, Australia*** Spatially resolved transcriptomics of human cortex reveals unique disease signatures and potential biomarkers for chronic traumatic encephalopathy
11:45 am	6.2	**Chelsie Osterman,** ***University of Auckland, Auckland, New Zealand*** Multiplex immunohistochemistry reveals focal glial reactivity in Chronic Traumatic Encephalopathy
12:00 pm	6.3	**Danica Hamlin,** ***University of Auckland, Auckland, New Zealand*** Characterising Cis Tau pathology in Chronic Traumatic Encephalopathy
12:15 pm	6.4	**Samantha Bureau, Concussion Legacy Foundation, Boston, USA** The Evolving Discussion on CTE Causation and the Quest to Develop a Clinical Diagnosis

12:30 pm BREAK
ANZSNP AGM

7A. PLENARY LECTURE

CHAIR: CATRIONA MCLEAN

1:30 pm 7A.1 **Arie Perry,** ***University of California San Francisco Parnassus Campus, San Francisco, USA***
Biomarkers in neuro-oncology

7B. QRW PARALLEL SESSION: MĀORI AND PACIFIC RESEARCH IN AOTEAROA

DART ROOM, L7,
RYDGES LAKELAND RESORT

1:30 pm	7B.1	**Prof Faafetai Tai Sopoaga,** ***University of Otago, Dunedine, New Zealand*** Tagata o Te Moana Nui a Kiwa – mental health and well-being of Pacific youth in Aotearoa
2:15 pm	7B.2	**Ainsleigh Cribb-Su'a,** ***National Hauora Coalition, Auckland, New Zealand*****, & Kahu Ama,** ***Iwi United Engaged Ltd., Auckland, New Zealand*** Hauora Hinengaro o te Whaea – Assessment tool development
3:00 pm	7B.3	**Miriama Ketu-Mackenzie,** ***University of Otago, Dunedine, New Zealand*** Starting well: Improving Māori mental health by focusing on the first 2000 days of life

8. DISORDERS OF THE NERVOUS SYSTEM

CHAIR: ASHIK BANSTOLA

2:30 pm	8.1	**Eleanor Bowley-Schubert,** ***The University of Adelaide, Adelaide, Australia*** Characterising the impact of pre-existing brainstem tau pathology on the development of cognitive deficits following a single mild traumatic brain injury
2:45 pm	8.2	**James Wiseman,** ***University of Auckland, Auckland, New Zealand*** Refining α-synuclein seed amplification assays to distinguish Parkinson's disease from Multiple System Atrophy
3:00 pm		AFTERNOON TEA

Sunday 1 September 2024

9. PLENARY LECTURE

CHAIR: VICTOR DIERIKS

3:30 pm	9.1	**Glenda Halliday,** ***The University of Sydney, Sydney, Australia*** Challenges and variability in the pathogenesis of neurodegenerative diseases: Insights and emerging concepts

10. SYMPOSIA: NEURODEGENERATION

CHAIR: VICTOR DIERIKS

4:15 pm	10.1	**Maurice Curtis,** ***University of Auckland, Auckland, New Zealand*** Reconstructing the olfactory system in humans to localize neurodegeneration's earliest events
4:30 pm	10.2	**Khushi Sehajpal,** ***University of Auckland, Auckland, New Zealand*** Characterisation of the substantia nigra in cases of X-linked Dystonia Parkinsonism
4:45 pm	10.3	**Jessica Collins,** ***University of Tasmania, Hobart, Australia*** Using mouse models of neurodegeneration to understand the relationship between blood biomarkers and pathology across disease progression and in response to interventions
5:00 pm	10.4	**Erin Cawston,** ***University of Auckland, Auckland, New Zealand*** The New Zealand-Dementia Prevention Research Clinics: Plasma biomarkers and the Alzheimer's disease continuum
5:15 pm	10.5	**Laura De Paoli,** ***University of Tasmania, Hobart, Australia*** NFH epitopes as blood biomarkers of neurodegenerative diseases
5:30 pm	10.6	**Chien-Hsiung (Alan) Yu,** ***Florey Institute of Neuroscience and Mental Health, Parkville, Australia*** Type I interferon response triggers programmed axonal degeneration in ALS

5:30 pm ANZSNP CLOSING REMARKS AND PRESENTATION OF PRIZES

Sunday 1 September 2024

5:45 pm	BREAK

QRW OPENING LECTURE

QUEENSTOWN & WAKATIPU ROOM,
LIVE STREAM CLANCY'S, L5
RYDGES LAKELAND RESORT

6:30 pm	**QRW Opening**
6:40pm	**Hons Judith Collins, *Minister for Research, Science and Innovation of New Zealand*** Opening address and Q&A
7.00 pm	**Prof Dame Jane Harding, *University of Auckland, Auckland, New Zealand*** Why planning a research career is futile but fun
7.40pm	**Prof Sir Ashley Bloomfield, *University of Auckland, Auckland, New Zealand*** How does research inform health policy and practice in New Zealand, and how can we do better?

AWCBR CONFERENCE DINNER

8:20 pm – 11:30 pm

BAZAAR QUEENSTOWN,
RYDGES LAKELAND RESORT

Tickets must be purchased in advance.
Tickets include food, drinks (including house wine, beer, and non-alcoholic options) and musical entertainment, so put on those dancing shoes!

Cash bar after 10pm

Monday 2 September 2024

8:45 am		COFFEE/TEA

11. PLENARY LECTURE

CHAIR: KYLA-LOUISE HORNE

9:00 am	11.1	**Jana Vukovic, *The University of Queensland, Brisbane, Australia*** Decoding the Role of Microglia in Brain Injury: Induction of Pro-Regenerative States

12. SYMPOSIA: GLIA AND CNS INJURY

CHAIR: JANA VUKOVIC

9:45 am	12.1	**Eryn Kwon, *Mātai Medical Research Institute, Gisborne, New Zealand*** Multimodal and multiscale – the rainbow of mild traumatic brain injury
10:00 am	12.2	**Marc Ruitenberg, *The University of Queensland, Brisbane, Australia*** Dissecting inflammation and spinal cord lesion site development at single-cell resolution
10:15 am	12.3	**Josh McGeown, *Mātai Medical Research Institute, Gisborne, New Zealand*** Longitudinal changes in network-based functional connectivity during a season of collision sport participation
10:30 am	12.4	**Samuel Stuart, *The University of Queensland, Brisbane, Australia*** Attenuating dopaminergic neurodegeneration following traumatic brain injury by modulating the innate immune system
10:45 am		MORNING TEA BREAK

11:15 am

SOCIAL ACTIVITIES

Skiing at Coronet Peak
Meeting point: 11:00 AM, NZSki Snow Centre,
25 Shotover St Queenstown
Finish: 02 Sep 2024 17.30 Queenstown
Pre-Booking and payment required

Hop on hop off wine and beer afternoon tour
Meeting Point: 12:05 PM, Queenstown - The Station,
Corner of Shotover & Camp Street, Queenstown
Last bus back is 4:55 PM
Pre-Booking and payment required

Frankton Arm walk (including Queenstown gardens)
Meeting point: 11:30 AM, Crowne Plaza Lobby
This is a 9.7-km out-and-back trail near Queenstown, Otago. Generally considered an easy route, it takes an average of 2 to complete but we can extend as time and inclination allows. This is a very popular area for hiking, mountain biking, and running, so you'll likely encounter other people while exploring. The trail is open year-round and is beautiful to visit anytime. We will likely stop at the Boatshed Café and Bistro for lunch before meandering on.
Contact Christina (021 174 2275) if you would like to join

13. DEVELOPMENT

CHAIR: KAREN WALDIE

5:30 pm	13.1	**Jieqi Wang, *Nanyang Technological University, Singapore*** Internet addiction: cortical hypertrophy and self-regulation
5:45 pm	13.2	**Francesca Pigatto, *University of Auckland, Auckland, New Zealand*** Cumulative risk of ACEs on depression symptoms in young people in the Growing Up in New Zealand study
6:00 pm	13.3	**Maitri Tomar, *University of Western Australia, Crawley, Australia*** Weakening of perineuronal nets following non-invasive brain stimulation

6:15 pm BREAK

14. NOVEL METHODS

CHAIR: CHRISTINA BUCHANAN

6:30 pm	14.1	**Catherine Morgan,** ***University of Auckland, Auckland, New Zealand*** The relationship between macro- and microvascular blood flow in cognitive decline
6:45 pm	14.2	**Sigrid Petautschnig,** ***Cyban Pty Ltd, Melbourne, Australia*** Assessment of cerebrovascular responses using a novel non-invasive brain pulse monitor in an acute stroke patient undergoing thrombectomy
7:00 pm	14.3	**Samuel McCullough,** ***University of Auckland, Auckland, New Zealand*** Human iPSC-derived brain pericytes exhibit differences in inflammatory activation compared to primary human brain pericytes
7:15 pm	14.4	**Hamid Abbasi,** ***Auckland Bioengineering Institute, Auckland, New Zealand*** Enhanced EEG seizure recognition after hypoxia-ischemia in fetal sheep using transformer-based deep learning

8:00pm **AWCBR Student Dinner**
Winnie's, Queenstown

Tuesday 3 September 2024

8:00 am		COFFEE/TEA

15. PLENARY LECTURE

CHAIR: KYLA-LOUISE HORNE

8:15 am	15.1	**Tim Anderson,** ***University of Otago, Christchurch, New Zealand*** Ian McDonald, NZP3 and is it worth the effort?

16. SYMPOSIA: BASAL GANGLIA

CHAIRS: ASHIK BANSTOLA/JOHN REYNOLDS

9:00 am	16.1	**Genevra Hart,** ***University of New South Wales, Sydney, Australia*** Local modulation of dopaminergic action signals during goal-directed learning
9:15 am	16.2	**Jay Bertran-Gonzalez,** ***University of New South Wales, Sydney, Australia*** Local cell-to-cell interactions protect predictive learning from counterproductive dopamine in the striatum
9:30 am	16.3	**Nathalie Dehorter,** ***The University of Queensland, Brisbane, Australia*** Novel immune-induced mouse model of Parkinson's disease
9:30 am	16.4	**John Reynolds and Bailee Ryan,** ***University of Otago, Dunedin, New Zealand*** Translational approaches to modulate basal ganglia circuits in brain disorders
10:00 am		MORNING TEA BREAK

17. CELLULAR MECHANISMS

CHAIR: SAM MCCULLOUGH

10:30 am	17.1	**Laura Carr,** ***The University of Adelaide, Adelaide, New Zealand*** Characterisation of phenotypic changes in aged microglia in the rodent and ovine brain
10:45 am	17.2	**Maggie Hames,** ***University of Otago, Dunedin, New Zealand*** Investigating the effect of CK2 phosphorylation of RyR2 on neuronal excitability
11:00 am	17.3	**Danielle Rutter,** ***University of Otago, Dunedin, New Zealand*** Altered L-type Ca2+ channel-mediated plasticity in dentate granule cells of PS19 mice.
11:15 am	17.4	**Shruthi Sateesh,** ***University of Otago, Dunedin, New Zealand*** Astrocyte-mediated trans-regional metaplasticity in the hippocampus
11:30 am		BREAK

18. COGNITION AND BEHAVIOUR

CHAIR: HAMID ABBASI

11:45 am	18.1	**Nicola Slater,** ***University of Otago, Christchurch, New Zealand*** Predictive value of cortical cholinergic pathway integrity on future cognitive change in Parkinson's disease
12:00 pm	18.2	**Karen Waldie,** ***University of Auckland, Auckland, New Zealand*** Functional magnetic resonance imaging reveals fidgeting in ADHD improves prefrontal cortex activation during executive functioning
12:15 pm	18.3	**Kyla-Louise Horne,** ***University of Otago, Christchurch, New Zealand*** Longitudinal trajectories and predictors of Visual hallucinations in the New Zealand Parkinson's Progression Programme
12:30 pm	18.4	**Shabah Mohammad Shadli,** ***Charles Sturt University, Bathurst, Australia*** Is lack of goal-conflict specific rhythmicity a biomarker for treatment resistance in generalized anxiety?

12:45 am	AWCBR AGM All attendees are invited to join
1:45 pm	BREAK FOR LUNCH
3:15 pm	AFTERNOON TEA

19. FLASH TALKS

CHAIR: NICOLA SLATER

The Flash Talk session is designed to maximise the exposure and discussion of each poster. Each presenter will be given 90 seconds and one static PowerPoint slide to introduce and promote their research. No questions will be answered after each Flash Talk presentation.

After the Flash Talks are finished, we invite all the speakers and audience to move through to the poster exhibition room for the poster session.

3:45 pm

Joseph Balfe, *University of Otago, Dunedin, New Zealand*
Katerina Gerasimenko, *University of Auckland, Auckland, New Zealand*
Suzanne Barker-Collo, *University of Auckland, Auckland, New Zealand*
Alexander Matthews, *University of Otago, Dunedin, New Zealand*
Christine Arasaratnam, *University of Auckland, Auckland, New Zealand*
Kiri Barr-Glintborg, *University of Canterbury, Christchurch, New Zealand*
Vanessa Alexandre da Silva, *Federal University of São Carlos, São Paulo, Brazil*
Georgia Peattie, *University of Otago, Dunedin, New Zealand*
Jonathan Zong, *University of Auckland, Auckland, New Zealand*
James Davies, *University of Otago, Dunedin, New Zealand*
Aimee Mills, *University of Auckland, Auckland, New Zealand*
Kreesan Reddy, *University of Auckland, Auckland, New Zealand*
Takanobu Yamamoto, *Tezukayama University, Nara, Japan*
Thomas Cawood, *University of Otago, Dunedin, New Zealand*
Guillaume Newburn, *Matai Medical Research Institute, Gisborne, New Zealand*
Blake Highet, *University of Auckland, Auckland, New Zealand*
Ashik Banstola, *University of Otago, Dunedin, New Zealand*
Madhu Kumar, *King George's Medical University, Lucknow, India*
Baraa Abuharbid, *University of Auckland, Auckland, New Zealand*
Anushka Chatterjee, *Western Sydney University, Campbelltown, Australia*

20. POSTER SESSION

4:30 pm-6:00 pm

All posters should be put up by 3:00 pm and remain up until 6:00 pm.

Presenters with odd numbers should be in attendance at their poster from 4:30 pm – 5:15 pm.

Presenters with even numbers should be in attendance at their poster from 5:15 pm – 6:00 pm.

All presenters need to remove their poster by 6:00 pm.

20.1 **Joseph Balfe,** ***University of Otago, Dunedin, New Zealand***
Non-invasive neuromodulation to alleviate bronchoconstriction

20.2 **Katerina Gerasimenko,** ***University of Auckland, Auckland, New Zealand***
Impacts of Friedreich's Ataxia on well-being, mood and social cognition

20.3 **Suzanne Barker-Collo,** ***University of Auckland, Auckland, New Zealand***
Calculating clinically reliable change in adults with post-stroke fatigue: an extension of the Fatigue After Stroke Educational Recovery (FASTER) trial

20.4 **Alexander Matthews,** ***University of Otago, Dunedin, New Zealand***
Using machine learning to quantify seizure behaviour in a tadpole model of developmental and epileptic encephalopathies

20.5 **Christine Arasaratnam,** ***University of Auckland, Auckland, New Zealand***
Neuropathology of the striatum in X-linked Dystonia Parkinsonism

20.6 **Kiri Barr-Glintborg,** ***University of Canterbury, Christchurch, New Zealand***
Comparative influence of rodent anterior thalamic nuclei, medial prefrontal cortex, and dorsal subiculum on episodic-like memory and spatial working memory

20.7 **Vanessa Alexandre da Silva,** ***Federal University of São Carlos, São Paulo, Brazil***
Exploratory analysis of ADAM10 isoforms levels and activity in neuron-like cell fractions.

20.8 **Georgia Peattie,** ***University of Otago, Dunedin, New Zealand***
Ketamine induces changes in hippocampal activity recapitulating changes seen in animal models of schizophrenia

20.9 **Jonathan Zong,** ***University of Auckland, Auckland, New Zealand***
Investigating EEG-derived biomarkers of Major Depressive Disorder: Lempel-Ziv complexity, spectral power and peak alpha frequency

20.10 **James Davies,** ***University of Otago, Dunedin, New Zealand***
Testing AAV-mediated sAPPa overexpression as a therapy in an AD mouse model

20.11 **Aimee Mills,** ***University of Auckland, Auckland, New Zealand***
Targeting connexin hemichannels and the inflammasome pathway in an induced mouse model of Alzheimer's disease

20.12 **Kreesan Reddy,** ***University of Auckland, Auckland, New Zealand***
Harnessing alpha synuclein polymorphs to investigate novel protein targets in Parkinson's disease

20.13 **Takanobu Yamamoto,** ***Tezukayama University, Nara, Japan***
Tryptophan metabolism and trans-diagnostic approach in childhood and adolescence ADHD/ASD comorbid patients with central fatigue

20.14 **Thomas Cawood,** ***University of Otago, Dunedin, New Zealand***
Neurobiology of Psychosis Risk

20.15 **Guillaume Newburn,** ***Matai Medical Research Institute, Gisborne, New Zealand***
Ultra-high contrast MRI (UHC-MRI): a new era in traumatic brain injury (TBI) diagnosis

20.16 **Blake Highet,** ***University of Auckland, Auckland, New Zealand***
The Neurological Foundation Human Brain Bank: Preparation of human brain tissue of neurodegenerative diseases

20.17 **Ashik Banstola,** ***University of Otago, Dunedin, New Zealand***
Developing new bilateral large animal model of Parkinson's disease: effects of asymmetrical 6-OHDA lesions of the substantia nigra in sheep

20.18 **Madhu Kumar,** ***King George's Medical University, Lucknow, India***
Utility of squash smear cytology in intraoperative diagnosis of central nervous system lesions: A tertiary care institute experience

20.19 **Baraa Abuharbid,** ***University of Auckland, Auckland, New Zealand***
Dissecting the substantia nigra & locus coeruleus from human brains

20.20 **Tracy Melzer,** ***University of Otago, Christchurch, New Zealand***
Tau PET in Parkinson's disease: interim findings

20.21 **Anushka Chatterjee, *Western Sydney University, Campbelltown, Australia***
The impact of Meriva® curcumin diet on glial activation and neuroinflammatory markers on a mouse model of chronic neuroinflammation

20.22 **Therese Mulligan, *University of Auckland, Auckland, New Zealand***
You only get one brain: An exploratory retrospective study on life after adolescent TBI

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21. SYMBIOTIC DEVICES STUDENT AND EARLY CAREER RESEARCHER SESSION

CHAIR: ROSS VAN DEWETERING & NICOLA SLATER

6:00 pm 21.1 **Promoting yourself on paper**

Open to all students and those who identify as an Early Career Researcher (ECR) attending AWCBR.

Join us for a drink and nibbles thanks to Symbotic Devices

Whether it is in a CV, cover letter, or grant application, being able to effectively highlight your skills and achievements in writing can enhance your career prospects and boost professional visibility. In this session, our three panellists will offer key insights and self-promotion tips from their experience in academia and industry, which will be followed by an interactive Q&A.

Panellists:

Dr Michelle van Rensburg, *Medical Science Liaison/Medical Manager, Eisai NZ, Auckland*

Dr Toni Pitcher, *Senior Research Fellow, University of Otago, Christchurch/ Research and Operations Manager, New Zealand Brain Research Institute, Christchurch*

Dr Robert Munn, *Director of Neuroscience / Lecturer, Department of Anatomy, Brain Health Research Centre, University of Otago, Dunedin*

9:00 am		COFFEE/TEA

22. DISORDERS OF THE NERVOUS SYSTEM
CHAIR: CHRISTINE ARASARATNAM

9:15 am	22.1	**Ben Moloney,** ***University of Auckland, Auckland, New Zealand*** Developing neuroinflammation biomarkers to assess the antidepressant effects of naltrexone in major depressive disorder with an inflammatory component
9:30 am	22.2	**Sophie Cawood,** ***University of Otago, Dunedin, New Zealand*** Plasma-derived microRNAs are altered with ketamine intervention for treatment-resistant Generalised or Social Anxiety disorders.
9:45 am	22.3	**Kyrah Thumbadoo,** ***University of Auckland, Auckland, New Zealand*** The clinical and genetic landscape of UBQLN2-linked ALS/FTD; a meta-analysis of variant pathogenicity and sex differences

10:00 am		MORNING TEA

23. COGNITION AND BEHAVIOUR
CHAIR: ROSS VAN DE WETERING

10:30 am	23.1	**Katerina Thompson,** ***University of Otago, Dunedin, New Zealand*** Beneficial effects of long-term agmatine supplementation in aged rats
10:45 am	23.2	**Olivia Haller,** ***The University of Adelaide, Adelaide, Australia*** The effect of 5-fluorouracil on immortalised neuronal and microglia-like cells: Laying the foundation for the development of an in vitro model of chemotherapy-induced cognitive impairment
11:00 am	23.3	**Hanna Friedlander,** ***University of Otago, Dunedin, New Zealand*** The central amygdala's involvement in processing appetitive stimuli
11:15 am	23.4	**Rob Munn,** ***University of Otago, Dunedin, New Zealand*** Hippocampal-prefrontal coherence is altered during behavioural strategy transitions, and is compromised in the maternal immune activation model of schizophrenia

11:30 am		BREAK

24. SENSORY AND MOTOR SYSTEMS

CHAIR: KYLA-LOUISE HORNE

11:45 am	24.1	**Ross van de Wetering,** ***Victoria University of Wellington, Wellington, New Zealand*** Novel analogues of the kappa opioid receptor agonist, U50488, have potent antinociceptive effects without tolerance or other side effects
12:00 pm	24.2	**Lily Bental,** ***University of Otago, Dunedin, New Zealand*** Basal ganglia-motor thalamus neuronal activity is altered by dyskinesia-inducing levodopa administration in parkinsonian rats
12:15 pm	24.3	**Jason Kerr,** ***Max Planck Institute for Neurobiology of Behavior, Bonn, Germany*** Deep cortical layers encode sustained changes in light conditions in freely moving mice

12.30 pm	CLOSING REMARKS AND PRESENTATION OF PRIZES LIGHT LUNCH, THREESIXTY RESTAURANT

Prize Winners

Goddard Prize and Poster Prize Winners (Students)

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 Connellly,** University of Otago, New Zealand **Bridget Simonson,** Victoria University of Wellington, New Zealand (Poster)
2010	**Tracy Melzer,** Van der Veer Institute, New Zealand **Yeri Kim,** University of Otago, New Zealand (Poster)
2011	**Kajsa Igelstrom,** University of Otago, New Zealand **Malinda Tantirigama,** University of Otago, New Zealand (Poster)

Prize Winners

2012	**Malinda Tantirigama,** University of Otago, New Zealand **Malvindar Singh-Bains,** University of Auckland, New Zealand (Poster)
2013	**Amy Smith,** University of Auckland, New Zealand **Peter Bosch,** Victoria University of Wellington, New Zealand **Laura Boddington,** University of Otago, New Zealand (Poster)
2014	**Emmet Power,** University of Otago, New Zealand **Lakshini Mendis,** University of Auckland, New Zealand (Poster)
2015	**Christine de Lance,** University of Canterbury, New Zealand **Christine Arasaratnam,** University of Auckland, New Zealand (Poster)
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It is exciting to see that this year the addition of targeted symposia on critical areas, including neurodegeneration, glia and CNS injury, and the Basal ganglia, is enhancing the depth and breadth of discussions at the already excellent conference.

The AWCBR is an invaluable platform that brings together researchers from New Zealand and abroad, fostering networking and collaboration. Research funded by the Foundation has significantly advanced the understanding of conditions such as Parkinson's, Alzheimer's, Huntington's, motor neurone diseases, stroke, multiple sclerosis, ALS, migraine, epilepsy, dementia, traumatic brain injury and many other debilitating conditions. Since the Foundation began its important work in 1971, over $70 million has been granted to neurological research.

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Abstracts in Presentation Order

Proceedings of the International Australasian Winter Conference on Brain Research, 2024, 40, will be published on the AWCBR website.

2.1

The New Zealand Parkinson's Environment and Genes Study (NZPEGS)

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Parkinson's disease is a neurodegenerative disorder with poorly understood etiology. Current theories assume an interaction between an individual's genetic risk, environmental exposures, and life-style factors to set someone on the path to Parkinson's. Our understanding of the role genetics plays in Parkinson's has greatly increased in recent times. Rare mutations across a number of genes are known to cause the disorder and genome-wide association studies have identified >90 alleles with greater expression in people with Parkinson's. The New Zealand Parkinson's Environment and Genes Study (NZPEGS) is an online nationwide cohort study focusing on collection of detailed environmental, lifestyle and genetic data to help us understand the interplay between genetic and non-genetic factors contributing to the development of Parkinson's. DNA extracted from saliva samples is genotyped on the Neurobooster Array, via the Global Parkinson's Genetics Program (GP2). As of June 2024, 301 people with Parkinson's and 281 control participants have completed the requirements of the study, with genotyping completed on 201 Parkinson's and 128 controls. Preliminary analysis indicates a low frequency of highly penetrant pathogenic genetic variants in the Parkinson's group, but as expected, they do show a higher polygenic risk score (PRS) compared to controls. We are now quantifying the environmental and lifestyle data into an environmental risk score and examining how this interacts with the PRS at the individual level for the development of Parkinson's in New Zealand.

2.2

Characterising chronic synergistic effects of traumatic brain injury and pesticide exposure on Parkinson's Disease development and progression in a novel rat model

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Traumatic Brain Injury (TBI) and pesticide exposure have been independently associated with increased risk of Parkinson's Disease (PD). However, it is increasingly clear that PD development is complex and multi-factorial. Currently, few preclinical models of neurodegeneration reflect this, thus elucidating mechanisms of disease pathogenesis presents challenges. This study aims to characterise chronic functional changes in a novel "two-hit" model of PD combining TBI and low-level rotenone exposure prior to injury. 8-10 week-old male Sprague-Dawley rats were randomly allocated to receive vehicle or rotenone treatment, and sham or TBI surgery (n=16/group). Animals were subcutaneously injected with 2% DMSO or rotenone (1.5mg/kg) every 48-hours for 12 days, followed by moderate-severe TBI using the Marmarou weight-drop model, or sham surgery, 24-hours after the final injection. Gross motor function, involuntary movement, forelimb dexterity and grip strength were not significantly affected by injury or rotenone, or the two in combination. Independently, TBI and rotenone significantly affected motor coordination, as assessed by latency to climb the inclined ladder, but balance, assessed by faults on the beam walk was affected by TBI only. Spatial and working memory, assessed with Barnes Maze and Novel Object Recognition Task, respectively, were not affected by TBI, rotenone or the two in combination. While motor and cognitive function were not synergistically affected by TBI and rotenone exposure 6-months post-injury, subtle tissue pathology may drive the development of deficits at later time-points. Further characterisation of our model is underway, including analysis of protein expression and neuronal integrity to assess chronic manifestations of disease.

2.3

More than a one-hit wonder: Exploring synergistic effects of genetic and environmental risk factors in the progression of Parkinson's disease

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Several genetic (e.g. GBA mutation; APOE4 allele) and environmental (history of traumatic brain injury (TBI); pesticide exposure) risk factors of Parkinson's Disease (PD) exist, but it is unknown whether they act synergistically to influence disease course. This study assessed whether such risk factors, alone or in combination, were associated with differences in baseline pathological, neuropsychiatric, or motor outcomes in newly diagnosed individuals with PD or were predictive of such outcomes at 5-year follow-up. Data were extracted from the Parkinson's Progression Markers Initiative (n=208). Extracted data included clinical measures, as well as CSF concentrations of alpha-syn, p-tau and amyloid-beta. A composite cognitive score was derived from principal component analysis. Baseline differences were assessed via Kruskal-Wallis for the following combinations: 1) No exposure; 2) TBI; 3) Genetic positivity (GBA or APOE4) or pesticide exposure and 4) two-hit, followed by post-hoc Dunn tests. Prediction of follow-up outcomes was assessed via multiple linear regression, with predictors including demographic information (age/sex/education), genetic and environmental risk factors, and their interactions. At baseline, synergistic effects corresponded to significantly reduced striatal DaT binding and CSF amyloid-beta for participants reporting both TBI and GBA or APOE4 positivity compared to the no exposure and TBI in isolation cohorts. Pesticide exposure interactions with APOE and GBA factors were significant predictors for follow-up CSF p-tau and cognitive ability, explaining 44% and 24% total variance respectively. Here we demonstrate established risk factors of PD may act synergistically to worsen underlying brain pathology and may have utility for predicting long-term prognosis of cognition in PD.

2.4

Harnessing Alpha Synuclein Polymorphs to investigate novel protein targets in Parkinson's Disease

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Parkinson's Disease (PD) is a debilitating neurodegenerative disorder with a rising global prevalence. Increasing aging populations, combined with genetic and environmental risk factors, contributes to a growing societal and economic burden that demands improved therapeutics. PD is defined by the progressive accumulation of alpha-synuclein in dopaminergic neurons. This accumulation leads to neuronal cell death and results in varying motor and non-motor symptoms, leaving patients with limited options beyond symptomatic relief. Alpha-synuclein accumulates as various conformational polymorphs, each with different pathogenic properties. Furthermore, recent research has established that non-neuronal cells such as pericytes are involved in the PD pathogenesis. We hypothesize that examining non-neuronal cells in a polymorph-specific context could identify novel proteins involved in PD pathogenesis. We exposed human brain-derived pericytes to five distinct alpha-synuclein polymorphs and conducted RNAseq analysis, which revealed specific changes in gene expression. These changes were validated at the protein level both in vitro and in situ using immunolabelling. We assessed the expression of 48 unique proteins using human pericytes and middle temporal gyrus tissue microarrays. In vitro analysis highlighted the expression of 7 proteins, with reduced BCL-XL signal in PD pericytes. In situ immunolabelling revealed eight proteins differentially expressed between control and PD tissues: ABCF1, ASAH1, BCL-XL, CSNK2A1, MEGF11, MTHFD1, NUCKS1, and PUM2. The notable changes in BCL-XL in both tissue and cells suggests that the anti-apoptotic protein may facilitate changes in PD pathogenesis, particularly around vascular cells. Continued investigation into BCL-XL may reveal its therapeutic potential in relation to PD.

5.1

Neuropathological features that differentiate CTE and Alzheimer's disease

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Chronic Traumatic Encephalopathy (CTE) is a neurodegenerative disease associated with repetitive head trauma and is characterised by the perivascular accumulation of hyperphosphorylated tau in the depths of cortical sulci. In our systematic review of CTE post-mortem histology literature, we found that few studies have directly compared the neuropathology of CTE and Alzheimer's disease (AD), despite both being mixed 3R-4R tauopathies. In this study, we sought to comprehensively characterise the CTE pathognomonic lesion to identify a neuropathological signature that better distinguishes CTE and AD pathology. We examined superior frontal gyrus sections from 15 CTE and eight Alzheimer's disease cases. Each section was labelled with 35 antibodies using multiplex immunohistochemistry to identify reactive gliosis, neuronal populations, axonal proteins, vasculature, ubiquitination, and tau. We compared the distribution and amount of labelling for each antibody in the sulcal depths of CTE and AD cases to identify differentially expressed markers. Co-labelling of all antibodies revealed CTE tau lesions were primarily located around arterioles in cortical layer II, while the tau in AD cases was concentrated in layer V. Markers of tau (AT8, T231, 4R, and 3R) and glial reactivity (CHI3L1, CD68, and HLADR) showed higher expression and more widespread distribution throughout the grey matter in AD cases. CTE cases showed focal expression of L-ferritin and NQO1 around tau lesion vessels. Therefore, the distribution of glial reactivity markers is a neuropathological hallmark of CTE and suggests that repeated head trauma leads to a chronic and localised neuroinflammatory environment around blood vessels in the sulci.

6.1

Spatially resolved transcriptomics of human cortex reveals unique disease signatures and potential biomarkers for chronic traumatic encephalopathy

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The condition 'chronic traumatic encephalopathy' (CTE) is an environmental tauopathy that is found almost exclusively in individuals with a history of repeated exposure to head trauma. CTE has risen to prominence in the public consciousness because of its link to professional contact sports. CTE is very poorly understood, and currently is only able to be diagnosed by post-mortem brain examination. There is a pressing need to understand the pathophysiology of CTE, and identify biomarkers for in-life diagnosis. CTE lesions are detected by visualising hyperphosphorylated tau deposition, and lesions are typically randomly distributed through the cortex, rendering bulk approaches to molecular analysis difficult and confounded. We have addressed this by performing spatially-resolved transcriptomics of CTE lesions in human prefrontal cortex using the Visium platform. Within densely tau-positive CTE lesions, we observed altered expression of hundreds of genes across multiple lesions; overexpression of four genes (GFAP, APNLR, AQP1, TNC) was universal. Together the alterations signify a complex molecular response to brain trauma, including heightened astrocytic activity, neuroinflammation, altered blood-brain barrier function, and extracellular matrix remodelling. When unaffected brain areas were compared to normal cortex and that from Alzheimer's disease there were intriguing changes in the first cortical layer, where increased expression of RELN and NDNF uniquely defined those brains with CTE. This may indicate a compensatory response to neuronal loss, offering valuable insights into the brain's adaptive mechanisms in CTE. The gene expression signature of CTE lesions described here provides multiple opportunities for biomarker and therapeutic discovery.

6.2

Multiplex immunohistochemistry reveals focal glial reactivity in Chronic Traumatic Encephalopathy

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Chronic traumatic encephalopathy (CTE) is a neuropathological diagnosis of hyperphosphorylated tau (p-tau)-related neurodegeneration, uniquely characterised by a focal, perivascular deposition within the depths of cortical sulci. The majority of CTE literature focusses on this p-tau pathology, however, other key pathological processes such as vascular dysfunction and neuroinflammation are left largely unexplored. This is surprising given vessel associated p-tau pathology is a defining feature of the disease and the cause is highly attributed to repetitive head injury. We examined features of vascular integrity and neuroinflammation in the CTE lesion microenvironment by using multiplex immunohistochemistry. The area of labelling for each marker was compared between tau-positive vessels and tau-negative vessels in the superior frontal gyrus of 9 CTE cases. We identified glial reactivity as a CTE lesion-associated feature with increased expression of astrocyte reactivity markers NQO1, CHI3L1 and GFAP, and microglial reactivity markers CD68 and HLADR around tau-positive vessels. Additionally, we observed an increase in L-ferritin in all glial cells in CTE, suggestive of iron imbalance in addition to microglial dystrophy. Markers of vascular structure, collagen IV (basement membrane marker) and GLUT1 (endothelial cell marker), showed no significant changes, although further investigation is required to validate vascular integrity. Overall, our findings suggest repetitive head injury leads to a focal neuroinflammatory environment around cerebral blood vessels at the depth of the cortical sulci, and this may be associated with increased exposure to iron, suggestive of increased vessel leakage.

6.3

Characterising Cis Tau Pathology in Chronic Traumatic Encephalopathy

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Tau protein is a hallmark pathology of both Alzheimer's Disease (AD) and Chronic Traumatic Encephalopathy (CTE), a neurodegenerative disease associated with repetitive traumatic brain injuries (TBI). Several modifications to tau occur in AD and CTE causing aggregation into neurofibrillary tangles. The earliest modification related to TBI is a shift from the physiological trans to the pathological cis conformation of tau phosphorylated at T231 (cis-p-tau). Cis-p-tau has been detected in postmortem human brain tissue as early as eight hours following severe TBI. We sought to establish whether cis-p-tau is a feature of the neurofibrillary tangles observed in CTE and AD by studying the relationship between cis-p-tau and other pathological tau species within neurons and astrocytes. Using multiplexed fluorescent immunohistochemistry, we labelled postmortem human brain tissue with antibodies targeting various tau epitopes, neurons and astrocytes. We compared CTE pathology to both neurologically normal and AD cases to examine differences in tangle composition between conditions. Cis-p-tau co-labelled with phospho202-205 tau, phospho231 tau and 4R tau, all of which were abundant within the CTE lesion area and in AD cases. We also identified cis-p-tau within astrocytes that showed markers of glial reactivity at the subpial border in CTE, a pattern consistent with age-related tau astrogliopathy. Our data supports the idea that cis-p-tau is a feature of neurotrauma associated pathology. Future investigations will examine how this early tau modification is influenced by inflammatory processes to provide insights into the mechanisms linking TBI and neurodegeneration.

6.4

The Evolving Discussion on CTE Causation and the Quest to Develop a Clinical Diagnosis

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Chronic Traumatic Encephalopathy (CTE) is a neurodegenerative disease diagnosed post-mortem in individuals with a history of exposure to repetitive head impacts (RHI). CTE has been diagnosed in individuals from a variety of populations, including contact and collision sport athletes, Veterans, and those with a history of domestic and interpersonal violence. CTE has been identified across the globe, with cases published by scientists in at least ten countries, representing at least 13 brain banks. In 2022, our group published Applying the Bradford Hill Criteria for Causation to Repetitive Head Impacts and Chronic Traumatic Encephalopathy, a literature review outlining the evidence to date to support the causal link between RHI and CTE. While the NIH, among others, recognizes that CTE is caused in part by repeated traumatic brain injuries, there is still substantial debate amongst the scientific and lay communities about CTE causation. Understanding CTE causation is an essential milestone for the development of prevention programs, a clinical diagnosis, and disease modifying therapies. Like other neurodegenerative diseases, definitive diagnoses cannot yet be made in the absence of post-mortem tissue analysis; however, over the past decade, substantial progress has been made to better understand how CTE presents in life, potential disease mechanisms, and the role of underlying pathology in symptom presentation. The CLF Global Brain Bank and our clinical research partners, particularly those at the Boston University CTE Center, have led much of the progress in the field. Combined, their insights have moved us closer than ever before to a clinical diagnosis.

7B.1

Tagata o Te Moana Nui a Kiwa – mental health and well-being of Pacific youth in Aotearoa

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Aotearoa New Zealand's past and future journey is integrally linked to the Pacific region through its historical context, location in the Pacific region, and an increasing proportion of its population with ancestral ties to the Pacific Islands. Tagata o Te Moana Nui a Kiwa is a reference to people of and from the Pacific Ocean, people in Aotearoa who whakapapa to one of the many islands in the Pacific region. They left the beautiful shores of their island nations for better education and employment opportunities in Aotearoa. They are however disproportionately represented in poor health and education outcomes. This presentation provides the context for Pacific young people in the tertiary environment in New Zealand. The Pacific population is young, a fast growing group making up 8% of New Zealand's population, and predicted to increase to 10% by 2038. This growth in the context of New Zealand's poor youth mental health statistics and global tertiary student mental health concerns, highlight the need to better understand and respond to the mental health and well-being needs of this group. This presentation presents a perspective from quantitative and qualitative work undertaken, and provides suggestions to consider for the way forward. It seeks to provide a balance between the reality for Pacific young people in the tertiary environment, while positioning the way forward for constructive and enabling approaches to enable Pacific youth in Aotearoa to thrive.

7B.2

Hauora Hinengaro o te Whaea – Assessment tool development

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Perinatal mental health and wellbeing is a critical component of hauora, influencing not only the well-being of māmā but also the developmental outcomes of their pēpi and whānau. Yet this has remained an under-researched and under-supported area of health, particularly for wāhine Māori. According to the Perinatal Mortality Review Committee report published Jan 2024, wāhine Māori were 2.91 times more likely to die by suicide as a direct result of maternal mortality than women of Pākehā ethnicity in the 2006–2020 period. Funded by Te Aka Whai Ora and hosted by the National Hauora Coalition (PHO), a group of Māori mental and maternal health experts have been developing via a Delphi study approach a mātauranga-Māori informed, perinatal mental health and wellbeing assessment tool. Incorporating kaupapa Māori methodologies, Whānau (mainly Māmā) focus groups were undertaken to understand the potential utility of the tool. The team proposes to seek funding to now test and iterate the tool in real world contexts. The assessment tool aims to assist perinatal healthcare providers in the early detection and timely support of Māori mothers experiencing psychological distress. There is a notable lack of culturally relevant and tailored tools and resources to support holistic assessment and support hapū Māmā in relation to mental health and psychological wellbeing. The presentation will incorporate lived-experience viewpoints and provoke considerations for the importance of this field of research.

7B.3

Starting well: Improving Māori mental health by focusing on the first 2000 days of life

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Adverse child experiences (ACEs) have been shown to accelerate the risk of developing a range of debilitating physical and mental health conditions in later life. Yet, they remain one of the most unaddressed risk factors in our society. In comparison with non-Māori, Māori living in Aotearoa New Zealand report significantly higher rates of child maltreatment including acts of omission (neglect) and commission (abuse). Consistent with the cumulative risks associated with adverse child experiences, Māori are also more likely than non-Māori to be hospitalised for a mental disorder, they are more likely to die by suicide, they are over-represented in our prison population, and they are more likely to die early of preventable, avoidable chronic diseases. This talk will broadly address factors that perpetuate poor mental (and physical) health outcomes for Māori, including engagement, service delivery and treatment modalities. It will also make the case for intervening earlier in development to reduce the likelihood of experiencing poor mental health outcomes later in life.

8.1

Characterising the impact of pre-existing brainstem tau pathology on the development of cognitive deficits following a single mild traumatic brain injury

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Traumatic brain injury (TBI) is one of the strongest environmental risk factors for the later development of neurodegenerative diseases, including Alzheimer's disease (AD). However, most people with a TBI do not develop neurodegeneration, instead, a TBI may accelerate disease progression in those with pre-existing pathology. The locus coeruleus (LC) is well-documented to be the first site of tau pathology in AD and is particularly susceptible to TBI due to its high metabolic demand and anatomical location. This study aimed to examine the effect of pre-existing inflammatory -induced tau pathology within the LC on the development of cognitive deficits following a mild TBI. 10-week-old male Sprague-Dawley rats (n=15-16/group) were randomly allocated to sham or LC injection and then to sham or diffuse TBI 7 days later. Three months following TBI rats underwent a behavioural battery to assess anxiety-like behaviour on the Elevated Plus Maze (EPM), cognition on the Barnes Maze and affective state via burrowing. Pre-existing LC inflammation and following TBI did not affect the development of cognitive deficits ($p=0.85$), anxiety-like behaviour on the EPM ($p=0.98$) or affective state ($p=0.67$). An overall main effect of injury was observed in latency to find the new escape box, with injured rats taking longer ($p<0.05$), with no effect of injury on anxiety ($p=0.76$) or affective state ($p=0.36$). Inflammation within the LC led to a significant decrease in burrowing behaviour ($p<0.05$), but no effect on any other measure. Future work will examine whether LC inflammation before TBI accelerates the spread of tau pathology and inflammation post-injury.

8.2

Testing AAV-mediated sAPPa overexpression as a therapy in an AD mouse model

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Soluble amyloid precursor protein-alpha (sAPPα) has been suggested as a treatment for Alzheimer's disease (AD) due to its myriad beneficial properties within the brain. However, the blood-brain barrier limits drug delivery. Modified adeno-associated viruses (AAVs) such as AAV.CAP-B10 can carry genes across this barrier, allowing gene therapy treatments to be administered systemically. This study tested the hypothesis that AAV-mediated sAPPα overexpression in the brain would improve disease-like symptoms in an AD mouse model. We injected intravenously 1x10^11 AAV.CAP-B10 viral vectors carrying the human sAPPα transgene into wild-type and 5xFAD mice, which carry five genetic mutations associated with familial AD. Control mice received a vector carrying the transgene for green fluorescent protein. Male and female mice were injected at two months of age, an early stage of the disease. At 8-9 months of age, behavioural, electrophysiological, and post-mortem assessments were conducted. Preliminary data indicates that untreated 5xFAD mice weigh less, explore more and are less anxious in the elevated plus maze and open field tests, have impaired spatial memory in the Y maze and Barnes maze, but improved novel object recognition, and equal motor performance on the RotaRod compared to wild-type mice. The magnitude of long-term potentiation within CA1 of the hippocampus was similar between groups. Unexpectedly, viral sAPPα treatment had no effect on virtually any of the measures. Future post-mortem analyses will investigate whether sAPPα treatment affects neuropathology in the transgenic mice. Overall, our findings to date do not support other studies showing therapeutic properties of sAPPα.

9.1

Challenges and Variability in the Pathogenesis of Neurodegenerative Diseases: Insights and Emerging Concepts

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Neurodegenerative diseases affect selective cells in the brain that cause progressively debilitating symptoms with fatal outcomes. They are considered the toughest diseases to treat due to the complexity of their biology and their clinical heterogeneity. Genetic studies show that heterogeneity is significant in non-genetic forms of neurodegenerative diseases, and from human studies each neurodegenerative disease has relatively poorly characterised, early selective dysfunction and loss of particular synapses and neurons, in addition to a predictable pathological spread of altered proteins, currently thought to be via a prion-like seeding mechanism involving neuron-to-neuron network transmission of pathological seeds. Three types of empirical data question these concepts. Assessment of the spread of pathological proteins shows high variability in both the initiation sites of protein deposition and spread. There is an extremely poor correlation between the initial sites of protein deposition and the sites of early selective neuronal loss. For most neurodegenerative diseases, comorbid pathologies of additional pathological proteins are the norm, with these additional proteinopathies having a substantial impact on disease trajectories. These variations in disease trajectories are changing consensus on the pathological diagnoses of (at least some) neurodegenerative diseases. Some of the variation observed may also be medication induced as the use of antihypertensive medications that independently reduce small vessel disease in the brain also ameliorate the progression of Ab and tau pathologies via different mechanisms.

10.1

Reconstructing the olfactory system in humans to localize neurodegeneration's earliest events.

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Olfactory sensory neurons directly sample the chemical composition of the external environment and their axons coalesce into glomeruli in the olfactory bulb. The olfactory bulb is one of the first neural structures to show pathological load and anatomical changes in Parkinson's disease. However, anatomical, and histological characterization of the normal human olfactory system is surprisingly lacking yet is critical to substantiate extrapolation of studies from rodents to humans. Here, we have combined histological studies of the human olfactory system with advanced imaging processing techniques. Starting with a 7.45 cm3 en-bloc specimen extracted from an embalmed human cadaver cut into 10 um thick sections, trained convolutional neural networks for automatic segmentation and a high-performance computer solution engineered to register the sections based on the fluorescence signal and structures segmented. The resulting multiresolution deformable 3D reconstruction offers several didactic capabilities in visualizing the human olfactory system with detailed anatomical structures in its native three-dimensional arrangement. In addition to this model, we have sectioned and immunostained the human olfactory system for neurodegenerative markers including a-synuclein and tau and have found a random localization pattern in cases that had pathology but were at the time of death asymptomatic. The results allow us to visualize early pathology in ageing and common neurodegenerative diseases such as Parkinson's disease.

10.2

Characterisation of the substantia nigra in cases of X-linked Dystonia Parkinsonism

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X-linked Dystonia Parkinsonism (XDP) is a newly discovered X-linked recessive neurodegenerative movement disorder clinically characterised by the presence of dystonia and parkinsonism. Despite a limited neuropathological understanding of the disease, previous research implicates basal ganglia dysfunction to underlie the core of XDP pathophysiology. The substantia nigra (SN) is a critical component of the basal ganglia, and is widely implicated in Parkinson's disease, a condition which shares partial symptomatology with XDP. This study investigated nigral changes in the XDP post-mortem human brain to elucidate the contribution to XDP neuropathology. Free-floating histological and fluorescent immunohistochemistry for known SN antibodies analysed with high-throughput semi-quantitative approaches were conducted in sections from the post-mortem SN of 12 XDP cases compared with age-matched controls. We revealed a significant loss of tyrosine hydroxylase+ neurons and reduced DARPP-32 expression in the XDP SN. We also report reduced substance P and enkephalin immunolabelling in the XDP SN, key peptides found on striatal projections into the SN. In contrast, immunoreactivity for the calcium-binding proteins parvalbumin and calbindin were unchanged in the XDP SN. Comparison of cases with short and advanced diseased durations demonstrated the extent of nigral tyrosine hydroxylase+ neuronal loss and reduced DARPP-32 expression tends to mirror the degree of striatal DARPP-32+ spiny projection neuronal loss. These findings are the first to point towards significant dopaminergic dysfunction and dysregulation of both nigrostriatal and striatonigral connectivity in the XDP brain, which may contribute towards the neuropathological signature of XDP.

10.3

Using mouse models of neurodegeneration to understand the relationship between blood biomarkers and pathology across disease progression and in response to interventions

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Neurofilament light (NFL), is a biomarker of neuroaxonal damage and neurodegeneration. Using mouse models, this study aimed to understand how NFL levels change in relation to neurodegenerative pathology across disease progression and in response to intervention. Serum NFL levels were analysed using Single molecule array in the APP/PSEN1dE9 (APP/PS1) model of amyloidosis, and the CamKII-TG4510 (TG4510) inducible tauopathy model, compared to wild-type mice (C57/Bl6). NFL levels increased with aging in both wild-type and APP/PS1 mice ($p<0.001$), however did not differ between the two groups. Serum NFL levels increased across disease progression in TG4510 mice ($p<0.001$) and were higher than wild-type mice from 18 months of age ($p<0.001$). When tauopathy was turned off in a subset of TG4510 mice at 18 months of age to mimic an effective intervention, serum NFL levels were lower at end-point in these mice compared to a group in which tauopathy induction continued ($p<0.05$). Male TG4510 mice showed significantly lower serum NFL levels following tauopathy cessation at end-point, compared to female mice ($p<0.05$), which corresponded to a significant reduction in hippocampal neuron loss ($p<0.001$), in male but not female mice. We demonstrate serum NFL levels correspond to overt neuron loss in the TG4510 model and detect reductions in neurodegeneration, in response to an effective intervention. They also demonstrate that NFL levels increase with ageing in mice but are not increased in the APP/PS1 model, which lacks overt neurodegeneration. These results support the use of serum NFL for monitoring intervention outcomes in pre-clinical models.

10.4

The New Zealand-Dementia Prevention Research Clinics: Plasma biomarkers and the Alzheimer's disease continuum

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Alzheimer's disease (AD), the most common cause of dementia, is a debilitating neurodegenerative condition that causes significant impairment of memory and cognition resulting in behavioural and functional changes in everyday life. Single molecule array (Simoa) technology enables the detection of biomarkers for AD neuropathology in blood. This study compared cross-sectional biomarker profiles for participants from the New Zealand-Dementia Prevention Research Clinics (NZ-DPRCs) who spanned the continuum from healthy older adults to a clinical diagnosis of AD. NZ-DPRC participants (n=253) were clinically classified as cognitively unimpaired adults (CU, n=34), subjective cognitive decline (SCD, n=65), non-amnestic mild cognitive impairment (single and multi-domain, non-aMCI, n= 23), amnestic MCI (single and multi-domain, aMCI, n=104), and AD (n=27). A cross-sectional analysis, using Simoa, quantified nine plasma biomarkers: amyloid-beta peptides (Aß1-40; Aß1-42); total and phosphorylated tau species (total-tau; brain-derived tau (BD-tau); p-tau181; p-tau217; p-tau231); neurofilament light (NfL); and glial fibrillary acidic protein (GFAP). Study participants had a mean age of 69.8 (SD[8.1]) years with 52% being female (n=131). Plasma biomarkers across the five clinical groups were assessed by linear regression adjusted for age and sex, with biomarkers p-tau217, p-tau181, p-tau231, GFAP, BD-Tau, Aß1-42, Aß1-42/Aß1-40 ratio and NfL, all showing group differences ($F(4,246)$; $P<0.05$). Tukey's HSD post-hoc test for pairwise clinical group comparisons showed significant differences ($P<0.05$) for specific clinical grouping comparisons for p-tau217, GFAP, p-tau181, BD-tau, p-tau231, Aß1-42 and Aß1-42/Aß1-40 ratio. Simoa-quantitated blood biomarkers in the NZ-DPRC cohort showed utility for differentiating cross-sectional groupings spanning the AD continuum.

10.5

NFH Epitopes as Blood Biomarkers of Neurodegenerative Diseases

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Neurofilament heavy (NFH), is amongst the most extensively phosphorylated neuronal proteins with multiple phosphorylation sites that differ across neuronal compartments. The dysregulation of NFH phosphorylation is implicated in the pathogenesis of neurodegenerative diseases (NDDs), including frontotemporal dementia (FTD), motor neuron disease (MND) and Alzheimer's Disease. We propose NFH phospho-epitopes are good candidate blood biomarkers that may demonstrate disease and region specificity for the differential diagnosis and monitoring of NDDs. Our objective was to develop assays with the sensitivity to characterise a non-phosphorylated (npNFH) and a highly-phosphorylated (hpNFH) epitope of NFH as blood biomarkers. Firstly, we developed sandwich enzyme-linked immunosorbent assays (ELISA) specific to each epitope, with limits of detection (LOD) of 47ng/ml and 23ng/ml, for npNFH and hpNFH respectively. To demonstrate the utility of these ELISAs, protein extracts of motor cortex (MC) and spinal cord (SC) from human MND tissue and frontal cortex (FC) from human FTD tissue, and controls were analysed. The ELISAs showed that npNFH was significantly higher in FTD FC, ($p=<0.01$), and hpNFH was trending higher in MND SC, compared to controls. Testing serum samples from a MND mouse model and wild-type controls on these ELISAs demonstrated that greater sensitivity was required to characterise the NFH epitopes. The ELISAs were then transferred over to the ultrasensitive SimoaÒ platform, creating novel assays for npNFH and hpNFH, with improved LODs of 11pg/ml and 9.7pg/ml, respectively. Once optimisation of the SimoaÒ assays is complete, upcoming experiments will aim to validate npNFH and hpNFH as biomarkers, in blood from NDD cohorts.

10.6

Type I Interferon response triggers programmed axonal degeneration in ALS

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Cytoplasmic build-up of TDP-43 proteins is a disease hallmark of amyotrophic lateral sclerosis (ALS), which is associated with a type I interferon (IFN-I) signature. Emerging evidence suggests that this inflammatory profile actively modulates disease progression *in vivo*. However, the molecular mechanisms underlying immune-mediated neurodegeneration remains to be elucidated. Here, we aim to identify the role of IFN-I in TDP-43 pathogenesis. We showed that genetic deletion of the type I IFNa/b receptor subunit 1 (Ifnar1) mitigates motor deterioration and neurodegeneration in a transgenic ALS mouse model expressing mutant TDP-43 (A315T). The gliosis and peripheral monocyte infiltration can be also prevented. Surprisingly, RNAscope and FACS analyses indicated that neuronal cells can also produce IFNB in addition to microglia in the brain. To this end, we hypothesised that these neuroinflammation events may be the secondary effect and whether neurodegeneration can occur within neurones. Indeed, we observed that TDP-43-induced phosphorylation of STAT1 correlated with exacerbated LDH release, axonal mitochondrial accumulation and tubulin polyglutamylation in our SH-SY5Y model of TDP-43 proteinopathy, as well as in iPSC-derived motor neurones from TDP-43-ALS patients. Importantly, this was associated with activation of the sterile alpha and TIR motif containing protein 1 (SARM1). These cell-autonomous degenerative cascades can be protected when IFNAR1 was deleted via CRISPR/Cas9 technology or using FDA-approved JAK small molecule inhibitors. We demonstrated a rationale to target IFN-I singalling to intervene in axonal degeneration. This will be foundational for new development of brain penetrant therapeutics to new clinical trials for TDP-43 proteinopathies.

11.1

Decoding the Role of Microglia in Brain Injury: Induction of Pro-Regenerative States

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Activation of microglia, the brain's resident immune cells, has been implicated in the progressive secondary tissue loss after brain injury, and also in the ongoing cognitive dysfunction and decline during the more chronic stages of injury. Much of this has, however, been based on correlative observations rather than direct evidence for a causal pathological role of microglia in these processes. To address this, we are using both genetic and pharmacologic approaches to conditionally deplete microglia from the brain, subsequently studying how absence of these cells influences the outcome from a moderate controlled cortical impact. Rather than exacerbating secondary damage, these cells appear to intrinsically lack the ability to support repair at secondary injury sites. However, a pro-regenerative type of microglia (namely repopulating microglia) can be obtained via the timing-dependent forced turnover of these cells. While pharmacological induction of repopulating microglia may not a viable treatment option for acquired brain injury, this specific microglial state offers an avenue into mechanisms of neuroprotection.

12.1

Multimodal and multiscale approaches to mild Traumatic Brain Injury

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Mild traumatic brain injury (mTBI) is a significant public health issue, often leading to long-term cognitive and neurological deficits. Despite its prevalence, the underlying mechanisms and effective treatments remain poorly understood. This presentation will cover the comprehensive range of mTBI research our group has undertaken over recent years. Our ultimate goal is to identify an optimised subset of biomarkers for brain injury, facilitating personalised (n-of-1) recovery plans. Our investigations span from controlled injuries in animal models to monitoring human contact sports athletes and conducting clinical follow-ups. Employing a multiscale approach, our research encompasses detailed histological examinations to whole-brain injury assessments. Additionally, we use a multimodal methodology, integrating clinical data, MRI, impact monitoring, and computational models. Multimodal research is important for mTBI as it combines various data types, enabling the identification of subtle changes across different modalities. By applying dimensionality reduction to our multimodal data, we can detect these changes with greater significance and precision. This process informs our computational models, leading to better personalisation and outcome targeting. Additionally, this extensive dataset informs both finite element modelling and machine learning analyses. In this talk, I will present our data collection methods, experimental framework, and the results from the first phase of our project. Through our experimentally informed models, we aim to advance the understanding and treatment of mTBI, paving the way for individualised recovery strategies.

12.2

Dissecting inflammation and spinal cord lesion site development at single-cell resolution

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Traumatic spinal cord injuries (SCIs) acutely induce a temporally-orchestrated recruitment of immune cell subsets to the lesion site. At least some elements of this inflammatory response negatively interfere with recovery. Neutrophils are of particular interest as their abundance inversely correlates with outcomes in human SCI patients, and antibody-mediated neutrophil depletion in experimental SCI improves recovery. Here we used in vivo tracking, single-cell and spatial omics approaches to better understand neutrophil function following SCI. We employed thymidine analogue labelling and transgenic approaches to assess neutrophil responses following thoracic level 9 (T9) contusive SCI in mice. Our results demonstrate increased bone marrow neutrophil precursor cell activity during the post-acute phase (>24 h) of SCI, which coincides with more immature neutrophil phenotypes at the lesion site. Single-cell RNA sequencing (1-7 days post-injury) revealed a high degree of neutrophil heterogeneity; the emergence and/or presence of neutrophil subsets varied with time. Visium spatial transcriptomics further indicated that neutrophil subsets may localise to different regions of the injured spinal cord. Cell-cell interaction analysis highlighted neutrophil-macrophage crosstalk via the pro-resolving molecule Annexin A1 as a key signalling event during early inflammation that may improve recovery. Our findings provide new insights into the complexity of the inflammatory response to SCI, with a particular focus on neutrophil biology. We posit that better understanding the spatiotemporal activity of distinct neutrophil subsets (or states) will assist the development of new strategies to promote the resolution of inflammation during spinal cord wound healing.

12.3

Longitudinal changes in network-based functional connectivity during a season of collision sport participation

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There is growing concern about the effects of exposure to repetitive head impacts (RHI) during collision sport on short- and long-term brain health; yet, prospective evidence exploring the relationship between RHI exposure and brain function remains limited. To address this, resting-state fMRI scans were acquired using a 3T MRI scanner from 47 adolescent male rugby players at the start and end of the school rugby season. A control group of 17 age- and sex-matched non-contact sport athletes were scanned once. Using an atlas-based technique, voxel-wise maps of 15 functional connectivity (FC) networks were derived for each participant. Our analysis explored cross-sectional differences in FC between rugby (collision sport) athletes at the beginning and end of the season versus controls. Additionally, longitudinal changes within the rugby cohort were investigated. No significant cross-sectional differences were observed between groups at either time point for any functional network. Furthermore, no cross-sectional differences in FC were detected between controls and rugby athletes stratified by high versus low RHI exposure, measured by the number of games played over the season. Longitudinal analysis of the rugby athletes revealed moderately increased inter-network FC at postseason relative to preseason within the anterior intraparietal sulcus, motor, secondary visual and temporal networks. Conversely, moderately decreased inter-network FC was observed within the cerebellar and basal ganglia networks over the season. These longitudinal findings suggest potential neuroplasticity processes in response to maturational processes and/or sport-related activities and underscore the need to assess the clinical implications of decreased FC associated with RHI exposure.

12.4

Attenuating dopaminergic neurodegeneration following traumatic brain injury through the innate immune system

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Traumatic brain injury (TBI) can increase an individual's likelihood for developing Parkinson's disease by up to 50%, representing a significant non-genetic risk factor. Previous studies have reported that TBI causes loss of dopaminergic neurons in the substantia nigra pars compacta (SN pc), a structure affected during Parkinson's disease pathogenesis. Here, we used a unilateral controlled cortical injury model of TBI in mice and delivered the injury to the motor cortex, a brain region often affected by TBI. We found that TBI resulted in significant loss of dopaminergic neurons in the SN pc, a site very distal to the initial injury location. We next investigated whether our recently discovered neuroprotective phenotype of repopulating microglia, induced by their replenishment shortly after injury (Willis et al., 2020), could mitigate dopaminergic neuron loss after TBI. Indeed, we found that repopulating microglia reduced the loss of dopaminergic neurons after TBI. Further, we found that such benefits were dependent upon microglial-derived IL-6 trans signalling. Further, transgenic induction of IL-6 trans signalling in resident microglia also recapitulated these benefits. Finally, pharmacological stimulation of IL-6 signalling using the designer cytokine Hyper IL-6 shortly after TBI was able to improve dopaminergic neuron survival following injury. Taken together, these results demonstrate the acute vulnerability of dopaminergic neurons in the SN pc, a site distant from the initial impact, and the protective effects of microglial IL-6 trans-signalling thereon.

13.1

Internet addiction: cortical hypertrophy and self-regulation

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While increasing studies have documented the link between self-regulation and internet addiction among young adults, not much is known about the neurobiological basis of this relationship. This study identified cortical regions whose thickness predicts self-regulation traits and whether such regions also explained internet addictive behaviour. The current study used data from MPI Leipzig Study or Mind-Body-Emotion Interactions (LEMON) database, in which a sample of 135 healthy participants (between 20 and 30 years of age) completed self-report measures of self-regulation variables (i.e., self-control, deliberate and spontaneous mind wandering, procrastination tendency, and boredom proneness) and internet addiction tendency, and underwent structural MRI scans. The structural scans were preprocessed using Freesurfer and vertex-wise cortical thickness measures were extracted and analyzed in a whole-brain vertex-wise manner. The vertex-wise analysis revealed two clusters in the right superior medial frontal gyrus and left superior medial orbital frontal gyrus, whose thickness was positively associated with internet addiction. Mediation analyses further indicated that both cortical thickness clusters partially mediated the relationship between two self-regulation variables (i.e., procrastination tendency and self-control) and internet addiction. No significant mediating effects were found for deliberate mind wandering, spontaneous mind wandering, or boredom proneness. Overall, the findings suggest that individual differences in cortical thickness of these brain regions might underlie difficulties in self-regulation, which in turn is linked to problematic internet use. The study provides new insight into the neurobiological basis of the relationship between self-regulation and internet addiction.

13.2

Cumulative risk of ACEs on depression symptoms in young people in the Growing Up in New Zealand study

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The prevalence of depression in young people has increased rapidly over the last decade and is associated with several adverse outcomes later in life. Identifying Adverse Childhood Experiences (ACEs) associated with depression may help design future treatment programs aimed to reduce the consequences of such experiences. The current study included 4563 young people from the Growing Up in New Zealand (GUiNZ) longitudinal study who completed a questionnaire on depression symptoms at age 12 years (Centre for Epidemiological Studies Depression Scale for Children (CESD-10). A Cumulative Risk (CR) score was used to assess the combined effect of multiple ACES on depression symptoms. The CR score was calculated by combining ACEs identified at ages 4.5 and 8 years that were significantly associated with depression symptoms. Three CR score categories were created, and their association with depression symptoms at age 12 years was investigated at the univariable level and in multivariable analyses, controlling for multiple covariates. Overall, 31.6% (n=1443) of our sample did not report any ACEs (no risk CR), 53.8% (n=2455) were exposed to one or two ACEs (low CR score), and 14.6% (n=655) to three or more ACEs (high CR score). In the adjusted analysis, exposure to the low and the high CR scores was associated with higher depression scores (beta 1.16, $p < 0.001$; and 2.35, $p < 0.001$, respectively) compared to no ACEs. The CR score is a useful approach to identifying a subgroup of young people who are most at risk for depression symptoms. Early mental health interventions addressing several ACEs are recommended.

13.3

Weakening of perineuronal nets following non-invasive brain stimulation

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Critical period is a time of heightened plasticity during development when the brain becomes sensitive to environmental cues which can influence structure and function . As this period is important in stabilizing neuronal projections, any negative environmental influence during this time can lead to abnormal brain organization which has been linked to several neurodevelopmental disorders. Therefore, enhancing, or prolonging plasticity during critical neurodevelopmental periods can be of therapeutic importance. We investigated the impact of low-intensity repetitive transcranial magnetic stimulation (LI-rTMS) on markers of critical period plasticity. We delivered LI-rTMS to the primary visual cortex (V1) in young ephrin-A2/A5+/- mice (sham: n=6, treatment: n=5), which have disorganised visual system projections, and in wildtype mice (sham: n=7, treatment: n=7), daily for two-weeks starting at postnatal day 28 (peak of critical period in V1). Following the treatment mice were euthanised, perfused and brains were cryosectioned. Sections containing V1 were immunostained for parvalbumin (PV)-expressing interneurons and their surrounding perineuronal nets (PNN) which are important determinants of the critical period. Although following LI-rTMS there was no significant change in the density of PV-expressing interneurons or PNNs, we observed changes in the intensity of the nets surrounding PV-expressing interneurons. Following TMS, there were more low intensity nets compared to high intensity nets in the ephrin-A2/A5+/- mice, suggesting that TMS might delay or prevent the maturation of these nets. As PNNs play an important role in closing the critical period, our findings suggest TMS might prolong critical period plasticity when abnormal brain wiring is present.

14.1

The Relationship Between Macro- and Microvascular Blood Flow in Cognitive Decline

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People with mild cognitive impairment (MCI) are at elevated risk of developing Alzheimer's disease (AD), therefore identifying brain alterations in this group presents an opportunity to intervene with targeted interventions. Mounting evidence suggests that cerebrovascular health is influential in AD. While reduced microvascular blood flow (i.e. capillary perfusion) in AD is reasonably well established, our aim was to investigate if macrovascular (i.e. large arterial vessel) flow is also affected in cognitive decline and better understand the interplay of these two haemodynamic aspects. Participants were recruited from the Auckland Dementia Prevention Research Clinic, comprising control (N=20), MCI (N=21) and AD (N=13) groups. Magnetic Resonance Imaging was used to assess cerebrovascular function non-invasively in vivo. Both macrovascular and microvascular flow were measured in the same session with 4D Flow and Arterial Spin Labelling respectively. Macrovascular blood flow was significantly different across groups in the middle cerebral, posterior cerebral and basilar arteries, and post-hoc pair-wise tests revealed a significant decrease in flow in AD compared to controls. Blood flow in the middle cerebral artery was positively correlated with total grey matter perfusion in controls (Pearson's r=0.62, p=0.003). However, this correlation was not present for people with MCI (r=0.18, p=0.426) or AD (r=0.10, p=0.739). Our results demonstrate that blood flow in the major cerebral arteries is reduced in AD. We provide new evidence on a disassociation between macro- and microvascular flow in both AD and MCI groups, suggesting cerebrovascular dysfunction also in those at risk of developing AD.

14.2

Assessment of Cerebrovascular Responses Using a Novel Non-Invasive Brain Pulse Monitor in an Acute Stroke Patient Undergoing Thrombectomy

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Early recognition and treatment of stroke or its complications significantly improves patient outcomes. Non-invasive continuous monitoring of brain blood flow could substantially improve stroke detection and management. Currently no viable continuous monitoring, point of care technologies exist for stroke. Optical brain pulse monitoring (OBPm) uses red and infrared light to non-invasively detect brain pulse waves associated with brain blood volume changes and brain movement. Bilateral OBPm sensors (Cyban, Melbourne Australia) were placed over the middle cerebral artery (MCA) territory in a patient undergoing thrombectomy for right internal carotid artery and distal MCA vessel occlusions. The OBPm continuously assessed brain pulse waveform changes and cerebral oxygenation whilst the clot from the right MCA area was aspirated, and the internal carotid lesion stented. Abnormal brain pulse waveforms with venous circulation features and low oxygen levels were observed at the time of carotid stenting. Subsequent hypertension and reperfusion of the brain was associated with brain pulse waveforms with arterial features. The venous waveforms and low oxygen levels observed may represent a period of low cerebral arterial pressure with low cerebral blood flow, where the venous pressure is the major influence the brain microcirculation and blood volume. This case highlights the potential of OBPm for stroke detection and continuous monitoring of complications. The abnormal brain pulse waveforms provide insights into the pathophysiological effects of low cerebral arterial levels on the brain.

14.3

Human iPSC-derived brain pericytes exhibit differences in inflammatory activation compared to primary human brain pericytes

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Brain pericytes are critical supporting cells of the brain's vasculature, providing trophic support to brain endothelial cells. Brain pericytes also play a unique role in the mediation of neuroinflammation. Pericyte dysfunction is observed in many diverse pathological conditions including Alzheimer's Disease, traumatic brain injury, and brain cancers such as glioblastoma. Human brain pericytes can be obtained from surgically resected brain tissue, however, access to tissue is limited. Another option is to generate brain pericytes from induced pluripotent stem cells (iPSCs). This study confirms our ability to generate iPSC-derived brain pericytes, but highlights differences in inflammatory activation compared to primary human brain pericytes. Human iPSCs were primed towards a neural crest stem cell (NCSC) lineage, before undergoing p75-directed isolation. Isolated p75+ NCSCs were differentiated into pericyte-like cells. We demonstrated the expression of pericyte markers PDGFRβ, NG2, αSMA, and CD13 in iPSC-derived pericytes using immunocytochemistry and qRT-PCR. Inflammatory activation of iPSC-derived pericytes with IL-1β or TNF revealed differences in the consistency of NF□B activation compared to primary pericytes. Additionally, cytometric bead array showed unique secretory profiles between iPSC-derived and primary brain pericytes. iPSC-derived pericytes also exhibited significantly higher rates of phagocytosis compared to primary brain pericytes. IL-1β and TNF reduced phagocytosis in primary human pericytes, but not iPSC-derived pericytes. These results highlight marked differences in the functional activity of iPSC-derived brain pericytes compared to primary brain pericytes. While iPSC-derived cells hold great potential as an in vitro disease modelling tool, care should be taken to ensure the cells recapitulate the desired phenotype.

14.4

Enhanced EEG Seizure Recognition after Hypoxia-Ischemia in Fetal Sheep Using Transformer-Based Deep Learning

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Hypoxic-ischemic (HI) events in newborns can trigger seizures, which are highly associated with later neurodevelopmental impairment. Precise detection of these seizures is complex and requires specialized expertise, highlighting the need for automated diagnostic methods. Our previous work demonstrated the effectiveness of deep convolutional neural networks (CNNs) in identifying post-HI electroencephalography (EEG) seizures in preterm fetal sheep, achieving a cross-validated accuracy of 97.19% (AUC=0.96). This study introduces transformer-based deep learning models as superior alternatives to CNNs for seizure detection in EEG recordings of pre- and near-term fetal sheep during the first 48 hours of recovery post-HI. We further show how these models excel in classifying varied and subtle seizure morphologies across different gestational age. We trained the models on data from four cohorts of Romney/Suffolk fetal sheep: HI-normothermia-term (n=7), HI-hypothermia-term (n=14), sham-normothermia-term (n=5), and HI-normothermia-preterm (n=14), totaling 31,015 EEG segments from 17,300 hours of recordings. The Transformer model exceeded the performance of the previous deep CNNs, achieving an overall accuracy of 99.60% accuracy with AUC of 0.992. More importantly, the transformers can adeptly distinguish between seizures in both the preterm and term brain, and under the influence of treatment with 99.92% accuracy (AUC=0.997). This study showcases the superior performance, efficiency, and robustness of Transformer models for generalized automated seizure detection, irrespective of the perinatal brain maturation stage and the influence of hypothermia, offering potential improvements for seizure detection after HI in newborns, at the cotside.

15.1

Ian McDonald, NZP3 and is it worth the effort?

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This lecture will present a personal viewpoint on the challenges encountered in neurological research in the New Zealand landscape. The discussion will be in the context both of New Zealand Neurologist Ian McDonald's illustrious career and our Parkinson's research in Christchurch with illustration from the 15 years longitudinal Parkinson's study – NZP[3] (New Zealand Parkinson's Progression Program). The theme will be; is it, and was it, worth the effort?

16.1

Local modulation of dopaminergic action signals during goal-directed learning

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A key difference in dopamine signalling between the ventral and dorsal regions of the striatum lies in the lateralized movement specificity of dopamine release in the dorsal striatum. This hemispherically lateralized signal cannot easily be reconciled with theories that propose that dopamine transients accord with reward prediction error (RPE) signals, which reflect a scalar reward value that back-propagates to reward-predictive stimuli or actions across learning. The predominant view is that dopamine release in the dorsal striatum signals, simultaneously and separately, a bilateral RPE and a lateralized movement signal. However, within this framework, it is unclear how movement and learning signals are disambiguated postsynaptically. We have recently proposed an alternative view, that lateralized action-related signals in the dorsomedial striatum reflect the specific action-outcome associations that underlie goal-directed action, arguing that dopamine learning and movement signals are integrated in the dorsal striatum. Here, we present new data suggesting that dopamine-mediated reward signals in the dorsomedial striatum emerge bilaterally, whereas action signals are locally modulated across learning, resulting in asymmetric, contralaterally dominant action-related signals, the magnitude of which accords with the rules of reward prediction error. Our data also suggest that this local modulation occurs through a feedback loop involving striatal direct pathway neurons. Together, these results support a model of global RPE's driving action-specific RPE's within local circuits.

16.2

Local cell-to-cell interactions protect predictive learning from counterproductive dopamine in the striatum

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The two main populations of spiny projection neuron (D1- and D2-SPNs) are interspersed in similar proportions across the striatum. We recently identified a novel modulatory interaction whereby D2-SPNs suppress plasticity in neighbouring D1-SPNs (D2-to-D1 transmodulation), a process that is critical for the updating of instrumental learning. Here, we studied plasticity territoriality in the mouse striatum by placing both neuron types in functional competition through pharmacological stimulation of D1- and D2-SPNs, respectively. Sequential administration of these drugs in either order blocked transcriptional activation in D1-SPNs, which contrasted with the summated increase in striatal dopamine (DA) induced by both drugs. Yet, in D1-SPNs, DA elevations did translate into an increase in cAMP, suggesting that D2-to-D1 transmodulation can intercept ongoing PKA signalling within D1-SPNs. Notably, molecular states did not align with changes in calcium transients in D1- or D2-SPNs, which instead correlated loosely with overall locomotor activity. We evaluated the primary role of this molecular cross-talk in instrumental learning by functionally manipulating D1- and D2-SPNs during acquisition of an action-outcome (A→O) contingency. Genetic ablation of D1-SPNs in the dorsomedial striatum disrupted original A→O learning, an effect that was mimicked by pharmacologically enhancing D2-SPN function only during training. Altogether our results uncover a prioritised cellular mechanism by which D2-SPNs exert determining influence over D1-SPN plasticity to mediate associative learning—a process that runs parallel to behavioural performance-related activity and that can override counterproductive DA input.

16.3

Translational approaches to modulate basal ganglia circuits in brain disorders

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Pharmacological treatments for Parkinson's disease (PD) aim to ameliorate the dopamine depletion underpinning the disease. However, oral administration of dopamine precursors or direct receptor agonists (e.g. D2 agonist ropinirole) results in widespread hyper-physiologic dopaminergic stimulation, leading to motor and impulse-control side-effects. Using a translational approach, we aim to improve the targeting and physiological timing of dopamine replacement in PD, utilising focused ultrasound-driven release from circulating ropinirole-loaded liposomes ('ropinisomes'). We prepared hemiparkinsonian Wistar rats (n=20; 250-380g) by injecting the neurotoxin 6-OHDA into the left medial forebrain bundle. The efficacy of ropinirole release from intravenously-delivered ropinisomes was assessed by measuring contralateral rotational motor responses following application of transcranial ultrasound, applied to the skull overlying the striatum. Significant ultrasound-mediated increase in contralateral turns was observed (1.08 turns per minute; $p<0.0001$), but absent at baseline or after isolated ultrasound application. This confirms the effectiveness of transcranial focused-ultrasound-mediated targeted release of ropinirole. However, the ultrasound/ropinisome relationship required to optimise behaviour is unclear. Therefore using fibre photometry we first recorded spontaneous calcium transients from striatum in anaesthetised rats to determine the effect of ropinirole (free and encapsulated) and varying ultrasound levels. Initial findings (n=5 rats) indicate that calcium transients, decreased by 65.3% following ropinirole (0.5-1 mg/kg subcutaneously), are fully restored by raclopride (dopamine D2 antagonist, 1 mg/kg). Next we will measure neural responses in awake rats to establish the relationship between ropinisome dose, ultrasound level, striatal activity and behaviour. This data will be critical to inform our ongoing translational research in sheep and eventual human application.

16.4

Novel immune-induced mouse model of Parkinson's disease

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Increasing evidence suggests that Parkinson's disease is an autoimmune disorder, with findings of elevated peripheral blood mononuclear cell in patients, and antigenic properties of α-synuclein driving both the innate and adaptive immunity. Yet, how the interaction of α-synuclein and a specific immune response participates to Parkinson's disease ontogenesis has remained unanswered. Here, we reveal that autoimmune response to an α-synuclein antigen underlies Parkinson's disease. We demonstrate that autoimmunity mediated by CD4+ T cell activation with α-synuclein α-syn61-75 antigen is required to lead to immune cell infiltration and localized inflammation in the substantia nigra, triggering dopaminergic cell neurodegeneration and deficits in locomotion and gait kinematics. This study offers the first immune-induced mouse model that recapitulates all features of Parkinson's disease to study the mechanisms triggering disease onset. It provides the basis for temporally tracking symptom development, exploring preventive strategies and prodromal therapeutic interventions in Parkinson's disease.

17.1

Characterisation of phenotypic changes in aged microglia in the rodent and ovine brain

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For neurodegenerative diseases (NDs), including Alzheimer's Disease and Parkinson's Disease, the most significant risk factor is age. We know microglia contribute to NDs, but age-related changes in microglia, and consequent impacts on ND pathology, are poorly characterised. This understanding is critical in uncovering the process by which ageing potentially contributes to the development and progression of NDs. Here, the brains of healthy Sprague Dawley rats at 3, 13, 16, and 18-months-old, and Merino sheep aged 1-1.5, 3-3.5, and 5-6 years-old, were used to assess age-related changes in microglia in the striatum, cortex, and hippocampus. Samples were fluorescently stained for: 1) IBA1, to assess microglial number and morphology; 2) MHCII, to assess activation; 3) Ki67, to assess microglial proliferation. Population analysis demonstrated region specific changes in microglial number with age in both rats and sheep. Morphologically, microglia in aged rats had changes in branch number and length compared to young rats and additionally, showed increase in cell size with age. In sheep, only cell area changed with age, but no other morphological changes were observed. Changes in microglial activation (MHCII) and proliferation (Ki67) with age, further reveals the altered phenotype of microglia in aged pre-clinical models. Critically, analysis of intracellular pathways, including NLRP3 and the ubiquitin-proteasome pathway, improves our understanding of the molecular changes in microglia during ageing. Future work, conducted at longer timepoints and in aged-matched diseased animals, is needed to isolate the independent effect of age-related changes in microglia compared to changes due to disease.

17.2

Investigating the effect of CK2 phosphorylation of RyR2 on neuronal excitability

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Dysfunctional calcium handling by the type 2 ryanodine receptor (RyR2) is an emerging mechanism underlying neuronal hyperexcitability. Previous studies have found that dysfunctional regulation of RyR2 can result in increased open time of the channel and spontaneous calcium release (SCR) from the ER, leading to increased neuronal excitability. This has been shown to occur in both seizures and Alzheimer's disease. Caesin kinase 2 (CK2) has been identified as a novel regulator of RyR2 function in the heart. In the heart, reduced phosphorylation of RyR2 by CK2 increased SCR, while permanent phosphorylation showed protection against SCR. As CK2 phosphorylation of RyR2 modifies SCR, this study investigated if CK2 phosphorylation of RyR2 controls the excitability of hippocampal CA1 pyramidal neurons. Mice expressing phosphomimetic RyR2 mutations mimicking either permanent phosphorylation of RyR2 by CK2 (CK2+) or no phosphorylation of RyR2 by CK2 (CK2-) were used to prepare brain slices containing the CA1. Using ex vivo calcium imaging we analysed the spontaneous firing in these two genotypes compared with wild type controls, measuring firing frequency and patterns to characterise excitability. Preliminary results suggest a trend towards higher excitability in CK2- neurons (CK2-=10, CK2+=6, WT=5) with ongoing experiments to increase the sample size. These results suggest a novel mechanism of hyperexcitability which could be further investigated in diseases exhibiting this phenotype such as seizures and early-stage Alzheimer's disease.

17.3

Altered L-type Ca2+ Channel-Mediated Plasticity in Dentate Granule Cells of PS19 mice.

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Frontotemporal dementia (FTD) refers to a group of progressive neurodegenerative diseases characterised often by hyperphosphorylated tau protein, leading to impaired microtubule binding and subsequent tau aggregation. PS19 mice, expressing FTD-related P301S human mutant tau, have been used to investigate FTD and related tauopathies. Synaptic dysfunction and altered plasticity of hippocampal neurons have been observed in FTD-related pathology, along with tau-associated dysregulation of L-type voltage-gated Ca2+ channels (L-VGCC). Utilising field potential electrophysiology in the hippocampal dentate gyrus, we investigated genotype-dependent alterations in population spike amplitudes (PSAs) recorded in slices from PS19 and wild-type (WT) mice following application of the L-VGCC agonist BAYK8644 (20 µM). Results revealed an increase in cell firing as indicated by increased PSAs from PS19, but not WT animals at 2-3-mo. However, slices from both genotypes at 6-mo demonstrated the effect. This was also seen at 8-9-mo, but the effect was now diminished in PS19 tissue. Experiments utilising the L-VGCC inhibitor nimodipine indicated that long-term potentiation (LTP) at synapses onto dentate granule cells in PS19 mice was largely L-VGCC-dependent. N-Methyl-D-aspartate receptors (NMDARs) were also required, but possibly only to provide depolarisation to open L-VGCCs. Conversely, nimodipine augmented LTP in WT tissue. Immunofluorescence demonstrated no difference in neuronal L-VGCC (Cav1.2 and Cav1.3) or NMDAR expression in the dentate gyrus between WT and PS19 mice at 2-3-mo. Genotype-dependent differences in plasticity may thus result from altered signalling cascades downstream of L-VGCC activation. We conclude that L-VGCCs are dominant triggers of plasticity in PS19 mice, which may contribute to Ca2+-driven toxicity.

17.4

Astrocyte-mediated trans-regional metaplasticity in the hippocampus

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The synaptic plasticity process of long-term potentiation (LTP) is vital for memory formation and overall neural health. However, mechanisms must be in place to prevent pathologically excessive LTP. Such regulation comes partly through metaplasticity, whereby neural activity at one point in time influences later plasticity. Recently we discovered a unique trans-regional mode of metaplasticity in the hippocampus, whereby “priming” activity in stratum oriens in area CA1 selectively inhibits later LTP at the synapses in the middle molecular layer (MML) of the dentate gyrus. While there are no known excitatory neuronal connections between CA1 and the dentate gyrus there is an astrocytic network known to cross the hippocampal fissure. To directly test the involvement of astrocytes, we undertook intracellular astrocyte patch clamping and extracellular field potential recordings in the MML of acute hippocampal slices taken from young adult male rats and mice. In rat slices, Ca2+ was buffered in individual patched astrocytes by dialyzing EGTA while recording local synaptic potentials in MML in the presence of glycine. Priming inhibited MML LTP compared to control while buffering astrocytic Ca2+ abolished this inhibitory effect on LTP. Finally, we found that the glial cytokine tumor necrosis factor-alpha (TNF), acting on TNF receptor-1, and glutamate acting on GluN2BRs, are critical signaling gliotransmitter molecules. Together, these data demonstrate a novel hippocampus-wide regulation of synaptic plasticity mediated by bi-directional astrocyte-neuron communication. We propose that such metaplasticity may play an important role in hippocampal information processing while also homeostatically counteracting excitotoxicity under extreme conditions.

18.1

Predictive value of cortical cholinergic pathway integrity on future cognitive change in Parkinson's disease

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Most Parkinson's disease (PD) patients experience cognitive impairment. Normal cognitive function is supported by the neuromodulatory mechanisms of the cholinergic system. There is evidence that integrity of the nucleus basalis of Meynert (NBM), the primary source of cortical cholinergic input, and PET cortical cholinergic function are associated with cognition in PD. Structural integrity of NBM projection pathways may influence cortical function and future cognitive status in PD. In a previous analysis, we found that cortical cholinergic pathway integrity, measured using anatomically constrained tractography from diffusion-weighted MRI (DWI), was associated with cognitive function in PD. In a sample of 107 PD participants, we performed Bayesian k-means clustering analysis using mean diffusivity in medial and lateral NBM projections. This cross-sectional analysis indicated three profiles of cortical cholinergic pathway integrity in PD. Follow-up using the Montreal Cognitive Assessment (MoCA) has been conducted in a subset of 44 PD participants, (mean follow-up=3.2years[0.7SD]). We found a greater reduction in MoCA scores in those with worse cortical cholinergic projection integrity at baseline (Probability[P] *(best>worst)* = 98% [mean change in MoCA = 0.4points; –1.9,respectively]) as well as those with intermediate baseline integrity (P*(best>intermediate)* = 97% [–1.3]), but no difference between those with intermediate and worse baseline integrity (P*(intermediate>worst)*=30%). PD patients with poorer cortical cholinergic projection integrity appear to be at greater risk of future cognitive decline. Ongoing follow-up of additional participants will seek to substantiate these findings. This evaluation adds to growing evidence suggesting cortical cholinergic input provides significant contribution to cognitive impairment in PD.

18.2

Functional magnetic resonance imaging reveals fidgeting in ADHD improves prefrontal cortex activation during executive functioning

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People with Attention Deficit Hyperactivity Disorder (ADHD) are often observed to fidget or display repetitive fine motor skills. Though it has been proposed that fidgeting may assist with concentration and sustained attention, there is little objective evidence to support this claim. This is the first study to evaluate the impact of fidgeting, using functional magnetic resonance imaging (fMRI), with neurotypical (n=30) and ADHD (n=30) adult volunteers while performing an executive functioning task (i.e., Erikson Flanker task). The default mode network (DMN) activations were contrasted using the standard network atlas Yeo20116 in the CONN toolbox. Comparative analyses revealed significant increases in medial prefrontal cortex brain activation while fidgeting during executive functioning in the ADHD participants relative to neurotypical controls. Specifically, activation in the frontal lobe increased significantly by 40% in the ADHD participants while fidgeting and performing the Flanker task (notably congruent conditions). In contrast, the neurotypical participants showed an 80% decline in activation in the same region while fidgeting and performing the Flanker task. This study has revealed that fidgeting may assist executive functioning in ADHD by increasing activation in the prefrontal cortex. This may assist those with ADHD shift from the DMN to other task-positive brain networks and offer clinicians an alternative to current medical interventions.

18.3

Longitudinal trajectories and predictors of Visual hallucinations in the New Zealand Parkinson's Progression Programme

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Many people with Parkinson's disease experience hallucinations. They are usually visual, ranging from sensing the presence of someone nearby to experiencing fully formed figures. Hallucinations can become distressing and escalate to paranoid psychosis which can precipitate hospital and rest home placement. To manage hallucinations effectively, and ultimately improve an individual's quality of life, we must understand *how* and *why* hallucinations occur. Detailed longitudinal hallucination data has been collected from 263 Parkinson's participants (sessions = 659) from the New Zealand Parkinson's Progression Programme. Bayesian regressions were used to examine cross-sectional associations between the presence of Parkinson's hallucinations and clinical and other factors. Within the sub-group who did not experience hallucinations at study entry (n = 67; 33 developed hallucinations; 2.8 years median follow-up), Bayesian regression models were used to identify factors that predict the development of hallucinations in Parkinson's participants. At any time, 58% of participants experienced hallucinations. Hallucinations were associated with lower cognitive ability (parameter estimate[PE]: -0.62 [95%CI: -1.04,-0.23]) and higher depression scores (PE: 0.40 [0.05,0.74]), but not gender, education, diagnosis age, disease duration, levodopa equivalent daily dose, motor impairment, or sleep disruption. When predicting the development of future hallucinations, the only feature which provided useful predictive information was levodopa daily dose (PE: 0.07 [0.01,0.14]). This suggests that although several features were associated with the presence of hallucinations, when examining the development of hallucinations in the future only current levodopa dose provided evidence of predictive information. Further examination is needed to determine the clinical utility of this predictive information.

18.4

Is lack of goal-conflict specific rhythmicity a biomarker for treatment resistance in generalized anxiety?

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Anxiety and depression cause major detriment to the individual, their significant others, and society as a whole. Such detriment is greater in treatment resistant (TR) cases, which are highly prevalent. Such TR prevalence may be due to failure of diagnostic frameworks. Current diagnoses are based on symptom lists and duration requirements that suffer from clinical subjectivity, comorbidity, and variation in symptom presentation. Goal Conflict Specific Rhythmicity (GCSR) measured using the Stop-Signal Task (SST) may help solve these problems by providing the first neural biomarker for an anxiety process. This GCSR has been validated with selective anxiolytics. So, we proposed that GCSR could differ between TR and non-TR individuals and do so differently between those diagnoses normally sensitive to selective anxiolytics and those not. We recorded electroencephalograms (EEG) from 20 TR participants (4 GAD, 5 SAD, 11 MDD) and 24 non-TR participants (4 GAD, 5 SAD, 15 Comorbid GAD/MDD (GMD)) while they performed the SST. There was significant positive GCSR in all groups except the GAD-TR group. GAD-TR lacked GCSR in the low frequency range. However, TR had little effect in SAD or MDD/GMD populations with apparent changes being increases not decreases. Overall, these results suggest that GAD may occur in two forms: one resulting from excessive GCSR and so being drug sensitive, and the other resulting from some other mechanism and so being TR. In SAD and MDD groups heightened GCSR could be a consequence rather than cause, driven by mechanisms that are normally more sensitive to non-selective panicolytic antidepressants.

20.1

Non-Invasive Neuromodulation to Alleviate Bronchoconstriction

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Every day, the lives of more than 1000 people are cut short because of an asthma attack. Unfortunately, many of these deaths are preventable due to a simple delay in obtaining help during the final attack. Therefore, the development of a novel therapeutic approach is urgently required to address the life-threatening nature of asthma attacks. Human airways are innervated by parasympathetic and sympathetic nerves that mediate bronchoconstriction and bronchodilation, respectively. Sympathetic fibres innervating the thoracic dermatomes have a segmental relationship with the small airways which are most implicated in asthma pathophysiology. Therefore, we investigated whether transcutaneous electrical nerve stimulation (TENS) induces bronchodilation of the small airways. Specific details are omitted due to commercial interest. In two randomised placebo-controlled trials, endurance-trained athletes (n=30) performed an exercise challenge on three different days to induce exercise-induced bronchoconstriction (proxy for asthma). Each study (n=15) investigated two TENS frequencies against placebo-TENS for six-minutes upon exercise cessation. Capnogram parameters (alpha-angle, beta-angle, phase-III-slope) were captured to analyse bronchial responses to TENS. The highest frequency appeared most rapid by significantly improving the absolute change in alpha-angle, beta-angle, and phase-III-slope (post-hoc) during 0-2 minutes ($p<0.03$) and 2-4 minutes ($p<0.02$) of stimulation onset. The lowest frequency significantly improved the absolute change in beta-angle and phase-III-slope (post-hoc) during 2-4 minutes ($p<0.03$) of stimulation onset. These findings contribute to the rationale for the development of a novel bronchodilator device to be utilised as an intervention for asthma attacks. Further experiments are planned to evaluate the efficacy of TENS among the asthmatic population.

20.2

Impacts of Friedreich's Ataxia on Well-being, Mood and Social Cognition

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Friedreich's ataxia (FRDA) is an autosomal recessive neurodegenerative condition with onset typically between ages 5 and 15, affecting balance, speech, vision, hearing, muscle control, and heart function. Research on cognition, particularly social cognition, and emotional wellbeing in FRDA is limited. Studies exploring depression have yielded inconsistent findings. The aims of this study were to investigate in FRDA participants (i) social cognition, executive functioning and processing speed; (ii) impacts of FRDA on mood and well-being (iii) the impact of low mood on social and executive function. Participants comprised 16 individuals with FRDA (aged 20-72) enrolled in Pūnaha Io the New Zealand Neurogenetic Registry and Biobank and 26 healthy control participants, age, gender, and education-matched. Measures assessed facial emotional recognition, theory of mind, verbal fluency, processing speed, inhibition of automatic responses, and depression, anxiety, irritability and well-being. Between-group differences were examined with parametric (t-test, ANOVA) and non-parametric (Mann-Whitney U) analyses as appropriate. The FRDA group had significantly poorer performance on the ability to infer the mental states of others, verbal fluency, and processing speed, but no difference in emotion recognition ability or inhibition. They also reported significantly lower mood and well-being than the matched control group. There were no significant associations between mood and social cognition or executive function. This group of FRDA participants did not show previously reported executive impairments but did show impairments in theory of mind and lowered mood. Targeted interventions to improve social functioning, mood and overall well-being in FRDA individuals may enhance quality of life.

20.3

Calculating clinically reliable change in adults with post-stroke fatigue: an extension of the Fatigue After Stroke Educational Recovery (FASTER) trial

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Fatigue is a significant and persistent consequence of stroke. The literature on post stroke fatigue (PSF) is limited to describing mean performances on common fatigue measures. There is no reference to clinical significance/clinically reliable change over time on an individual level in relation to PSF. Using data from the Fatigue After STroke Educational Recovery (FASTER; N=100 fatigue management (FMG), N=100 educational control(EC)) trial, we describe clinically reliable change in Fatigue Severity Scale (FSS), and Multidimensional Fatigue Inventory (MFI-20) from baseline to post-treatment. Tabulated data includes all the figures required to calculate reliable change. Mean FSS and MFI-20 scores remained stable over time. However, ≥50% of participants had clinically reliable reductions in fatigue and about 30% had reliable increases in fatigue across measures and groups. Potential confounders (e.g., age, gender, mood) did not impact FSS overall or in the treatment group. Those whose FSS fatigue reduced/improved started the EC group with higher subjective pain than those whose fatigue got reliably worse ($F[69]=4.752, p=0.033$). Those whose MFI-20 scores increased significantly were likely to be male (n=24 vs 9 female; ($Chi2(1)=4.179, p=0.041$), an effect derived from the treatment group ($Chi2(1)=4.849, p=0.028$) . Baseline pain in the treatment group was greater in those whose MFI-20 improved compared to those who declined. Null statistical findings do not necessarily equate to the absence of clinically relevant improvements or declines. The findings indicate that trials of PSF interventions must consider the impact of spontaneous recovery and should also consider including components related to confounders such as post-stroke pain.

20.4

Using Machine Learning to Quantify Seizure Behaviour in a Tadpole Model of Developmental and Epileptic Encephalopathies

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Developmental and Epileptic Encephalopathies (DEE) are a set of clinically defined disorders caused by mutations in over 100 different genes. These mutations, along with the drugs used to treat them, can significantly slow brain development, making accurate diagnosis and treatment critical to avoid compounding developmental delays. Identifying effective drugs for treating DEE is challenging. Recently, gene-edited Xenopus laevis tadpole models have shown promise in reliably producing DEE phenotypes. These models are advantageous for drug testing because tadpoles absorb drugs through their skin and can be mass-produced. However, the rapid nature of seizure behaviours (occurring in less than 1/50th of a second) necessitates frame-by-frame video analysis, which is time-consuming. To address this, we utilised a convolutional neural network (CNN) to extract positional data from multiple tadpoles in identifying seizure behaviours such as C-shaped contractions based on human definitions. The preliminary CNN successfully detected these behaviours. In an exploratory run of 72 different 20 minute videos of tadpole seizure behaviour, the frames requiring human examination were reduced to 2.19% of the total. We will present data comparing manual scoring of seizure postures to automatic detection. Future work will employ unsupervised learning on the extracted tadpole locations to identify additional behaviours indicative of seizures. This method presents a highly efficient approach for collecting extensive behavioural data on seizures in Xenopus laevis, which can be leveraged to examine the vast number of gene-drug combinations necessary for treatment of DEE.

20.5

Neuropathology of the striatum in X-linked Dystonia Parkinsonism

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X-linked dystonia-parkinsonism (XDP) is a newly described recessive neurodegenerative disease discovered in Panay Island (Philippines). XDP is hypothesised to be a disorder of the basal ganglia, however, neuropathological studies of the basal ganglia nuclei, including the striatum, are limited. To advance our understanding of the human striatum in XDP, immunohistochemistry coupled with automated analysis was conducted on post-mortem striatal tissue from 12 XDP and 5 age-matched neurologically normal cases to detail (1) the neurochemical architecture and (2) neuronal and glial populations of the striatal sub-compartments. Neuroanatomical delineation of the XDP striatal compartments, through enkephalin, DARPP-32, and GABAA receptor β2/3 immunolabelling, revealed 'patches' of enhanced immunoreactivity, likely to be preserved striosomes. Furthermore, calbindin expression, normally localised to the matrix, appeared upregulated within the XDP striosomes. Together, these observations suggest pathological restructuring of the XDP striatal sub-compartments. However, whether these altered immunoreactivity patterns reflect striosome-specific protein upregulation or a selective loss of matrix immunoreactivity is unclear. Additionally, the XDP striatum presented with selective neuronal vulnerability, indicated by >50% loss of calbindin+ medium spiny neurons and ChAT+ interneurons. Morphometric analysis of XDP ChAT+ interneurons revealed a reduction in somal size and process number. Furthermore, the presence of astrocytosis and microgliosis was identified within the caudate nucleus of the XDP striatum. This study is part of an ongoing investigation to elucidate the neurochemical and phenotypical dysfunction of the human XDP striatum. Subsequent studies will investigate key striatal outputs and other basal ganglia nuclei to further understand XDP neuropathology and identify potential future therapeutic targets.

20.6

Comparative influence of rodent anterior thalamic nuclei, medial prefrontal cortex, and dorsal subiculum on episodic-like memory and spatial working memory

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The comparative influence of the anterior thalamic nuclei (ATN), medial prefrontal cortex (mPFC) and dorsal subiculum (dSUB) for learning and memory are not fully understood. To characterise the functional significance of each structure within this distributed network, we compared the contributions of the ATN, mPFC, or dSUB in an object-place-context (OPC) task to assess rodent episodic-like memory, and a modified T-maze task to assess spatial working memory. Performance was compared between four groups of male Piebald Virol Glaxo cArc (PVGc) rats after bilateral excitotoxic lesions to the ATN (N=11), mPFC (N=11), or dSUB (N=8), and sham-lesion controls (N=11). There was no significant Group main effect in the episodic-like memory task (p=0.09), although only the sham-lesion control group was significantly different to chance when scores were averaged across testing sessions (p=.01). In the T-maze, the ATN (p<.001) and dSUB (p=0.02) groups made more spatial working memory errors compared to sham-lesion controls, while the mPFC group only made more errors during initial learning. Furthermore, both ATN (p<.001) and dSUB (p=.004) groups made more errors in 'same start-arm' trials compared to controls, while only the ATN (p=.004) group made more errors in 'opposite start-arm' trials. These results indicate the dSUB and, especially, the ATN are essential for spatial working memory while the mPFC supports initial acquisition. Together, these results further our understanding about the involvement of ATN, mPFC, and dSUB in learning and memory and provide insights into when these structures may interact together to support episodic-like memory and spatial working memory.

20.7

Exploratory analysis of ADAM10 isoforms levels and activity in neuron-like cell fractions.

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Alzheimer's disease (AD) pathology involves the accumulation of amyloid-beta (Aβ) peptides into senile plaques generated by Amyloid Precursor Protein (APP) cleavage by β-secretases. When APP is cleaved by ADAM10 instead, neuroprotective fragments are released. ADAM10 possesses three isoforms: a zymogen (proADAM10), a proteolytically active mature (mADAM10), and a soluble (sADAM10) isoform. Our group has shown that sADAM10 levels and activity are altered in the plasma of persons with AD. Thus, we aimed to investigate the levels and activity of ADAM10 isoforms in neuron-like cells to understand their central functioning. SH-SY5Y cells were differentiated into neuron-like cells using retinoic acid. The media was collected, and the cells were fractionated into cytoplasmic, membrane-bound, and nuclear protein-rich portions. Western blotting (WB) experiments were performed on each fraction to detect ADAM10 isoforms and assess fraction purity using anti-GAPDH (cytoplasm), anti-VDAC (membranes), and anti-Lamin A/C (nuclei) antibodies. Antibodies targeting the N-terminal and C-terminal regions of ADAM10 were used to detect the soluble and membrane-bound isoforms, respectively. Additionally, enzymatic activity assays were conducted. The characterization of the fractioning process and preliminary results of the activity assays show feeble sADAM10 activity in the cell medium, compared to mADAM10 in the membrane and cytoplasm fractions and recombinant ADAM10 ($p < 0.001$). These preliminary results show that sADAM10 has feeble activity in neuron-like cells, which agrees with our previous findings, validating the potential use of plasma ADAM10 as a blood-based AD biomarker.

20.8

Ketamine induces changes in hippocampal activity recapitulating changes seen in animal models of schizophrenia

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Schizophrenia is a debilitating psychological disorder with a range of cognitive deficits. However, our knowledge about the neural mechanisms governing this disorder is still incomplete. An animal model of schizophrenia (the MIA model) suggests that the coherence of theta and gamma in the hippocampus are abnormal in this condition. Importantly, these animals also fail to discriminate when they are under the influence of ketamine, despite successfully discriminating other drug states. This suggests that low dose ketamine recapitulates the cognitive state of schizophrenia to some degree. This study aims to investigate if low doses of ketamine also recapitulate the neural changes seen in this model. Sprague Dawley rats with implanted tetrode multielectrode microdrives in the CA1 region of the hippocampus were recorded while animals freely explored. Electrophysiological analyses indicate low-dose ketamine reduces coherence of theta and gamma in the CA1 region of the hippocampus. This indicates ketamine recapitulates the changes within the hippocampus seen in the MIA model, suggesting that theta and gamma coherence in hippocampus may be central to the improper binding of sensory information central to schizophrenia.

20.9

Investigating EEG-Derived Biomarkers of Major Depressive Disorder: Lempel-Ziv Complexity, Spectral Power and Peak Alpha Frequency

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Major Depressive Disorder (MDD) is a prevalent and debilitating mental health disorder, yet its diagnosis often relies on subjective assessments. Current treatments are ineffective for about one third of patients, highlighting the need for improved diagnostic tools and more tailored treatment plans. Identifying objective biomarkers with electroencephalography (EEG) could enhance diagnostic accuracy and provide insights into underlying neurobiological mechanisms and inform treatment options. Resting-state EEG was recorded from a preliminary cohort of 16 patients with MDD and 16 healthy controls. Preprocessed data were analysed to compare spectral power changes, peak alpha frequency, and Lempel-Ziv Complexity (LZc) between the two groups. LZc across centro-parietal regions was higher in the depressed group than in the non-depressed group with a maximal effect at electrode CP4 ($t(30) = 2.4431$, $p = 0.0142$). No significant changes were seen in spectral power or peak alpha frequency between the groups. The findings of increased LZc in the depressed cohort are consistent with previous research, suggesting this heightened complexity may reflect impaired neural communication and processing efficiency. This could serve as a potential biomarker for MDD, offering insights into its neurobiological underpinnings. Having established this biomarker in this cohort, future research will assess LZc before and after administering low-dose naltrexone, an emerging adjunct treatment for MDD. This will help determine if LZc can be modulated by treatment and if changes correlate with antidepressant effects.

20.10

Testing AAV-mediated sAPPa overexpression as a therapy in an AD mouse model

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Soluble amyloid precursor protein-alpha (sAPPα) has been suggested as a treatment for Alzheimer's disease (AD) due to its myriad beneficial properties within the brain. However, the blood-brain barrier limits drug delivery. Modified adeno-associated viruses (AAVs) such as AAV.CAP-B10 can carry genes across this barrier, allowing gene therapy treatments to be administered systemically. This study tested the hypothesis that AAV-mediated sAPPα overexpression in the brain would improve disease-like symptoms in an AD mouse model. We injected intravenously 1x10^11 AAV.CAP-B10 viral vectors carrying the human sAPPα transgene into wild-type and 5xFAD mice, which carry five genetic mutations associated with familial AD. Control mice received a vector carrying the transgene for green fluorescent protein. Male and female mice were injected at two months of age, an early stage of the disease. At 8-9 months of age, behavioural, electrophysiological, and post-mortem assessments were conducted. Preliminary data indicates that untreated 5xFAD mice weigh less, explore more and are less anxious in the elevated plus maze and open field tests, have impaired spatial memory in the Y maze and Barnes maze, but improved novel object recognition, and equal motor performance on the RotaRod compared to wild-type mice. The magnitude of long-term potentiation within CA1 of the hippocampus was similar between groups. Unexpectedly, viral sAPPα treatment had no effect on virtually any of the measures. Future post-mortem analyses will investigate whether sAPPα treatment affects neuropathology in the transgenic mice. Overall, our findings to date do not support other studies showing therapeutic properties of sAPPα.

20.11

Targeting Connexin Hemichannels and the Inflammasome pathway in an induced mouse model of Alzheimer's Disease

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Pathologically opened connexin hemichannels can establish a self-propagating inflammasome activation loop that may contribute to Alzheimer's disease (AD) pathogenesis. This project investigated the effect of connexin hemichannel blockade in mice with acute onset of AD characteristics such as neurodegeneration, neuroinflammation, and memory deficits induced by aggregated amyloid beta 1-42 (Aβ1-42). One day after intrahippocampal injection of Aβ1-42, mice (n = 9) were administered connexin hemichannel blocker, Tonabersat, in peanut butter for 16 days before tissue collection. Aβ1-42- and vehicle-injected mice (n = 8 each) received peanut butter pellet only, while Naïve controls received no pellet or Tonabersat only (n = 8 each). Fluorescent immunohistochemistry and densitometry analysis were used to quantify the response of astrocytes, microglia, and neurons as well as expression of inflammasome-associated proteins. In the hippocampus, Aβ1-42 induced an elevated microglial response compared to naïve mice (*p = 0.0150) and a reduction in neuron area compared to vehicle-injected controls (*p = 0.0185). Mice treated with Tonabersat following Aβ1-42 injection showed a reduced microglial response compared to untreated (*p = 0.0430). Tonabersat also prevented the decrease in neuron area caused by Aβ1-42 (*P = 0.0493). This data demonstrates the ability of connexin hemichannel blockade to modulate the inflammatory response of microglia to Aβ1-42 and result in a neuroprotective outcome. This highlights connexin hemichannels as a potential therapeutic target for nflammasome-related neurodegenerative diseases such as AD.

20.12

Harnessing Alpha Synuclein Polymorphs to investigate novel protein targets in Parkinson's Disease

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Parkinson's Disease (PD) is a debilitating neurodegenerative disorder with a rising global prevalence. Increasing aging populations, combined with genetic and environmental risk factors, contributes to a growing societal and economic burden that demands improved therapeutics. PD is defined by the progressive accumulation of alpha-synuclein in dopaminergic neurons. This accumulation leads to neuronal cell death and results in varying motor and non-motor symptoms, leaving patients with limited options beyond symptomatic relief. Alpha-synuclein accumulates as various conformational polymorphs, each with different pathogenic properties. Furthermore, recent research has established that non-neuronal cells such as pericytes are involved in the PD pathogenesis. We hypothesize that examining non-neuronal cells in a polymorph-specific context could identify novel proteins involved in PD pathogenesis. We exposed human brain-derived pericytes to five distinct alpha-synuclein polymorphs and conducted RNAseq analysis, which revealed specific changes in gene expression. These changes were validated at the protein level both in vitro and in situ using immunolabelling. We assessed the expression of 48 unique proteins using human pericytes and middle temporal gyrus tissue microarrays. In vitro analysis highlighted the expression of 7 proteins, with reduced BCL-XL signal in PD pericytes. In situ immunolabelling revealed eight proteins differentially expressed between control and PD tissues: ABCF1, ASAH1, BCL-XL, CSNK2A1, MEGF11, MTHFD1, NUCKS1, and PUM2. The notable changes in BCL-XL in both tissue and cells suggests that the anti-apoptotic protein may facilitate changes in PD pathogenesis, particularly around vascular cells. Continued investigation into BCL-XL may reveal its therapeutic potential in relation to PD.

20.13

Tryptophan metabolism and trans-diagnostic approach in childhood and adolescence ADHD/ASD comorbid patients with central fatigue

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Adults with ADHD have been reported to experience greater fatigue than healthy controls. However, this is not known for children and adolescents, thus this study was conducted. In an animal model of ADHD, Nagase analbuminemic rat, a rat that is easily fatigued, has a reduced ability to inactivate tryptophan to 5-HIAA in the striatal extracellular fluid. As a result, tryptophan, a fatigue-causing substance, increased. The urinary excretion rate of brain-derived 5-HIAA is therefore a biomarker for central fatigue. 38 males and 8 females aged 5-18 years were studied using a self-report questionnaire. Of these, 11 had ADHD only, 16 had ADHD/ASD comorbidity and the remaining 19 had ADHD and various psychiatric disorders. 85% of these three groups showed mainly central/mental fatigue. In addition, 63% had difficulties with sustained and transitive attention functions and muscle tone regulation, which interfered with working skill. Urinary 5-HIAA excretion rates were significantly reduced and correlated with pronounced central fatigue symptoms. In conclusion, ADHD and ASD share many common symptoms, and from a trans-diagnostic approach, it is necessary to confirm the presence of central fatigue before starting therapeutic medication. This study was supported by a JSPS Grant-in-Aid for Scientific Research to Takanobu Yamamoto (project number 20K03013).

20.14

Neurobiology of Psychosis Risk

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Psychosis spectrum disorders such as bipolar disorder or schizophrenia are severe psychiatric disorders with complex aetiologies. Precursors like schizotypal personality traits and psychosis experiences often emerge before formal diagnosis, indicating elevated risk, which if identified early can help mitigate future harm. This longitudinal study employed magnetic resonance imaging (MRI) to examine the relationship between brain structure and risk factors for psychosis spectrum disorders. We hypothesized that individuals with higher schizotypy scores would show alterations in brain structure and neurochemistry. Twenty-one undergraduate students underwent MRI scans and completed assessments for schizotypy and psychosis experiences at two time points, one year apart. T1-weighted MRI and proton magnetic resonance spectroscopy measured brain tissue volumes and striatal glutamate concentrations. Participants were categorized into low-risk and high-risk groups based on questionnaire scores. The neuroimaging data were analysed using FMRIB Software Library (FSL). Two-way mixed effect ANOVAs tested for differences between groups across time points. Preliminary analyses revealed significantly lower white matter ($p = 0.01$, $\eta^2 = 0.17$) and whole brain volumes ($p = 0.03$, $\eta^2 = 0.12$) in the high-risk group, which remained stable over time. No significant differences were found in grey matter volumes ($p = 0.2$) or striatal glutamate concentrations ($p = 0.13$). These findings suggest decreased white matter volume may be present in subclinical populations experiencing psychosis-like symptoms, even before the onset of clinical disorders. However, the small sample size limits generalizability. Ultimately, this research could inform early identification strategies and targeted interventions for individuals at risk of developing psychosis spectrum disorders.

20.15

Ultra-high contrast MRI (UHC-MRI): a new era in traumatic brain injury (TBI) diagnosis.

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TBI is common in NZ with annual prevalence 0.79%, a likely underestimate given that many groups, e.g. victims of intimate partner violence, do not report their injuries. The majority of cases are mild TBI (mTBI). Over 30% of these have enduring symptoms, constituting a major public health issue. Many are considered to have a functional disorder, with this view supported by the frequent lack of abnormality found on brain imaging. In modelling studies, UHC-MRI of small increases in the T1 of tissues using divided Subtracted Inversion Recovery (dSIR) sequences show ten times the contrast seen with conventional sequences. These sequences are useful in imaging normal appearing white matter where there may be small changes in T1 and/or T2 insufficient to produce useful contrast with conventional sequences. Our study shows positive findings in patients with enduring symptoms, when conventional MRI is negative. This can aid clinicians in diagnosis and management, as well as mTBI patients and their families in acceptance. In our case control series of 29 patients with enduring symptoms and 37 un-matched healthy controls we have shown an odds ratio for mTBI history (2 scorers) of 120 (95%CI:14-1038) and 67 (95%CI:16-482) giving greater certainty to diagnostic practice and placing increased value on the elicited histories. It is unclear what neuropathology is being observed, but neuroinflammation, as the commonest neuropathological cascade triggered by mTBI, is the most likely candidate. Tissue fluid changes may be important pathologies. We are addressing animal gyrencephalic models to further study the aetiology of the changes.

20.16

The Neurological Foundation Human Brain Bank: Preparation of human brain tissue of neurodegenerative diseases

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The Neurological Foundation Human Brain Bank was formed in 1993 by Sir Richard Faull, with the purpose of facilitating neuroscientific research. Unique protocols have been developed by Brain Bank personnel for the optimal preservation of tissue from neurologically normal brains and those affected by a wide range of neurodegenerative diseases. Here, we outline the process of brain donation, beginning with the acceptance of brain donation from suitable candidates, to processing the tissue in a variety of manners best suited for different laboratory techniques including both anatomical and molecular studies. This tissue is made available to researchers, both within New Zealand and internationally. We have received over 800 brains spanning from neurologically normal, to those affected by neurodegenerative diseases including Huntington's, Alzheimer's, Parkinson's, Motor Neuron, Frontotemporal dementia and Multiple sclerosis. Here, we highlight some of the techniques routinely used by the brain bank, including immunohistochemistry and in situ hybridization, as well as outline some future developments including single cell RNA sequencing and spatial transcriptomics. The success of the Brain Bank relies on the close relationship with the community. It is only with the wonderful support of donors and their families across New Zealand that the Brain Bank has been possible.

20.17

Developing new bilateral large animal model of Parkinson's disease: effects of asymmetrical 6-OHDA lesions of the substantia nigra in sheep

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterised by the loss of dopamine-producing neurons in the substantia nigra pars compacta (SNpc), leading to reduced dopamine and, initially, imbalanced motor deficits. Unilateral stereotaxic injection of the neurotoxin 6-hydroxydopamine (6-OHDA) between SNpc and striatum is the usual method of inducing dopamine loss in small-animal experimental models. In these models, the unlesioned side supports normal motor activity during recovery and provides a control hemisphere, however the bilateral signs observed in PD are absent. In the present study, we aimed to establish a novel bilateral sheep model of PD by asymmetrically infusing 6-OHDA bilaterally into the SNpc Slowed movements and varying levels of asymmetric behaviour, were induced in all sheep to Parkinsonian signs. The dopaminergic receptor agonists apomorphine (0.25 mg/kg) and ropinirole (0.08 mg/kg) were administered subcutaneously to enhance reduced motor activity, induce rotational behaviour (or correct spontaneous rotation), and confirm parkinsonian. Behavioural assessments were conducted using automated movement tracking via GPS and video recordings. The extent of lesions was quantified through tyrosine hydroxylase immunohistochemistry to evaluate the cellular effects of 6-OHDA lesioning. Our novel sheep model emulates early to mid-clinical PD, where slowness in initiating and executing movements starts on one side but progresses to both. It offers several regulatory, ethical, and economic advantages over other large animal models, such as non-human primates.

20.18

Utility of Squash Smear Cytology in Intraoperative Diagnosis of Central Nervous System Lesions: A Tertiary care Institute Experience

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Squash smear cytology is universally accepted technique in diagnosing a wide range of central nervous system lesions and is presently employed for both therapeutic and prognostic reasons. The biggest advantage of squash smear cytological diagnosis is rapid intraoperative diagnosis which further helps the neurosurgeon to plan the extent of surgery and modify accordingly. To study the diagnostic accuracy of squash smears cytology with histopathological and clinico-radiological correlation. Total 100 cases were included, which was paediatric and adult central nervous system lesions. Biopsy tissue subjected to squash smear cytology, stained with Geimsa, Haematoxylin & Eosin stain and remaining tissue processes for histopathological diagnosis. Squash smear cytological diagnosis was correlated with histopathological diagnosis. The most common site of central nervous system lesions was brain 90% followed by spinal cord lesions was 10%. The age of patient ranged from 3 months to 65 years, maximum number of cases was aged between 21 to 50 years (56%). Most common presenting symptom was headache (70%) followed by nausea and vomiting. Clinical diagnosis provided diagnostic accuracy of 84% with histopathological diagnosis. Radiological investigations provided diagnostic accuracy of 88% with histopathological diagnosis. Cytological diagnostic accuracy of 90% with gold standard histopathological diagnosis. For discordant cases, Squash cytology diagnosis also not match (0%) with histopathology for anaplastic astrocytoma, anaplastic meningioma, desmoplastic medulloblastoma, germinoma and oligoastrocytoma. Squash cytology should be used as a preliminary investigation and should always be confirmed with histopathological examination which is the gold standard. This study shows a very high degree (90%) of cytohistological correlation.

20.19

Dissecting the Substantia Nigra & Locus Coeruleus from Human Brains

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Parkinson's disease (PD) and Alzheimer's disease (AD) are the most prevalent neurodegenerative diseases, affecting over 64 million people globally as of 2020. Studies suggest that these diseases are rooted in the substantia nigra (SN) of the midbrain and the locus coeruleus (LC) of the pons. In addition to their key physiological roles producing critical neurotransmitters, studies have identified a correlation between neuronal loss within these structures and illness duration for both PD and AD. The study of post-mortem brains has played a key role in mapping and enhancing our understanding of the neuroanatomy of these disorders. This dissection can be tricky. This paper describes a clear method for dissecting these nuclei while keeping the cerebral hemispheres intact. Using basic surgical instruments, the brainstem can be safely and efficiently extracted from the inferior surface. Several key landmarks are used to guide the extraction. The incisions begin at the lateral geniculate bodies of the thalamus, the first running rostrally to the posterior surface of the optic chiasm, anterior to the mammillary bodies. The second incision posteriorly to the rostral surface of the corpus callosum. This method was developed as part of a larger neuroradiological study on PD. We expect to see the SN and LC clearly on MR imaging, as the brainstems are intact. Having a reliable method for extracting the brainstem allows for consistency in sampling, and preserves the remaining cerebral structures. This study is advancing our understanding of these disorders, which will contribute to reducing their global burden.

20.20

Tau PET in Parkinson's disease: interim findings

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Parkinson's disease (PD) research has focused on the neuropathological hallmarks associated with the death of dopamine-producing neurons and the deposition of misfolded α-synuclein protein. The multisystem neurodegeneration that eventuates in dementia in PD may, however, also reflect neuropathology beyond α-synuclein. Alzheimer's disease neuropathology, defined by the accumulation of misfolded beta-amyloid and tau proteins, may contribute to the emergence of dementia in PD, at least in a subset of PD patients, perhaps through synergistic interaction with α-synuclein. Recent developments in positron emission tomography (PET) now allow in vivo imaging of abnormal tau. We therefore investigated the presence of misfolded tau in PD using a 2nd generation tau ligand, PI-2620. Of 17 participants imaged thus far (15 with PD and two controls), only one PD participant demonstrated abnormal tau deposition, showing increased uptake in bilateral medial temporal lobes (a characteristic Alzheimer-like pattern) and right temporal-occipital areas. Recruitment is ongoing. Future work will associate tau deposition with cognitive impairment in PD, which may facilitate a more complete understanding of dementia in Parkinson's, and may reveal shared neurodegenerative pathways with other diseases, e.g. Alzheimer's.

20.21

The impact of Meriva® curcumin diet on glial activation and neuroinflammatory markers on a mouse model of chronic neuroinflammation

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Chronic neuroinflammation is a pathological hallmark for neurodegenerative disorders triggered by internal or external stimuli leading to altered central nervous system (CNS) homeostasis, production of proinflammatory cytokines, chronic glial activation, overexpression of neuroinflammatory markers and protein misfolding. This multifaceted nature of neurodegenerative disorders demands therapeutic strategies which will have an impact on the cellular and molecular phenotype without causing deleterious effects. Therefore, in this study, we explored a highly bioavailable phytosomal curcumin formulation in a mouse model of chronic neuroinflammation (GFAP-IL6). A comprehensive approach combining transcriptomic analysis of the cerebellum, hippocampus, amygdala and prefrontal cortex and immunohistochemistry along with stereology was employed to investigate the effect of curcumin supplementation on neuroinflammatory markers and glial activation on mice at 9 months age. Meriva® curcumin (MC) feeding was able to interfere with the neuroinflammatory pathways by downregulating the mRNA levels of pro-inflammatory markers P2rx7 and Nfkb1 in the hippocampus as compared to the animals on control diet. In female GFAP-IL6 mice, the amygdala was the region that MC feeding had the greatest impact with genes such as Aif1, C3, Nfkb1, S100a10, Tmem119 being downregulated. MC diet also had a positive impact on the glial activation with lower microglial numbers in the cerebellum along with lower microglial and astrocyte numbers in the hippocampus as compared the mice on control diet. Our study on phytosomal curcumin supplementation in GFAP-IL6 mice mostly showed positive effects on neuroinflammatory markers and glial cells therefore making it a therapeutic potential against chronic neuroinflammation either by reversing or slowing down the neuroinflammatory process.

20.22

You only get one brain: An exploratory retrospective study on life after adolescent TBI

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There is a scarcity of literature regarding adolescent experiences of traumatic brain injury (TBI). This qualitative study explored how TBI at this unique stage of development might impact how young people navigate the challenges of adolescence and transition to adulthood, and what might support recovery. Thirteen adolescents who sustained a mild-moderate TBI (aged 13–17years), approximately 7.7 years (range=6.7–8.0years) prior, participated. Semi-structured individual interviews were conducted to explore participants' experiences surrounding and following their TBIs. Thematic analysis produced five key themes: 1) Participants experienced problems with cognitive (e.g. forgetfulness, concentration), physical (e.g. migraines, fatigue) and emotional (e.g. depression, anxiety) functioning, which were often endured into adulthood. 2) TBI-related problems adversely affected important areas of life for the participant (i.e., school, work, friendships). 3) Changes following TBI commonly impacted identity formation. 4) Recovery processes evolved over time as participants coped initially by just 'getting on with it', before accepting new limitations and, ultimately, growing from their experiences. 5) While friends and family assisted recovery, struggles were exacerbated by lack of emotional support from others, and the absence of assistance/ information-provision from professionals regarding what to expect. The findings suggest that even mild TBI sustained during adolescence can have consequences for an individual's functioning, engagement in life and identity development, whilst also giving rise to post-traumatic growth. Recovery following adolescent TBI might be maximised by facilitating greater understanding of the injury and acknowledging its impacts on important areas of life, as well as the provision of emotional support and facilitating self-reflection and meaning-making.

22.1

Developing neuroinflammation biomarkers to assess the antidepressant effects of naltrexone in major depressive disorder with an inflammatory component

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Current treatments for major depressive disorder (MDD) are ineffective in approximately one-third of patients. Increased inflammation may reflect an MDD sub-type which would benefit from adjunctive anti-inflammatory treatment such as low-dose naltrexone (LDN). However, there is a lack of validated tools to assess treatment effects for neuroinflammation. The objectives of this study were to determine if magnetic resonance imaging (MRI) and spectroscopy (MRS) markers sensitive to neuroinflammation in brain regions known to be impacted by inflammation in MDD (anterior cingulate gyrus (ACG) and insula) are different between patients with low C-reactive protein (CRP), those with high CRP, and healthy controls. Participants with moderate MDD and CRP≤1mg/L (n=18) or CRP≥3mg/L (n=7) and healthy controls (n=13) were recruited. MRS and diffusion-weighted MRI data were collected to evaluate local brain temperature, metabolites and diffusion metrics. Low-CRP MDD exhibited significantly higher temperature and free-water fraction in the ACG than controls, p=0.016 and p=0.011. High-CRP MDD showed significantly higher myo-inositol/creatine ratio in the right insula compared to low-CRP MDD, p=0.014. These results suggest that MRI/MRS-measured neuroinflammation may occur in MDD without elevations in serum CRP. These markers will be tested after the MDD participants have been administered LDN to determine their sensitivity to treatment effect.

22.2

Plasma-Derived MicroRNAs are Altered with Ketamine intervention for Treatment-Resistant Generalised or Social Anxiety Disorders.

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Low-dose subcutaneous infusions of the glutamate N-methyl-D-aspartate (NMDA) receptor antagonist ketamine have been shown to act as a rapid and persistent anxiolytic in over 80% of those with refractory Generalised Anxiety Disorder and Social Anxiety Disorder. However, neural correlates of such disorders and their treatment response have yet to be defined. As microRNAs regulate neural function, are released from neurons, and enter the bloodstream, plasma-derived microRNAs may function as useful biomarkers. We assessed the plasma-derived microRNAs in patients with treatment-resistant Generalised or Social Anxiety Disorders pre- and 72 hours post-ketamine intervention, as well as in a group of healthy control subjects using custom-designed TaqMan arrays representing 188 anxiety-related microRNAs. We performed nonparametric tests to investigate the differences in microRNA expression between the healthy and pre-ketamine anxiety groups, as well as longitudinally pre- and post-ketamine in the anxiety group. Following this analysis, we found that 21 microRNAs were significantly upregulated in the anxiety group (n=14) compared to controls (n=12). Of those 21 microRNAs, 20 were significantly downregulated in the anxiety group following ketamine intervention (n=8). These microRNAs are implicated in inflammation and serotonergic pathways. Overall, this exploratory study indicates that further investigation into these pathways may be of interest in understanding treatment-resistant anxiety symptomology, and subsequent novel therapies such as ketamine.

22.3

The clinical and genetic landscape of *UBQLN2*-linked ALS/FTD; a meta-analysis of variant pathogenicity and sex differences

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Ubiquilin 2, encoded by the UBQLN2 gene, is a trafficking protein involved in protein quality control. Pathogenic *UBQLN2* variants cause X-linked amyotrophic lateral sclerosis and/or frontotemporal dementia (ALS/FTD) however the demographic and clinical phenotype of ALS/FTD caused by pathogenic *UBQLN2* variants shows striking inter- and intra-familial heterogeneity. Further, the contribution of *UBQLN2* variants of uncertain significance to disease is unclear. To clarify this heterogeneity, a meta-analysis of published literature describing demographic, clinical, and genetic features of *UBQLN2*-linked ALS/FTD was conducted, alongside evolutionary conservation and in silico analysis to infer biological and clinical variant pathogenicity. Immunohistochemistry was performed in brain tissue of 3 related individuals harbouring a pathogenic p.T487I *UBQLN2* variant to quantify ubiquilin 2 aggregation burden. From 28 published studies, 156 affected individuals and 46 non-symptomatic carriers harbouring one of 41 unique *UBQLN2* variants were identified. Pathogenic *UBQLN2* variants showed a sex-specific age of onset disparity wherein males develop disease 17.5 years prior to females (30.24±12.06 versus 47.71±13.37; $p<0.0001$), with no change in disease duration ($p=0.3301$). Further, *UBQLN2* variants of uncertain significance show a bimodal distribution of onset age for males and females suggesting these are a mixture of true benign and pathogenic variants. In human brain tissue, male p.T487I *UBQLN2* cases showed a greater burden of ubiquilin 2 aggregation compared to a female case. This is the first and largest cohort meta-analysis of *UBQLN2*-linked ALS/FTD. The predictable sex-specific clinical differences of pathogenic *UBQLN2* variants may support the reclassification of variants of uncertain significance and inform predictions of ALS/FTD risk.

23.1

Beneficial effects of long-term agmatine supplementation in aged rats

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Aging is a multi-factorial process leading to cognitive decline. It has been well documented that synaptic and cerebrovascular dysfunction contributes to age-related learning and memory deficits. Recent research has indicated anti-aging and memory enhancing properties of agmatine (decarboxylated arginine). The present study systematically investigated the effects of long-term agmatine supplementation on neurovascular coupling and synaptic function in aged rats. Sprague-Dawley rats at 14 months of age were supplemented daily with or without agmatine (50 mg/kg) via food chow for 4-6 months, and a group of 4 months old rats with normal food chow were used as younger age controls. We found significantly reduced spontaneous alternations in the Y-maze test and neurovascular coupling response in aged rats relative to young rats. Intriguingly, such age-related reductions were normalised and attenuated respectively by agmatine supplementation. Synaptosomes enriched with synaptic nerve terminals were then prepared to measure chemically-induced long-term potentiation (cLTP) and F- and G-actin levels using Western bot. Aged rats displayed significantly reduced cLTP, F-/G-actin ratio and actin regulator phospho-LIM-kinase1 protein expression relative to young rats. Interestingly, agmatine supplementation normalised age-related decreases in all three variables determined. Moreover, our preliminary immunohistochemical work indicated the potential of agmatine in rescuing age-related reduction in hippocampal capillary. Taken together, our results demonstrate that oral supplementation of agmatine is able to rescue synaptic and cerebrovascular dysfunction in aged rats, further supporting its anti-aging and memory enhancing properties.

23.2

The effect of 5-fluorouracil on immortalised neuronal and microglia-like cells: Laying the foundation for the development of an in vitro model of chemotherapy-induced cognitive impairment

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Chemotherapy-induced cognitive impairment (CICI) significantly affects patients' quality of life, causing issues with memory, concentration, and processing speed. CICI research is often conducted in animal models to isolate the effects of chemotherapy on cognition and develop therapeutic strategies. Currently however, no gold standard animal model for CICI research exists, translating to considerable heterogeneity in methods employed. This study therefore aimed to characterise the effects 5-flurouracil (5-FU) chemotherapy exerts on two cell populations (SH-SY5Y differentiated neurons and BV2 murine microglia-like cells), which has not been conducted and is an important first step to developing an in vitro model of CICI. Cell viability was assessed through MTT and ATP assays, while functional changes were investigated using ELISA to measure IL-6 release in BV2 cells and IL-8 in neurons. Morphological changes were examined via confocal imaging. Results showed higher cell death in BV2 cells compared to neurons following 5-FU treatment, but no changes in IL-6 or IL-8 release. In BV2 cells, changes to all assessed morphological features (process number, length, branching number and soma and cell size), were evident at all time-points, particularly at 24-hours. Interestingly, no significant changes were noted in the neurons at either time-point, suggesting a more profound effect of 5-FU on microglia in the acute treatment period. While this study represents a first step towards a new model for CICI research, further work is required to refine and validate this through the use of primary and co-culture models, while also delving further into the mechanistic changes occurring causing this.

23.3

The Central Amygdala's Involvement in Processing Appetitive Stimuli

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Research into the neural basis of associative learning has primarily focused on the traditional reinforcement circuit, such as the nucleus accumbens and ventral tegmental area. Most accounts of such learning propose that it is a gradual process; however, some studies suggest that animals often exhibit an abrupt learning pattern, which presents an opportunity to investigate the neurobiological changes that occur before and after acquisition. In the present studies, a novel statistical approach was used to pinpoint the trial at which rats acquire an association, thereby quantifying the abrupt change in behavior during a classical conditioning task. Immunohistochemical analysis revealed that the central amygdala was most prominent at the time of acquisition and decreased both before and after this point. Subsequently, electrophysiological recordings demonstrated changes in both the level and nature of neural activity that were focused on the acquisition point. These findings point to the central amygdala being maximally involved in the acquisition of newly acquired information, providing insight into a novel role for the central amygdala in

23.4

Hippocampal-prefrontal coherence is altered during behavioural strategy transitions, and is compromised in the maternal immune activation model of schizophrenia

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Communication between hippocampus and prefrontal cortex is thought to be critical for behavioural selection from several alternatives. Experiments in hippocampus typically treat free-foraging sessions as unitary behaviour, but there are distinct states that animals change between; highly tortuous paths at slow speed that animals employ to exploit a local resource, and relatively straight higher-speed strategies when animals transition from one local region to another. Here, we examine paths taken by animals with electrodes in hippocampus and prefrontal cortex and divide each session into "search" and "transition" behavioural epochs. We find that just prior to transition between states there is communication between these two regions that is absent during non-transition times. This suggests that these behavioural states are distinct, and that communication between hippocampus and prefrontal cortex is associated with the switch in strategy. Critically, in an animal model of a schizophrenia risk factor (the MIA model) there is a disruption in the communication between these regions at the transition points. This finding is consistent with the notion that schizophrenia is associated with a deficit in the "binding" or integration of information and results in maladaptive explore/exploit dynamics.

24.1

Novel analogues of the kappa opioid receptor agonist, U50488, have potent antinociceptive effects without tolerance or other side effects

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Mu opioid receptor (MOR) agonists such as morphine are efficacious analgesics. However, severe side effects including respiratory depression, addiction, and tolerance, limit their clinical viability to manage chronic pain. Another class of opioids, kappa opioid receptor (KOR) agonists, also have analgesic properties, but they are not addictive, nor do they cause respiratory depression. Other side effects including sedation, anxiety, and aversion, have limited their clinical development, however. G-protein signalling bias may be the key to developing efficacious KOR agonists without these side effects. In this study, we determined the analgesic and side effects of three novel U50488-derived KOR agonists, LDK93, LDK95, and LDK276, in adult male C57BL6J mice. Firstly, the acute, antinociceptive potency and duration of action of each drug was determined using the warm-water tail-flick assay. Next, we investigated the efficacy of each drug at attenuating chronic, paclitaxel-induced mechanical and thermal allodynia. Lastly, the lead compound (LDK276) was assessed for side effects including sedation, anxiety, reward, and motor incoordination using the open field, elevated zero maze, conditioned place aversion, and rotarod tests, respectively. In the warm-water tail withdrawal assay, all novel KOR agonists were more potent than U50488 and had a similar duration of effect. All KOR agonists also significantly reversed chronic paclitaxel-induced mechanical and thermal allodynia, without any evidence of tolerance. Moreover, unlike U50488, LDK276 had no significant side effects. These results suggest novel KOR agonists may provide a promising, safer alternative to MOR agonists for the management of chronic pain.

24.2

Basal ganglia-motor thalamus neuronal activity is altered by dyskinesia-inducing levodopa administration in parkinsonian rats

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Prolonged levodopa administration in Parkinson's disease (PD) causes debilitating hyperkinetic levodopa-induced dyskinesia (LID) side-effects in 80% of patients. This study investigated network mechanisms underlying levodopa-triggered dyskinesia onset in the basal-ganglia thalamocortical motor pathway. Single cell and population electrophysiological recordings were simultaneously recorded from substantia nigra pars reticulata (SNpr) and motor thalamus (Mthal) from control and PD model rats that were levodopa-naïve, or received levodopa (4.75 mg/kg, 3 weeks) and did (LID+) or did not (LID-) exhibit LIDs. Baseline SNpr GABAergic output to the Mthal in LID+ rats was higher than other groups ($P= 0.0048$), and decreased significantly following levodopa administration ($p = 0.0241$). SNpr firing pattern became more bursty in all groups after levodopa ($p>0.0001$). For Mthal, baseline firing rate was higher in LID+ groups than others ($p=0.0183$) and had greater spontaneous low threshold calcium spike (LTS) burst occurrence ($p = 0.0021$). Levodopa injection increased Mthal firing rate, however, this was disorganised with increased general burstiness ($p = 0.0027$) and decreased LTS burst occurrence ($p<0.001$). SNpr-Mthal paired recordings were critical to understand coherence between nuclei. Baseline coherence was high in LID and decreased following levodopa injection, showing chronic levodopa decreases network organisation. Results show that the levodopa dose inducing dyskinesia decreased SNpr activity in LID+ rats, resulting in disorganized Mthal hyperactivity. These changes differed significantly from LID- and naïve PD model rats, indicating long term levodopa use induces chronic pathological activity in the basal ganglia-Mthal network. These findings highlight potential targets to delay LID onset or reduce dyskinesia symptoms.

24.3

Deep cortical layers encode sustained changes in light conditions in freely moving mice

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Many mammalian species, such as the mice, switch between lit and dark environments during exploration of their environment in search of food and while avoiding predators by moving in and out from dark spaces. How neuronal activity encodes visual features in the primary visual cortex (V1) of many mammalian species in lit environments and under various luminance levels has been well studied. However, how the functionally distinct superficial and deep cortical layers of the V1 encode abrupt sustained changes in light conditions in freely exploring animals remains unclear. To address this question, we recorded neuronal activity from populations of V1 neurons located across the different layers (L2-L6) in freely exploring mice using our recently developed head-mounted 3-photon microscope that allows imaging in light or dark conditions. Using different mouse lines (Scnn1a-cre, Ntsr1-cre and wild-type), the activity from V1 layers 2/3, 4, 5 and 6 was recorded from neurons labelled with a genetically encoded calcium indicator (GCaMP7f), for up to 3 months, while mice were free to explore a linear track (0.8 x 0.1 m) under different sustained lighting conditions ranging from bright light (1.1 cd/m²), to complete darkness (>0.001 cd/m²). Initial analysis indicates that lighting conditions are differentially encoded across cortical layers, with sub-populations located in deep (L5 and 6) but not superficial (L2/3 and 4) layers displaying sustained activity during dark-conditions. Additionally, this activity is sustained in the dark-condition for the dark condition entirety (>7 min) and is not dependent on the animal's speed or head motion.