2025 Programme

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SYMBIOTIC DEVICES

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SYMBIOTIC DEVICES

2025 Programme at a Glance

SUNDAY 31ST AUGUST (GREAT HALL)									
			AWCBR REGISTRATION (4:30-6:00PM)	AWCBR OPENING RECEPTION (4:30-5:30PM)	AWCBR CONFERENCE OPENING (5:30-5:40PM)	PLENARY: PROF BILKEY (5:45-6:45PM)	DISORDERS OF THE NERVOUS SYSTEM (6:45-7:45PM)		
MONDAY 1ST SEPTEMBER (TE PAE, DOBSON D4)									
CELLULAR MECHANISMS (8:45-10:00AM)	MORNING TEA (10:00-10:30AM – DONSON FOYER)	DISORDERS OF THE NERVOUS SYSTEM (10:30AM-12:00PM)	LUNCH (12:00-1:00 PM– DONSON FOYER)	SYMPOSIA: NEUROIMAGING (1:00-3:00PM)	BREAK (3:00-3:30PM)	AWCBR AGM (3:30-4:30PM – AFTERNOON TEA FOR ATTENDEES AT 3:15PM IN THE – DONSON FOYER)	STUDENT & ECR EVENT (4:30-6:00PM)	AWCBR CONFERENCE DINNER (7:00-MIDNIGHT - DELILAH)	
TUESDAY 2ND SEPTEMBER (TE PAE, DOBSON D4)									
WORKSHOP: HORIZON'S EUROPE (8:30-9:15AM)	DEVELOPMENT (9:15-10:00AM)	MORNING TEA (10:00-10:30AM – EXHABITION HALL)	SENSORY AND MOTOR SYSTEMS (10:30AM-12:00PM)	LUNCH & TRADE DEMO (12:00-1:30PM – EXHABITION HALL)	FLASH TALKS (1:30-2:15PM)	POSTER SESSION 1 (2:15-3:30PM – EXHABITION HALL)	TEA/COFFEE (3:30-4:00PM – EXHABITION HALL)	POSTER SESSION 2 (4:00-5:15PM – EXHABITION HALL)	AWCBR STUDENT DINNER (7:00-10:00PM) / QRW SOCIAL MIXER (6:30-8:30PM – EXHABITION HALL)
WEDNESDAY 3RD SEPTEMBER(TE PAE, DOBSON D4)									
AWCBR 3KM FUN RUN (8:00-8:30AM)	PLENARY: PROF SHULTZ (9:00-10:00AM)	MORNING TEA (10:00-10:30AM – EXHABITION HALL)	COGNITION AND BEHAVIOUR (10:30AM-12:0PM)	LUNCH (12:00-1:00 PM – EXHABITION HALL)	SOCIAL ACTIVITIES (12:30-5:30PM)		QRW PANEL DISCUSSION & PLENARY (5:30-7:40PM - AUDITORIUM)	QRW SOCIAL MIXER & QUIZ (7:45-9:30PM – EXHABITION HALL)	
THURSDAY 4TH SEPTEMBER (TE PAE, DOBSON D4)									
DISORDERS OF THE NERVOUS SYSTEM (8:30-10:00AM)		MORNING TEA (10:00-10:30AM – EXHABITION HALL)	NOVEL METHODS (10:30AM-12:00PM)	LUNCH & TRADE DEMO (12:00-1:30PM – EXHABITION HALL)	PLENARY: PROF MONTGOMERY (1:30-2:30PM)	AWARDS & CLOSE (2:30-3:00PM)			

Sunday 31 August 2025

The Great Hall

4:30 pm-6:00 pm	Registration, The Great Hall, The Arts Centre, 2 Worcester Boulevard, Christchurch
4:30 pm-5:30 pm	Opening Reception, Drinks and Light Nibbles, The Great Hall
5.30 pm	Co-Chair's Opening Remarks, The Great Hall (Kyla-Louise Horne)

1. SYMBIOTIC DEVICES PLENARY LECTURE

CHAIR: ROB MUNN

5:45 pm 1.1 **David Bilkey,** ***University of Otago, Dunedin, New Zealand,***

Disorganized phase coding as a mechanism underlying sequential processing deficits in schizophrenia

Session sponsored by Symbiotic Devices

2. DISORDERS OF THE NERVOUS SYSTEM

CHAIR: SIMON O'CARROLL

6:45 pm 2.1 **Ali Rezaei,** ***Ludwig-Maximilians-Universität (LMU), Munich, Germany***

Cyclodextrin-mediated lipid normalisation rescues oligodendrocyte transcription and lifespan in female poly-GA C9orf72 ALS mice

7:00 pm 2.2 **Jim Davies,** ***University of Otago, Dunedin, New Zealand***

AAV-mediated sAPPa overexpression does not affect disease-like symptoms in the 5xFAD mouse model of Alzheimer's disease

7:15 pm 2.3 **Samantha Murray,** ***Lincoln University, Christchurch, New Zealand***

Dose response of intracerebroventricular and intravitreal CLN5 gene therapy in sheep

7:30 pm 2.4 **Frances Corrigan,** ***The University of Adelaide, Adelaide, Australia***

Evolution of axonal injury in the closed head impact model of engineered rotational acceleration in adult ferrets

3. NEURAL EXCITABILITY, SYNAPSES, AND GLIA: CELLULAR MECHANISMS

CHAIR: BLAKE HIGHET

8:45 am	3.1	**Bins Kathanadan Chackochan,** ***Cochin University of Science and Technology, Kerala, India*** The interplay between neurotrophic factor, CNTF, and transcription factor, Prrx-1, regulates adult neurogenesis in CNTF - treated mouse subventricular zone-derived neurosphere cultures
9:00 am	3.2	**Courtney Westlake,** ***University of Otago, Dunedin, New Zealand*** The influence of the neuromodulator sAPPα and derived peptides on NMDA-glutamate receptor expression in rodent and human neurons
9:15 am	3.3	**Laura McNamara,** ***University of Auckland, Auckland, New Zealand*** Assessing the impact of miniscopes in an in vivo Alzheimer's disease model
9:30 am	3.4	**Shadrina Asssegaf,** ***University of Otago, Dunedin, New Zealand*** Targeting soluble TNFα in the PS19 tauopathy mouse model
9:45 am	3.5	**Ross van de Wetering,** ***Victoria University of Wellington, Wellington, New Zealand*** Effect of cuprizone-induced demyelination on Alzheimer's-like pathology in 5xFAD mice
10:00 am		MORNING TEA BREAK (Dobson Foyer)

4. DISORDER OF THE NERVOUS SYSTEM

CHAIR: TAYLOR STEVENSON

10:30 am	4.1	**Sharon Olsen,** ***Auckland University of Technology, Auckland, New Zealand*** Aerobic exercise and concussion: Rethinking how we report and prescribe aerobic exercise in concussion rehabilitation

10:45 am	4.2	**Toni Pitcher,** ***University of Otago, Christchurch, New Zealand*** Preserved life expectancy in females with Parkinson's disease in an Aotearoa New Zealand cohort
11:00 am	4.3	**Tiphaine Saulnier,** ***University of Bordeaux, Bordeaux, France*** Understanding Parkinson's disease progression through patients' eyes: a study of quality of life decline over time
11:15 am	4.4	**Angus McNamara,** ***University of Adelaide, Adelaide, Australia*** Individuals with a prior history of traumatic brain injury present with more symptoms of prodromal Parkinson's disease than those without such a history
11:30 am	4.5	**Lyndsey Collins-Praino,** ***University of Adelaide, Adelaide, Australia*** Baseline striatal dopamine transporter binding and levels of CSF amyloid beta and hyperphosphorylated tau predict trajectory of cognitive change over a 5-year period in Parkinson's disease
11:45 am	4.6	**Daniel Myall,** ***New Zealand Brain Research Institute, Christchurch, New Zealand*** Frequency of Parkinson's genetic risk variants in New Zealand

12:00 pm LUNCH
(Dobson Foyer)

5. SYMPOSIA: AOTEAROA ADVANCED NEUROIMAGING RESEARCH SHOWCASE

CHAIRS: SAMANTHA HOLDSWORTH, WILLIAM SCHIERDING & TRACY MELZER

This symposium presents a national cross-section of leading-edge MRI developments and their clinical applications in neurological research across Aotearoa New Zealand. Attendees will be introduced to a broad spectrum of neuroimaging research interfaces using established and robust MRI methods, spanning gene therapy, cognitive prediction, and neurodegenerative disease mapping. Novel MRI techniques and hardware developments are also featured, including next-generation neuroimaging systems and the integration of novel MRI sequences with mathematical modelling of brain dynamics, immunohistochemical imaging validation, and applications in substance use recovery and brain injury. The program concludes with an introduction to MRI processing tools and data analysis. Attendees will hear from neuroimaging research groups working across New Zealand about their latest findings, discover collaborative opportunities that transcend geography, and explore ground-breaking innovations poised to reshape diagnostic precision, treatment approaches, and the broader landscape of neuroscience research.

Each presenter will speaker for 10 minutes and a collective Q&A will follow for 30 minutes.

1:00 pm	5.1	**Tracy Melzer,** ***University of Canterbury, Christchurch, New Zealand*** Tracking CLN5 gene therapy efficacy with brain MRI
1:10 pm	5.2	**Narun Pat,** ***University of Otago, Dunedin, New Zealand*** Boosting ability for brain MRI to predict cognitive functioning viamultimodal fusion
1:20 pm	5.3	**Cameron Heyman,** ***University of Auckland, Auckland, New Zealand*** Tract-specific WMH burden in groups spanning the clinical Alzheimer's continuum
1:30 pm	5.4	**Ben Parkinson,** ***Victoria University of Wellington*****, Wellington, New Zealand** A novel 0.7 T ultra-compact brain MRI scanner
1:40 pm	5.5	**Alireza Sharifzadeh-Kermani,** ***University of Auckland, Auckland, New Zealand*** Better than a hole in the head: a computational model of intracranial hypertension
1:50 pm	5.6	**Mangor Pedersen, Auckland** ***University of Technology, Auckland, New Zealand*** Imaging mild Traumatic Brain Injury: what is the role of iron and inflammation?
2:00 pm	5.7	**Miriam Scadeng,** ***University of Auckland, Auckland, New Zealand*** Validation of ultra high contrast neuroinflammatory MRI changes using immunohistochemistry
2:10 pm	5.8	**Maryam Tayebi,** ***Mātai Medical Research Institute, Gisborne, New Zealand*** Multi-parametric MRI mapping of brain changes in early-abstinent methamphetamine users
2:20 pm	5.9	**Eryn Kwon,** ***Medical Research Institute, Gisborne, New Zealand*** From data to discovery in mTBI: FAIR and CARE-aligned multimodal MRI pipelines and federated analysis
2:30 pm		**Q&A with the panel of speakers**
3:00 pm		BREAK
3:30 pm		**AWCBR AGM** All attendees are invited to join. Afternoon tea will be provided for AWCBR AGM attendees only at 3:15pm, Dobson Foyer

6. STUDENT AND EARLY CAREER RESEARCHER SESSION

CHAIRS: ROSS VAN DEWETERING & NICOLA SLATER

4:30 pm 6.1 **Navigating ethical dilemmas in neuroscience**

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

Join us for a social drink and nibbles in the Dobson Foyer before the presentation.

Being a neuroscientist often involves discussing sensitive topics about your research to friends, family, or the public. This session will cover to how to best communicate about research ethics, explain the role of human and animal ethics committees, and address common misconceptions . A brief presentation from our guest speaker will be followed by a Q&A.

Speaker:

Associate Professor Anna Mitchell, *University of Canterbury, Christchurch, New Zealand*

AWCBR CONFERENCE DINNER

7:00 pm – Midnight

DELILAH

122 Oxford Terrace, Christchurch

Tickets must be purchased in advance.

Tickets include food, drinks (including selected wine, beer, and non-alcoholic options) and musical entertainment, so put on those dancing shoes!

Cash bar after 10pm

7. WORKSHOP: HORIZON EUROPE – BRAIN HEALTH PARTNERSHIP IN NEW ZEALAND

CHAIR: KYLA-LOUISE HORNE

8:30 am 7.1 **Louise Parr-Brownlie, *Ministry of Business, Innovation and Employment, Wellington, New Zealand***

Come along to hear about the Horizon Europe–Brain Health Partnership, what you can do now to prepare for the upcoming opportunities, the expected activity in the next year, how to stay connected for updates, and to have your questions answered.

8. DEVELOPMENT

CHAIR: VICTOR DIERIKS

9:15 am 8.1 **Kseniia Konopkina*, University of Otago, Dunedin, New Zealand***
Harnessing multimodal MRI for cognitive functioning: Unpacking between-individual differences and longitudinal change

9:30 am 8.2 **Christian John Saludar, *University of Auckland, Auckland, New Zealand***
Effect of head acceleration events on microstructural organisation of brain cortical and deep grey matter: a diffusion MRI investigation

9:45 am 8.3 **Tristan Hurzeler, *University of Sydney, Sydney, Australia***
Neurobehavioral effects of cannabidiol (CBD) in individuals with alcohol use disorder: A double-blind, randomised control trial

10:00 am MORNING TEA BREAK
(Exhibition Hall)

9. SENSORY AND MOTOR SYSTEMS

CHAIR: ROBERT MUNN

10:30 am	9.1	**Damian Wallace,** ***Max Planck Institute for Neurobiology of Behavior, Bonn, Germany*** Eye saccades align optic flow with intended heading during object pursuit in freely moving mammals
10:45 am	9.2	**Emil Rosenov Peshtenski,** ***The University of Queensland, Brisbane, Australia*** Anti-CD14 improved functional outcomes, reduced neuroinflammation and seizures in a mouse model of severe traumatic brain injury
11:00 am	9.3	**Lily Bentall,** ***University of Otago, Dunedin, New Zealand*** EEG/LFP waveform shape asymmetry as a future biomarker for Parkinson's disease or levodopa-induced dyskinesia disease states
11:15 am	9.4	**Ann Holden,** ***University of Otago, Christchurch, New Zealand*** Do people with Parkinson's disease have increased perception of pareidolia?
11:30 am	9.5	**Aliesha Kemp,** ***University of Otago, Dunedin, New Zealand*** Treatment-Refractory Anxiety disorders: Altered activity and connectivity with emotional stimuli
11:45 am	9.6	**Eloïse Fairbairn,** ***University of Canterbury, Christchurch, New Zealand*** Characteristics of stuttered disfluencies in Parkinson's disease

12:00 pm	LUNCH (Exhibition Hall)
	EXHIBITOR LUNCHTIME PRESENTATIONS (Exhibition Hall)
12.10 pm-12.25 pm	**Decode Science** *One Solution with Decode - Discover your biomarkers and get the most out of your single cell and spatial data. Come hear the latest on Quanterix, Parse, STOmics and MGI from Alayna, Chris and Ebru and win some spot prizes too*
12.40 pm-12.55 pm	**Mediscope** *Empowering Healthcare and Science: Mediscope*

1.10 pm-1.25 pm **Mediray NZ Ltd & Eppensorf & Miltenyi**
Workflow solutions to prepare cells and nuclei for genomic analysis by Miltnenyi. Improved sample quality makes the difference. We have a solution for every step in the preparation of cells and nuclei for excellent genomic analysis results. From tissue storage to quality control, our technology will help your research achieve new heights.

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10. 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 60 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 Trade exhibition Hall for the poster session.

1:30 pm **Nicola Slater,** *University of Otago, Christchurch, New Zealand*
Kate Hitpass Romero, *University of Auckland, Auckland, New Zealand*
Joseph Balfe, *University of Otago, Dunedin, New Zealand*
Luke Bialostocki, *University of Otago, Dunedin, New Zealand*
Jazmine Brash, *Lincoln University, Christchurch, New Zealand*
Neda Nasrollahi, *University of Otago, Dunedin, New Zealand*
Taylor Stevenson, *University of Auckland, Auckland, New Zealand*
Benjamin Watkin, *University of Auckland, Auckland, New Zealand*
Irina Buianova, *University of Otago, Dunedin, New Zealand*
Christina Pike, *University of Otago, Christchurch, New Zealand*
Georgia Westfall, *Victoria University of Wellington, Wellington, New Zealand*
Jyot Kaur, *University of Auckland, Auckland, New Zealand*
Jenny Hamilton, *University of Canterbury, Christchurch, New Zealand*
William Parton, *University of Otago, Dunedin, New Zealand*
Charlotte Greenaway, *University of Otago, Dunedin, New Zealand*
Lisa Berriman, *University of Canterbury, Christchurch, New Zealand*
Isabella Culshaw, *University of Otago, Dunedin, New Zealand*
Ella Harris, *Lincoln University, Christchurch, New Zealand*
Catherine Sheat, *New Zealand Brain Research Institute, Christchurch, New Zealand*
Miriam Collins, *New Zealand Brain Research Institute, Christchurch, New Zealand*
Jean Yu Lim, *University of Auckland, Auckland, New Zealand*
Mikayla Chetty, *University of Auckland, Auckland, New Zealand*

Jasmine Sahota, *University of Otago, Dunedin, New Zealand*
Boglarka Varga, *University of Auckland, Auckland, New Zealand*
Ezra Muir, *University of Otago, Christchurch, New Zealand*
Manu Henderson, *University of Otago, Dunedin, New Zealand*
Isabella Cowie, *University of Otago, Dunedin, New Zealand*
Imogen Richards, *University of Auckland, Auckland, New Zealand*
Nisha Suresh, *Auckland University of Technology, Auckland, New Zealand*

11. POSTER SESSION

2:15 pm-5:30 pm

All posters should be put up in the Exhibition Hall between noon and 1:30 pm. They should remain up until 5:15 pm.

Presenters with odd numbered abstracts should be in attendance at their poster from 2:15 pm – 3:30 pm.

Presenters with even numbered abstracts should be in attendance at their poster from 4:00 pm – 5:15 pm.

All presenters need to remove their poster by 5:30 pm.

Velcro dots to hang your poster will be provided.

Poster board will be labelled P1, P2, P3 etc. Please refer to your poster board number in the programme below.

11.1 **Kate Hitpass Romero, *University of Auckland, Auckland, New Zealand* (P1)**
Age-related meningeal extracellular matrix remodelling compromises CNS lymphatic function

11.3 **Luke Bialostocki, *University of Otago, Dunedin, New Zealand* (P3)**
From signals to symptoms: infraslow triple-network brain dysconnectivity linked to pain in chronic knee osteoarthritis

11.5 **Neda Nasrollahi, *University of Otago, Dunedin, New Zealand* (P5)**
Ketamine effects on EEG and their links to therapy differ across treatment-resistant major depression, post-traumatic stress disorder, and obsessive-compulsive disorder

11.7 **Benjamin Watkin, *University of Auckland, Auckland, New Zealand* (P7)**
Development of patient-derived tumour organoids as a drug discovery model

11.9 **Christina Pike, *University of Otago, Christchurch, New Zealand* (P9)**
Diabetes, insulin, and Parkinson's disease risk: findings from two complementary population-based cohort studies

11.11	**Jyot Kaur,** ***University of Auckland, Auckland, New Zealand*** **(P11)** Investigating the effects of allopregnanolone and estradiol on cortical excitation using visually induced long-term potentiation
11.13	**William Parton,** ***University of Otago, Dunedin, New Zealand*** **(P13)** Electroencephalographic brain adaptations in individuals with chronic patellofemoral pain: Protocol for a source-localised neuroimaging investigation
11.15	**Lisa Berriman,** ***University of Canterbury, Christchurch, New Zealand*** **(P15)** Enrichment, episodic-like memory, and neuronal immediate-early gene expression
11.17	**Ella Harris,** ***Lincoln University, Christchurch, New Zealand*** **P17)** Cardiolipin and Batten disease: Investigating phospholipid alterations in ovine models
11.19	**Miriam Collins,** ***New Zealand Brain Research Institute, Christchurch, New Zealand*** **(P19)** Increased frequency of head injury in New Zealand Parkinson's disease cohort
11.21	**Mikayla Chetty,** ***University of Auckland, Auckland, New Zealand*** **(P21)** The effect of an impaired blood-brain barrier on microglial phenotype in Alzheimer's Disease
11.23	**Jasmine Sahota,** ***University of Otago, Dunedin, New Zealand*** **(P23)** Exploring tear fluid as a source of diagnostic biomarkers for Parkinson's Disease
11.25	**Ezra Muir,** ***University of Otago, Christchurch, New Zealand*** **(P25)** The mechanisms by which cholinesterase inhibitors improve apathy in dementia
11.27	**Isabella Cowie,** ***University of Otago, Dunedin, New Zealand*** **(P27)** Effects of an intravenously idministered sAPPα gene therapy on neuropathology in the 5xFAD mouse model of Alzheimer's disease
11.29	**Nisha Suresh,** ***Auckland University of Technology, Auckland, New Zealand*** **(P29)** Literature review on the effects of Yoga Nidra on the nervous system and sleep

3:30 pm	TEA/COFFEE BREAK (Exhibition Hall)

11.2 **Joseph Balfe, *University of Otago, Dunedin, New Zealand* (P2)**
A case for vagus nerve stimulation in modern medicine

11.4 **Jazmine Brash, *Lincoln University, Christchurch, New Zealand* (P4)**
The therapeutic evaluation of trehalose in sheep models of Batten disease

11.6 **Taylor Stevenson, *University of Auckland, Auckland, New Zealand* (P6)**
Cerebrospinal fluid and dural accumulation of alpha synuclein impairs CNS clearance in Parkinson's disease

11.8 **Irina Buianova, *University of Otago, Dunedin, New Zealand* (P8)**
Multimodal MRI marker of cognition explains the association between cognition and mental health in UK Biobank

11.10 **Georgia Westfall, *Victoria University of Wellington, Wellington, New Zealand* (P10)**
Effort, motivation and the medial prefrontal cortex: A neuropsychological study of brain tumour patients

11.12 **Jenny Hamilton, *University of Canterbury, Christchurch, New Zealand* (P12)**
Noradrenergic modulation of thalamocortical interactions in decision-making

11.14 **Charlotte Greenaway, *University of Otago, Dunedin, New Zealand* (P14)**
Function of cohesin in brain development

11.16 **Isabella Culshaw, *University of Otago, Dunedin, New Zealand* (P16)**
GLP-1 Receptor Agonism Modulates Local Field Potential in Lateral Septum and Alters Motivated Behavior in Rats

11.18 **Catherine Sheat, *New Zealand Brain Research Institute, Christchurch, New Zealand* (P18)**
Increased sleep disturbances in a New Zealand Parkinson's cohort

11.20 **Jean Yu Lim, *University of Auckland, Auckland, New Zealand* (P20)**
Investigating the role of microglial dysfunction in Alzheimer's Disease: Regulation of GPNMB Expression

11.22 **Nicola Slater, *University of Otago, Christchurch, New Zealand* (P22)**
Dominantly Inherited Alzheimer Network (DIAN) in New Zealand

11.24 **Boglarka Varga, *University of Auckland, Auckland, New Zealand* (P24)**
BDNF as a biomarker of neuroplasticity in LSD microdosing for Major Depressive disorder

11.26	**Manu Henderson, *University of Auckland, Auckland, New Zealand* (P26)** Development of a fluorescence-based assay to screen novel synthetic cathinones
11.28	**Imogen Richards, *University of Auckland, Auckland, New Zealand* (P28)** AAV serotype-promoter selection and implications for transduction efficiency in diverse human-derived GBM cell cultures
11.30	**Arunesh Mohandas, *Miltenyi Biotec, Bergisch Gladbach, Germany* (P30)** Maximizing spatial biology - A workflow combining 3D imaging with 2D multiparameter analysis of adult mouse brain

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6.00-8.00pm	**Evening Social Mixer** *Exhibition Hall E1+E2* Everyone welcome. No fee *Sponsored by Decode Science*

7:00pm	**AWCBR Student Dinner** The Church Pub 124 Worcester Street, Christchurch

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Wednesday 3 September 2025

Te Pae, Dobson D4

8:00 am

3km AWCBR Fun Run

3km fun run/walk along the Avon river/Otakaro, past the Canterbury Earthquake Memorial Wall, into the Christchurch Botanic Gardens to ring the NZ World Peace Bell before looping back to Te Pae.

Meeting Place and Time: Te Pae Lobby, Wednesday 3rd Sept 8:00AM.

No registration required.

12. PLENARY LECTURE

CHAIR: SIMON O'CARROLL

9:00 am 12.1

Sandy Shultz, *Monash University, Melbourne, Australia*

Translational insights into the aftermath and treatment of brain injuries caused by intimate partner violence

10:00 am

MORNING TEA BREAK
(Exhibition Hall)

13. COGNITION AND BEHAVIOUR

CHAIR: JENNY HAMILTON

10:30 am 13.1

Jessica Gu, *University of Auckland, Auckland, New Zealand*

Relationship between task-based fMRI activity during working memory task and mTBI-related symptoms in Adolescent Rugby Players: A Longitudinal Neuroimaging Study

10:45 am 13.2

Sam Guy, *The Auckland University of Technology, Auckland, New Zealand*

Cognitive effects of traumatic brain injury in a New Zealand prison

11:00 am 13.3

Ben Bristow, *Matai Medical Research Institute, Gisborne, New Zealand*

Multimodal MRI reveals brain structural deficits and executive dysfunction in early methamphetamine abstinence

11:15 am	13.4	**Kyla-Louise Horne, *University of Otago, Christchurch, New Zealand*** The structural integrity of nucleus basalis of Meynert and its association with hallucinations in Parkinson's disease
11:30 am	13.5	**Alina Tetereva, *New Zealand Brain Research Institute, Christchurch, New Zealand* (P27)** Source-space EEG functional connectivity and prediction of cognition in Parkinson's disease: No added benefit of individualized head models over standard templates
11:45 am	13.6	**Lee-Anne Morris, *University of Otago, Christchurch, New Zealand*** Decision cost hypersensitivity underlies Huntington's disease apathy

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12:00 pm	LUNCH (Exhibition Hall)
	EXHIBITOR LUNCHTIME PRESENTATIONS (Exhibition Hall)
12.40 pm-12.55 pm	**Thermo Fisher Scientific** *Quick and easy imaging on the new EVOS M3000 system.* *Presenter: Jason Lee*

12:30 pm

SOCIAL ACTIVITIES

Biking at the Christchurch Adventure Park

Come and experience the Southern hemisphere's largest mountain bike park. The lift-accessed mountain bike trails range from beginners through to advanced and the onsite coaches will ensure you have the best experience (https://christchurchadventurepark.com/).

Meeting Place: Christchurch Adventure Park, 50 McVicar Drive, Cracroft, Christchurch 8022

Finish: Variable depending on the package selected

Pre-Booking and payment required

Waipara Wine Tour

This tour explores three of North Canterbury's boutique vineyards all producing a fine selection of both white and red wines. Tour includes platter lunch and tastings at Waipara Springs, followed by further tastings at George's Road and Torlesse.

Meeting Place and Time: Te Pae Lobby Wednesday 3rd Sept 12:30PM

Duration: 4 hours approximately

Pre-Booking and payment required

Port Hills Walk
A guided walk from the Sign of the Takehe to Sign of the Kiwi return. Iconic elevated views of Lyttleton on one side of the Port Hills, out across the Canterbury Plains to the Southern Alps. Option to stop for afternoon tea at Sign of the Kiwi.
Meeting Place and Time: Te Pae Lobby Wednesday 3rd Sept 1:30PM
Duration: 4 hours approximately
Contact Christina (021 174 2275) if you would like to join

5:30 pm 14.1 **QRW 2025 Plenary Lecture**

Auditorium, Te Pae

Panel Discussion on Aotearoa New Zealand's future research, science & innovation sector:

Sir Peter Gluckman ONZ KNZM FRSNZ, *University of Auckland*
Professor Emily Parker FRSNZ, *Victoria University of Wellington*
Mark Piper CEO, *Transitional CEO, Bioeconomy Science Institute*
Professor David R. Grattan FRSNZ, *University of Otago*
MC: Dr Marie Bradley Director of strategy, *AgResearch*

6.30pm 14.2 **Prof. Tak Mak, *University of Toronto and Centre of Oncology and Immunology, University of Hong Kong***

Beyond immune checkpoint blockade: emerging strategies

Tak W. Mak is internationally reknown for his pioneering work on the genetics and molecular biology of cancer and the immune system. In 1984, his group cloned the gene encoding the human TCRβ chain, providing the basis for CAR-T treatment. His team also showed that CTLA4 negatively regulates T cell activation, paving the way for checkpoint inhibitor immunotherapy. Most recently, his team established that the brain communicates with the immune system via T and B cells producing acetylcholine. In the biotech arena, Dr. Mak co-founded Agios Pharmaceuticals and Treadwell Therapeutics. These companies specialize in delineating metabolic vulnerabilities in tumour cells that can be exploited as novel cancer therapies. Two IDH inhibitors are now FDA-approved for AML treatment, and two first-in-class agents targeting aneuploidy in advanced tumours are now in phase II clinical trials. Dr. Mak has published over 1000 peer-reviewed research papers, holds dozens of patents, and has won numerous awards.

Plenary Lecture sponsored by Mediscope International Limited

7.45-9.30pm	**Evening Social Mixer** *Exhibition Hall E1+E2* *Everyone welcome. No fee*
8.00-8.30pm	**The Great Trivia Night with Pierre de Cordovez** *Exhibition Hall E1+E2* *Sponsored by Thermo Fisher Scientific*

15. DISORDERS OF THE NERVOUS SYSTEM

CHAIR: ROSS VAN DE WETERING

8:30 am	15.1	**Luca Vinnell,** ***University of Auckland, Auckland, New Zealand*** Investigating the disruptive role of T-cells in Parkinson's disease
8:45 am	15.2	**Rebecca Hartley,** ***University of Auckland, Auckland, New Zealand*** Adeno-associated virus vector targeting of striatal astrocytes and neurons
9:00 am	15.3	**Kirsten Carter,** ***Victoria University of Wellington, Wellington, New Zealand*** Relevance of the kappa opioid receptor as a potential dual-regulatory therapeutic for Multiple Sclerosis
9:15 am	15.4	**Sam McCullough,** ***University of Auckland, Auckland, New Zealand*** Characterising changes in immune cell populations at the brain borders after traumatic brain injury
9:30 am	15.5	**Amitai Zuckerman,** ***University of Auckland, Auckland, New Zealand*** The kor receptor nalfurafine improves inflammation in a rodent model of spinal cord injury
9:45 am	15.6	**Victor Dieriks,** ***University of Auckland, Auckland, New Zealand*** Neuronal α-synuclein toxicity drives degeneration in Multiple System Atrophy

10:00 am — MORNING TEA
(Exhibition Hall)

16. NOVEL METHODS AND TECHNOLOGY DEVELOPMENT

CHAIR: LILY BENTALL

10:30 am	16.1	**Jason Kerr,** ***Max Planck Institute for Neurobiology of Behavior, Bonn, Germany*** Simultaneous 2- and 3-photon multiplane imaging across cortical layers in freely moving mice

10:45 am	16.2	**William Aye, *University of Otago, Christchurch, New Zealand*** Streamlining neurodegenerative imaging: Early-phase amyloid PET as a one-stop modality, comparisons with FDG PET and ASL MRI
11:00 am	16.3	**Timofei Vorozhbit, *University of Otago, Dunedin, New Zealand*** Investigating a potential “viability switch” in a juvenile-onset ATP13A2-associated Parkinson’s disease model
11:15 am	16.4	**Muna Dhakal, *University of Auckland, Auckland, New Zealand*** Mapping Nurr1’s functional domains for targeted gene activation and therapeutic use in Parkinson’s disease
11:30 am	16.5	**Farzane Lal Khakpoor, *University of Otago, Dunedin, New Zealand*** Benchmarking different MRI phenotypes for ethnic bias in cognitive-functioning prediction
11:45 am	16.6	**Eileen Lueders, *University of Auckland, Auckland, New Zealand*** From menarche to menopause: estradiol and brain aging in women

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12.00 pm	LUNCH (Exhibition Hall) EXHIBITOR LUNCHTIME PRESENTATIONS (Exhibition Hall)
12.40 pm-12.55 pm	**Thermo Fisher Scientific** *Simple steps to greener choices in the lab.* *Presenter: Sabine Audigé*
1.10pm-1.25pm	**Custom Science** *Illuminating Innovation: Flexible Imaging with Azure Biosystems’ Sapphire FL and Azure 600 Content* *Speaker: Nicole Cheah Regional Business Director (APAC) Azure Biosystems Inc, United States* *Join us for a 15-minute presentation that delves into the cutting-edge imaging technology of the Sapphire FL Biomolecular Imager and the Azure 600, showcasing their advanced capabilities in fluorescence, chemiluminescence, near-infrared, and phosphor imaging. With broad application flexibility—from Western blotting and gel documentation to multiplex protein analysis, in-cell western and radiolabeled sample detection, these platforms deliver high sensitivity, reproducibility, and workflow efficiency. Discover how these instruments can help you "see" more in your research and accelerate your path to discovery.*

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17. PLENARY LECTURE

CHAIR: KYLA-LOUISE HORNE

1:30 pm	17.1	**Joanna Montgomery,** ***University of Auckland, Auckland, New Zealand*** The role of plasticity in the central and peripheral nervous systems	

2:30 pm – 3:00 pm AWARDS AND CLOSING REMARKS

2025 QRW Events

QRW MIHI WHAKATAU
Tuesday 2 September, Conway C5, 7.30 am-8.00 am
Registration required. No fee.

QRW POSTER SESSIONS
Tuesday 2 September, Exhibition Hall, 6.00 pm-8.30 pm
Block A meetings Poster Session (AI, AMR, ASI NZ, Heart and Indigenous Genomics)
Free to attend. No registration required

Wednesday 3 September, Exhibition Hall, 3.00pm-5.00pm
Medsci Poster Session
Free to attend. No registration required

Thursday 4 September, Exhibition Hall, 4.00pm-6.00pm
QMB Poster Session
Free to attend. No registration required

MEDSCI NZ MEEING (THURSDAY ONLY)
MedSci - NZ Medical Sciences Congress incorporates the annual meetings of the NZ Society of Endocrinology and Physiological Society of NZ.
Free for AWCBR Delegates to attend on Thursday only. No registration required

QRW EVENING MIXERS
Tuesday 2 September, Exhibition Hall, 6.00-8.00pm
Evening Social Mixer
Everyone welcome. No fee
Sponsored by Decode Science

Wednesday 3 September, Exhibition Hall, 7.45-9.30pm
Evening Social Mixer & The Great Trivia Night
Everyone welcome. No fee
Sponsored by Thermo Fisher Scientific

SCIENCE MEDIA SAVVY EXPRESS
Science Media SAVVY Express offers one-on-one training for researchers to improve the way they communicate key ideas from their work with the wider public. These 15 minute sessions are an opportunity to practice speaking on-camera in a safe environment, with helpful advice and practical tips from experienced and supportive media experts. As an added bonus, you can request a copy of your videos that you are free to reuse. Participation is open to all New Zealand-based scientists and researchers attending any QRW meeting, and is free of charge - however places are limited and entry is by selection. We will be on-site at the conference venue on the mornings of **Wednesday 3 September and Thursday 4 September only**. You must be a New Zealand-based researcher to apply. **Register here** to express your interest in participating. Entry is by selection.

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)
2016	**Jennifer Robertson,** Australian National University, Australia **Allanah Kenny,** University of Canterbury, New Zealand (Poster)
2017	**Hannah Best,** University of Otago, New Zealand **Ashwini Hariharan,** University of Otago, New Zealand (Poster)
2018	**Jarred Griffin,** University of Auckland, New Zealand **Alice McDouall,** University of Auckland, New Zealand (Poster)
2019	**Mohammed Ibrahim,** University of Otago, New Zealand **Kendra Boyes,** Victoria University of Wellington, New Zealand (Poster) **Nikita Lyons,** University of Auckland, New Zealand (Infoblitz)
2020	**Karan Govindpani,** University of Auckland, New Zealand (by zoom)
2021	**Sophie Farrow,** University of Auckland, New Zealand (Press Release)
2022	**Maize Coa,** University of Auckland, New Zealand **Kyrah Thumbadoo,** University of Auckland, New Zealand (Poster)
2023	**Kate Witt,** Victoria University of Wellington, New Zealand **Oliver Burnett,** University of Auckland, New Zealand (Poster)
2024	**Chelsie Osterman,** University of Auckland, Auckland, New Zealand **Baraa Abuharbid,** University of Auckland, Auckland, New Zealand (Poster) **Thomas Cawood,** University of Otago, Dunedin, New Zealand (Flash Talk)

Prize Winners

Aotearoa Brain Project Speaker and Poster Prize Winners (ECR)

2022 **Macarena Pavez,** University of Otago, New Zealand
Ruth Monk, University of Auckland, New Zealand (Poster)

2023 **Michael Kendig,** University of Technology Sydney, Sydney, Australia
Taylor Stevenson, University of Auckland, Auckland, New Zealand (Poster)

2024 **James Wiseman,** University of Auckland, Auckland, New Zealand
Christine Arasaratnam, University of Auckland, Auckland, New Zealand (Poster)

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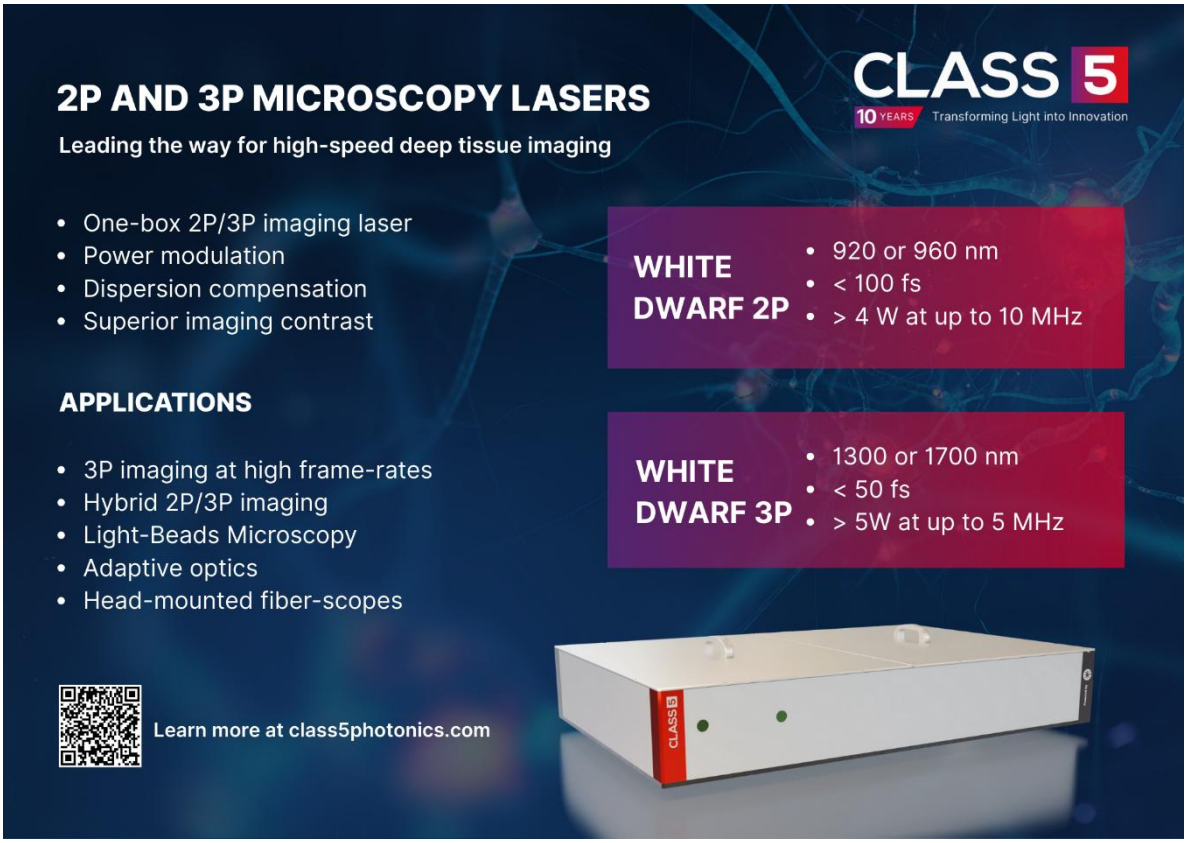

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Abstracts in Presentation Order

Proceedings of the International Australasian Winter Conference on Brain Research, 2025, 41, will be published on the AWCBR website.

1.1

Disorganized phase coding as a mechanism underlying sequential processing deficits in schizophrenia

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Many neural processes, including episodic memory, require that information is stored and recalled in sequential order. Some of these sequencing processes appear to be disrupted in schizophrenia. Phase precession has been proposed as a biological mechanism that might underlie the sequential ordering of experience at timescales suitable for supporting neural plasticity. Work from our lab has examined these mechanisms using single unit recording in the hippocampus of freely moving animals. A comparison of control animals and those manipulated using a maternal immune activation (MIA) model of a schizophrenia risk factor revealed that precession was altered by MIA. Although the phase precession of hippocampal CA1 neurons against local theta activity was preserved in MIA animals, the phase offset was considerably more variable when compared to controls. A critical theoretical consequence of this variability is that the ordered representation of experience, encoded via theta sequences, becomes disorganized. Phase precession was also observed in neurons recorded from the lateral septum, however, in MIA animals, the phase trajectory was altered and appeared to be less coupled to reward location in the environment. Changes in phase precession may, therefore, underlie aspects of disordered sequencing and aberrant reward salience in schizophrenia, although, the evidence so far is correlational. Several recent studies will be described that are starting to close this gap by linking phase precession to human memory and experience.

2.1

Cyclodextrin-mediated lipid normalisation rescues oligodendrocyte transcription and lifespan in female poly-GA C9orf72 ALS mice

Ali Rezaei[1,2,3], Virág Kocsis-Jutka[1], Zeynep I. Gunes[2,3,4,5], Qing Zeng[1,3], Georg Kislinger[1,2], Franz Bauernschmitt[2,4,5], Huseyin Berkcan Isilgan[1], Laura R. Parisi[6], Tuğberk Kaya[1,2,7], Sören Franzenburg[8], Jonas Koppenbrink[1], Julia Knogler[1], Thomas Arzberger[9,10], Daniel Farny[1], Brigitte Nuscher[11], Eszter Katona[1,2,3], Ashutosh Dhingra[12], Chao Yang[1], Garyfallia Gouna[1,3,13], Katherine D. LaClair[1], Aleksandar Janjic[14], Wolfgang Enard[14], Qihui Zhou[1,2], Nellwyn Hagan[6], Dimitry Ofengeim[6], Eduardo Beltrán[2,4,5], Ozgun Gokce[2,3,15], Mikael Simons[1,2,3,13], Sabine Liebscher[2,3,4,5,16] and Dieter Edbauer[1,2,3]

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Altered cholesterol handling is increasingly implicated in amyotrophic lateral sclerosis (ALS), yet cell-type-specific mechanisms and therapeutic leverage points remain elusive. We combined bulk RNA-seq, single-nucleus transcriptomics, AI-assisted immuno-electron microscopy, targeted lipidomics and behavioural phenotyping across three ALS mouse lines (poly-GA GA-Nes, neuron-restricted GA-Camk2a, TDP-43ΔNLS rNLS8) and post-mortem spinal cord. Cross-species meta-analysis revealed a conserved repression of sterol-biosynthetic enzymes and induction of cholesterol export, esterification and lipid-droplet genes, indicating intracellular cholesterol overload. Oligodendrocytes adopted a previously unrecognised disease-associated state marked by Serpina3n, Plin4 and ApoD that encompassed ~40 % of mature cells and mirrored signatures in Alzheimer's and multiple sclerosis. Daily subcutaneous 2-hydroxypropyl-β-cyclodextrin (2 g/kg) from postnatal day 21 selectively benefited the fast-progressing GA-Nes line: in females it normalised cholesteryl-ester species (CE18:1, CE22:4), halved serum neurofilament-light, restored myelin-gene expression, increased corpus-callosum myelinated-axon density by 45 %, shifted microglia from a myelin-DAM to an amyloid-DAM profile, and extended median survival from 43 to 52 days (+21 %). Interestingly, male mice did not exhibit statistically significant benefits from CD treatment. Single-nucleus RNAseq analyses confirmed that cyclodextrin primarily dampened oligodendroglial cholesterol-stress programmes and partially rescued neuroblast axonogenesis pathways without altering poly-GA aggregation. Collectively, our data identify cholesterol-loaded oligodendrocytes as modulators of axonal vulnerability and demonstrate that pharmacological reduction of free cholesterol confers a sex-dependent, disease-modifying benefit in ALS, supporting stratified clinical trials of cyclodextrin derivatives for cholesterol-overloaded patient subtypes.

2.2

AAV-mediated sAPPa overexpression does not affect disease-like symptoms in the 5xFAD mouse model of Alzheimer's disease

James W.T. Davies[1], Bruce G. Mockett[1], Connor J. Nicholls[1], Lucia Schoderboeck[2], Stephanie M. Hughes[2] and Wickliffe C. Abraham[1]

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Soluble amyloid precursor protein-alpha (sAPPa) 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 is the first study assessing whether AAV-mediated sAPPa overexpression in the brain would improve disease-like symptoms in 5xFAD mice. We injected intravenously 1x10^11 AAV.CAP-B10 viral vectors carrying the human sAPPa transgene into wild-type and 5xFAD mice. Control mice received a vector carrying the transgene for green fluorescent protein. Male and females were injected at two months of age, before overt pathology emerged. At 8-9 months of age, behavioural, electrophysiological, and post-mortem assessments were conducted. There was no treatment effect on the behavioural phenotype of 5xFADs, which included altered anxiety-like behaviour, exploration, and spatial memory. In vitro hippocampal field recordings revealed a reduction in long-term potentiation in the dentate gyrus of 5xFADs which treatment partially rescued, but no group differences in CA1. Post-mortem analyses revealed upregulated sAPPα expression in the brain but also, unexpectedly high basal levels of sAPPa in 5xFADs, thus possibly limiting the phenotype and treatment efficacy. These results suggest that while AAV.CAP-B10 enabled gene delivery to the brain, the relatively small degree of sAPPα overexpression was insufficient to ameliorate the AD-like phenotypes in this model. Further post-mortem analyses are underway to assess viral transduction efficiency and effects on plaque load and neuroinflammation processes.

2.3

Dose response of intracerebroventricular and intravitreal CLN5 Gene therapy in sheep

Samantha J Murray[1], Madeleine J Palmer[1], Jazmine Brash[1], Martin P Wellby[1] and Nadia L Mitchell[1]

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Neuronal ceroid lipofuscinoses (NCLs) are a group of rare, inherited, and fatal neurodegenerative disorders that primarily affect children. Sheep with a naturally occurring CLN5 variant of NCL exhibit clinical and pathological features closely resembling those seen in human patients. Previous trials using combined intracerebroventricular (ICV) and intravitreal (IVT) gene therapy, administered at varying doses and treatment ages, have shown mixed results. The current trial aimed to optimize therapeutic outcomes by delivering high-dose treatment during the early symptomatic stage of disease progression. Sheep received either a very high dose (VHD; 1.3×1013 viral genomes (vg) ICV and 9.0×1010 vg IVT) or a high dose (HD; 2.6×1012 vg ICV and 1.8×1010 vg IVT) treatment at 6 months of age. Both doses were well-tolerated and all treated sheep survived until the pre-determined endpoint of 36 months of age. In-life assessments showed stabilised clinical scores, brain volumes, and vision in the majority of treated sheep. Post-mortem analysis confirmed amelioration of disease associated neuropathology and retinal pathology. Collectively these findings further validate the safety and long-term efficacy of combined CLN5 gene therapy, and inform on optimal doses for the clinical trial currently underway for children with CLN5 disease (clinicaltrials.gov NCT05228145).

2.4

Evolution of axonal injury in the closed head impact model of engineered rotational acceleration in adult ferrets

Frances Corrigan[1], Justin L Krieg[1], Kosta Antolis[1], Carl Hooper[1], Hasini Kapuwelle[1], Rebecca George[1], Anna V Leonard[1], and Renée J. Turner[1]

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Concussion-related symptoms such as impaired balance, slower processing speed, attention deficits, memory dysfunction, and irritability are thought to result from diffuse axonal injury (DAI), characterised by selective damage to white matter axons. Axons subjected to this mechanical stretch injury exhibit diverse pathological changes, including disruption of axonal transport, neurofilament compaction and degradation, myelin sheath disruption, and loss of sodium channels required for action potential generation and propagation. These distinct forms of axonal pathology may evolve differentially over time and preferentially localise to specific white matter tracts. In this study we employed the clinically relevant ferret model of concussion using the Closed Head Impact Model of Engineered Rotational Acceleration (CHIMERA). 55 male ferrets were randomly allocated to sham or injury groups and then to either 24h, 72h or 14d survival time-points. We confirmed that axonal transport disruption and neurofilament pathology represent independent processes, with minimal co-localisation, but a shared peak of around 72 hours following injury. Furthermore, we observed a persistent loss of ankyrin-G, a critical anchoring protein for sodium channels at the node of Ranvier, up to 14 days post-injury, suggesting that the resultant impairment in axonal transmission may underlie many concussion symptoms. Indeed, injured ferrets displayed significant deficits in balance, working memory, spatial memory, and recognition memory over the same period. These findings demonstrate that the CHIMERA model in ferrets recapitulates key axonal pathologies and their associated clinical manifestations following concussion. This model offers a valuable platform for investigating the temporal evolution of axonal injury and developing targeted therapeutic interventions to mitigate concussion-related deficits.

3.1

The interplay between neurotrophic factor, CNTF, and transcription factor, Prrx-1, regulates adult neurogenesis in CNTF - treated mouse subventricular zone-derived neurosphere cultures

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Neural Stem Progenitor Cells (NSPCs) maintenance and neuronal cell differentiation are two key aspects of sustained neurogenesis in the adult mammalian brain. Transcription factors (TFs) are known to regulate these biological processes under the influence of various neurotrophic factors. Although several molecular mechanisms leading to adult neurogenesis have been reported, details on its transcriptional regulation are still limited. Our results showed that Ciliary Neurotrophic Factor (CNTF) reduced the overall proliferation of NSPCs at the expense of differentiating them to both GFAP+ve glial progenitors and Tuj1+ve neurons. Our co-labeling studies revealed that Tuj1+ve neurons arose from GFAP+ve glial progenitors. To identify the key regulators of this glia-to-neuron switch, whole transcriptome RNA-sequencing analysis of CNTF-treated NSPCs revealed 483 differentially expressed genes and identified paired-related homeobox protein (Prrx-1) as a significantly upregulated TF gene in CNTF-treated neurosphere cultures. To further investigate the interplay between the transcription factor, Prrx1, and CNTF in differentiating GFAP progenitors to neurons, lentiviral knockdown of the Prrx1 gene was carried out in SVZ-derived NSPCs. Prrx-1 ablation significantly reduced the differentiation of GFAP+ve progenitors into Tuj1+ve neurons, and the CNTF treatment showed no pro-neural effect. This could suggest that Prrx1 may act as a critical regulator in the intrinsic transcriptional networks driving the adult neurogenesis process under the influence of CNTF and warrants further investigations to elucidate the molecular mechanisms underlying their interactions. In the future, research on their interplay can be further explored to generate a homogenous population of neuronal progenitors in translational stem cell research.

3.2

The influence of the neuromodulator sAPPα and derived peptides on NMDA-glutamate receptor expression in rodent and human neurons

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Secreted amyloid precursor protein-alpha (sAPPα), an endogenous neuromodulator, and CTα16, a bioactive sAPPα-derived peptide, rescue synaptic plasticity deficits in rodent Alzheimer's Disease (AD; Tuapaemahara) models. This positions sAPPα as a potential therapeutic for AD, although its efficacy in human neurons remains unclear. This work aims to understand the molecular mechanisms underpinning sAPPα's plasticity-promoting effects. We first examined altered synthesis and cell surface expression of plasticity-related N-methyl-D-aspartate receptor (NMDAR) subunits in cultured rodent hippocampal neurons in response to 1nM sAPPα. To bridge the translational gap between rodent models and clinical application, we next examined the ability of sAPPα and CTα16 to alter NMDAR surface expression in excitatory and inhibitory iPSC-derived human neurons (iPSC-HNs). Using a combination of immunocytochemistry and Fluorescent Non-Canonical Amino Acid Tagging with Proximity Ligase Assay (FUNCAT-PLA), we show sAPPα biphasically increases surface de novo GluN2B-containing NMDARs in rodent neuronal dendrites (1.6-fold, 30 min, p=0.0068; 1.8-fold, 240 min, p=0.011). Furthermore, we show sAPPα and CTα16 enhanced GluN2B surface expression in a time- and cell-type-specific manner in iPSC-HNs (1.24-fold in excitatory neurons, 120 min, p<0.0001; 1.37-fold in inhibitory neurons, 240 min, p<0.0001). These findings complement established understanding that sAPPα rapidly traffics AMPA-glutamate receptors, priming the synapse for activity, suggesting NMDARs may contribute to priming activity and also support sustained synaptic changes. Demonstrating efficacy of sAPPα in human neuronal models represents a critical step toward translating sAPPα-based therapies. The novel finding of differential responses in excitatory versus inhibitory human neurons suggests sAPPα may target the excitatory-inhibitory imbalance implicated in early-AD.

3.3

Assessing the impact of miniscopes in an in vivo Alzheimer's Disease model

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Alzheimer's disease (AD) is the most common neurodegenerative condition worldwide, resulting in an insidious cognitive decline. There is limited evidence of real-time circuit and subcellular changes as AD progresses, requiring in vivo acquisition of cellular activity during behavioural tasks. Head-mounted miniaturised microscopes (miniscopes) allow chronic recording of in vivo calcium activity in freely moving rodents. However, the potential physiological and behavioural impact of the miniscope itself is unreported in all literature to date. We aimed to elucidate the relationship between pyramidal cellular activity and behavioural paradigms in a murine AD disease model and how this could be altered utilising miniscopes in vivo. AD (APPswe/PS1dE9) and control mice received adeno-associated viral plasmid injections for the calcium activity reporter (GCaMP7s) into the CA1 hippocampus, were superiorly implanted with a gradient-index lens and affixed with a miniscope baseplate. Genotype-matched mice without implants were also utilised for experiments. Mice performed open field, y-maze, and novel object recognition behavioural tests, with calcium data concurrently collected via miniscopes. Our findings indicated AD animals exhibit increased ambulation, reduced peak widths and diminished peak amplitudes from time of implantation. Brain tissue was collected for immunohistochemical analysis of neuronal counts, GCaMP expression, microglial activation, plaque distribution and synaptic density. Implanted animals exhibited significant microgliosis in the corpus callosum and elevated synaptic density in the CA1 stratum pyramidale. Our results indicate the use of miniscopes as an in vivo technique produces significant alterations to brain function and structure, which could influence the disease phenotype being investigated in resulting experiments.

3.4

Targeting soluble TNFα in the PS19 tauopathy mouse model

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Neurodegenerative diseases are characterised by progressive neuronal loss, and behavioural dysfunction. In recent years, soluble tumour necrosis factor-alpha (sTNFα) has been identified as a key mediator of inflammation and synaptic pathology in Alzheimer's disease, yet its role in tauopathies such as frontotemporal dementia remains unclear. We therefore investigated whether inhibition of sTNFα using XPro1595 (INmuneBio) can rescue physiological and behavioural impairments in the PS19 tauopathic mouse model. XPro1595 was designed to cross the blood-brain barrier and inhibit soluble TNFα while sparing transmembrane TNFα. Mice were divided into four groups based on genotype (wild-type vs transgenic) and treatment (saline vs XPro1595). Male and female mice received twice-weekly subcutaneous injections at 4 months of age, continuing until the end of experimentation. At 6 months of age, behavioural tests were conducted to assess locomotion, anxiety and memory, including the open field test, elevated plus maze, rotarod, Barnes maze, and Y-maze. Following behavioural testing, electrophysiological recordings were performed in hippocampal slices, targeting the CA1 stratum radiatum. Synaptic plasticity was assessed using a theta-burst stimulation protocol to elicit long-term potentiation (LTP). Although the group allocations remain blinded, preliminary analyses reveal an emerging pattern of possible treatment effects. Preliminary trends suggest that mice treated with solution 'D' displayed improved memory performance in behavioural tasks and improved LTP compared to mice treated with solution 'C', for both genotypes. If confirmed upon unblinding, these results would align with findings in Alzheimer's models and extend the therapeutic relevance of sTNFα inhibition to tauopathies and potentially broader neurodegenerative contexts.

3.5

Effect of cuprizone-induced demyelination on Alzheimer's-like pathology in 5xFAD mice

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Exacerbated demyelination has been observed in Alzheimer's disease (AD) as well as in animal models of AD. Some studies have found that demyelination can precede hallmark AD pathologies and have suggested that demyelination may play a more causative role. Previous efforts to directly investigate this, however, were limited by the choice of demyelination model and potential confounds related to disrupted copper homeostasis. In the current study, we addressed these issues and examined the causal role of demyelination on the development of AD-like pathology in a genetic mouse model of AD. Male and female, 12-week-old 5xFAD mice were fed a diet containing 0.2% cuprizone for 8 weeks, with or without 0.1% CuSO4 supplementation. Mice were perfused at either 8 or 12 weeks, and coronal sections were immunohistochemically labelled for myelin (MBP), microglia (IBA1), and amyloid-beta (6E10). Compared to controls, cuprizone-treated mice showed widespread demyelination and significant microgliosis within white matter regions at week 8, which partially recovered by week 12. Cuprizone treatment also caused significant time- and region-dependent increases in amyloid-beta, which was accompanied by reduced microglia co-localisation with amyloid plaques. These findings support a region-dependent causal link between demyelination and amyloid plaque aggregation that may be driven by a diversion of microglial activity toward the clearance of myelin debris at the expense of amyloid plaques.

4.1

Aerobic exercise and concussion: Rethinking how we report and prescribe aerobic exercise in concussion rehabilitation

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Concussion cases in Aotearoa New Zealand have surged and nearly half of concussion sufferers have persistent symptoms at 12 months. Current guidelines recommend a 21-day sport standdown with light aerobic activity, and research supports the use of sub-symptom aerobic exercise to support recovery. However, the optimal aerobic exercise parameters (i.e., session duration, frequency per week, challenge level) and underlying mechanisms are unknown, although improvements in autonomic dysfunction are postulated. Before exploring the optimal aerobic exercise parameters, they first need to be clearly identified and reported. This presentation will summarise two studies that have explored: i) the reporting of aerobic exercise parameters in RCT literature (systematic review), and ii) the prescription of aerobic exercise parameters by NZ physiotherapists (online survey). Within concussion RCT literature, aerobic exercise parameters are often incompletely reported, particularly concerning the session duration, warm up/cool down time, challenge level, and progression/regression. Despite the varied needs of individuals with concussion, personalisation of aerobic exercise—considering cultural, psychological, or environmental factors—is rarely addressed in the literature. In contrast, many NZ physiotherapists prescribe a specific duration and challenge level of aerobic exercise, and a proportion also use personalisation strategies. This reflects a gap between research and clinical practice. This presentation makes the case for improved standardisation and reporting of dosage and personalisation parameters in aerobic exercise research, to ensure research reflects the complexities of real-world clinical practice and to facilitate the exploration of optimal exercise parameters after concussion and their underlying mechanisms.

4.2

Preserved life expectancy in females with Parkinson's disease in an Aotearoa New Zealand cohort

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Neurodegenerative disorders are often associated with a reduced life expectancy. Using the New Zealand Parkinson's Progression Programme (NZP[3]), a longitudinal study of the progression of Parkinson's, we examined the life expectancy of people with Parkinson's and identified the main causes of death. Over 17 years, 401 (277 males and 124 females) people with Parkinson's have been recruited into NZP[3]. During this time we have recorded 174 deaths (139 males, 35 females). At the time of death, people with Parkinson's were an average of 78.2 years of age and 12.0 years since diagnosis. Using survival models we compared the life expectancy of those with Parkinson's to a randomly generated control sample using the New Zealand life tables, matched for year of birth and sex. Life expectancy was preserved in females with Parkinson's but was reduced by three years in males. When examining the main causes of death in Parkinson's, respiratory, cardiovascular, and cancer were most common, which is slightly different to the general population where cancer and cardiovascular causes were more common than respiratory. Future work will extend this analysis to the national level, including the entire New Zealand Parkinson's population.

4.3

Understanding Parkinson's disease progression through patients' eyes: a study of quality of life decline over time

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Patient perceptions of disease represent an important source of information offering insights to better understand progression and improve care through support for patients' needs. However, health-related quality of life (Hr-QoL) studies often rely on patient-reported questionnaires with ordinal items that are typically summarized into scores, leading to a loss of information. Moreover, missing responses, questionnaire multidimensionality, and patient dropout during follow-up further complicate analysis. In this work, we describe Hr-QoL changes in Parkinson's disease (PD) using the 4S method – a comprehensive item response theory-based strategy that captures traits underlying responses to items while addressing those analytical challenges. We analyzed data from the New Zealand Parkinson Progression Programme (NZP[3]), including over 400 PD patients with regular follow-up over 16 years. Hr-QoL was assessed using the PDQ-39 questionnaire, covering motor and non-motor spheres. The 4S method comprises four successive steps: (1 – structuring) identify scale dimensions, (2 – sequencing) describe each dimension's progression and associated factors, (3 – staging) compare progression across clinical stages, and (4 – selecting) highlight the most informative items. Five dimensions were identified: mobility, daily activities, psycho-social, stigma, and cognition/communication/bodily discomfort. All, except stigma, showed progressive decline, with patterns notably varying by sex and age at onset. Items related to walking, dexterity, anxiety, and communication were found to be particularly sensitive manifestations during PD stages and may guide clinicians in providing appropriate support. Therefore, patient perceptions of PD provide valuable information on disease progression and offer avenues for enhancing patient-centered care.

4.4

Individuals with a prior history of traumatic brain injury present with more symptoms of prodromal Parkinson's disease than those without such a history

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While prior history of traumatic brain injury (TBI) is associated with increased risk of developing Parkinson's Disease (PD), it is not yet understood who will develop this outcome. PD is associated with prodromal symptoms that present years, or decades, prior to clinical onset. This study assessed whether prodromal presentation differs in individuals with and without a history of TBI. Data from the Forecasting Impairment and Neurodegenerative Disease risk following Traumatic Brain Injury (FIND-TBI) study were used. Participants were categorised as: control (n = 104), TBI (n = 126) or PD (n = 45). Positive predictive likelihood scores for prodromal PD (PPL scores) were calculated by summing weighted scores (based on Movement Disorders Society criteria) for: male sex, REM-sleep behaviour disorder questionnaire (RBDSQ), hyposmia (Sniffin' Sticks Identification score), constipation, daytime somnolence, orthostatic hypotension, erectile dysfunction (if male), urinary urgency, depression (CESD-10), global cognitive impairment (Montreal Cognitive Assessment), history of Type II diabetes and having a first-degree relative with PD. Linear regression assessed whether prior history of TBI predicted PPL score. Individuals with prior history of TBI had significantly higher PPL scores relative to controls without such a history. When controlling for age, education, male sex and PD diagnosis, prior history of TBI was predictive of total prodromal score ($\beta = 3.37$, 95% CI [2.20-4.54], $p = 0.003$), with $R2 = 0.421$. This suggests that assessing for prodromal PD symptoms in those with a prior history of TBI could lead to earlier identification of PD risk, allowing for more personalised management strategies.

4.5

Baseline striatal dopamine transporter binding and levels of CSF amyloid beta and hyperphosphorylated tau predict trajectory of cognitive change over a 5-year period in Parkinson's disease

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Cognitive impairment, ranging from mild cognitive impairment (MCI) to dementia, impacts a large percentage of individuals with Parkinson's disease (PD) and is a major predictor of quality of life. Despite its significant burden, however, it is largely unknown what predicts risk of cognitive impairment in PD. The current study assessed whether baseline striatal dopamine transporter (DaT) binding or levels of biofluid-based biomarkers predict mild cognitive impairment (MCI) or dementia diagnosis at 5-year follow-up in PD. Data for 256 individuals with PD were extracted from the Parkinson's Progression Markers Initiative (PPMI) study. Year 5 cognition was determined from self/informant-report and neuropsychological test performance. Participants were categorised as: no cognitive impairment (n = 182), self-reported cognitive complaint (n = 46), PD-MCI (n = 15) or PD-dementia (n = 13). Logistic regression and receiver operating characteristic (ROC) analysis assessed whether baseline clinical measures, striatal DaT binding or CSF levels of alpha-syn/p-tau/amyloid beta predict cognitive status at five-year follow-up. Cognitive categorisation at year 5 follow-up was predicted by reduced striatal DaT binding, decreased CSF amyloid beta and increased CSF p-Tau, at baseline. Other significant predictors included lower cognitive function and increased mood dysfunction at baseline. The model accounted for 33.8% of the variance, with an AUC of 0.96 (CI = 0.93-0.99). Including assessment of key biomarkers, in addition to clinical measures, at time of PD diagnosis may help clinicians to better understand an individual's risk of developing cognitive impairment. This is key for informing more effective personalised management strategies.

4.6

Frequency of Parkinson's genetic risk variants in New Zealand

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Genetics are known to play an important role in a person's risk of developing Parkinson's. The aim of this research was to explore the genetics of Parkinson's in a New Zealand context. As part of the New Zealand Parkinson's Environment and Genes Study and New Zealand Parkinson's Progression Study, 556 people with Parkinson's and 337 control participants have been genotyped through the Global Parkinson's Genetics Programme using the NeuroBooster array and with direct sequencing of GBA. The raw data was processed using standard pipelines including plink, and TOPmed for imputation. Parkinson's risk variants were identified and the Parkinson's polygenic risk score was calculated. The Parkison's group had a higher mean Parkinson's polygenic risk score (z=0.5, Probability > 99.99%). Parkinson's risk variants were found in 12% of the Parkinson's group compared to 5% in the control group, with variants in the GBA, LARRK2 and PRKN genes most commonly identified. As expected, the Parkinson's group had a greater number of risk variants and a higher polygenic risk score. The next steps are to examine how these genetic variations interact with environmental exposures and lifestyle factors to further increase the risk of Parkinson's.

5.1

Tracking CLN5 gene therapy efficacy with brain MRI

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Neuronal ceroid lipofuscinoses (NCL; Batten disease) are rare inherited neurodegenerative disorders caused by mutations in one of 13 CLN genes, presenting with motor and cognitive decline, vision loss, and seizures. A naturally occurring model of CLN5 NCL in New Zealand Borderdale sheep closely mirrors human clinical symptoms and pathology. Prior trials using combined intracerebroventricular and intravitreal gene therapy have shown therapeutic benefit. Here, we assessed brain MRI as a measure of treatment efficacy in CLN5-affected sheep. Sheep treated pre-symptomatically underwent five structural MRI scans between 5 and 18 months of age. We used linear mixed effects modelling to compare brain volume among control sheep (n=3), untreated affected sheep (n=3), and treated affected sheep (n=9). Pre-symptomatically treated sheep showed intracranial growth comparable to healthy controls. While grey matter volume declined and CSF volume increased, these changes were milder than in untreated sheep. Most cortical regions remained stable, except for the cerebellum. Early and advanced symptomatic treated sheep had intracranial volumes similar to untreated affected sheep, but early treated animals had significantly greater grey and white matter volumes and reduced CSF volumes. Regional volumes demonstrated an age-at-treatment and dose-dependent effect. These findings support MRI as a practical and useful tool for monitoring therapeutic efficacy in large animal models of CLN5 NCL, both longitudinally and cross-sectionally.

5.2

Boosting ability for brain MRI to predict cognitive functioning via multimodal fusion

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Recent research has raised concerns about the robustness of brain MRI in capturing individual differences in cognitive functioning, thereby challenging its utility as a biomarker. To address this limitation, we introduced a machine learning approach that leverages large-scale datasets to integrate brain MRI data across multiple modalities—including task-based fMRI contrasts, functional connectivity during tasks and rest, structural MRI and diffusion MRI—into a unified predictive model. We validated this multimodal fusion method across various contexts. For example, using lifespan data (ages 22–100) from the Dunedin Study and Human Connectome Projects-Young Adults and Aging, we demonstrated that multimodal integration consistently enhances the psychometric properties of brain MRI in assessing cognition. Specifically, it improves: (1) predictive accuracy, with out-of-sample correlations reaching up to r = .6, and (2) test-retest reliability, with intraclass correlation coefficients (ICC) exceeding .75. Additionally, the model exhibits substantial heritability and generalises effectively to pediatric populations, including children with ADHD, as shown in the Adolescent Brain Cognitive Development (ABCD) Study (n>11,000). We further explored its utility in elucidating the relationship between cognition and mental health in both ABCD and UK Biobank (n > 20,000) cohorts. Notably, neuroimaging explained 48–66% of the observed association between cognitive performance and mental health outcomes. These findings suggest that multimodal fusion is a promising strategy for developing robust brain-MRI biomarkers of cognitive functioning.

5.3

Tract-specific WMH burden in groups spanning the clinical Alzheimer's continuum

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White matter hyperintensities (WMHs) on MRI are a marker of cerebral small vessel disease and prevalent in aging. However, the impact of WMH volume and location in groups at increasing risk of dementia is not well understood. We investigated WMH burden in specific WM tracts in groups at increasing risk for Alzheimer's disease (AD). Participants (*N*=369) from the NZ Dementia Prevention Research Clinics were classified as control, subjective cognitive decline, single-domain amnestic mild cognitive impairment (MCI), multiple-domain amnestic MCI, or early AD-dementia. "Overlap scores" (percentage of tract voxels containing WMHs) were calculated using a 140-subject atlas (www.megatrackatlas.org) in ten major WM tracts: the superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), uncinate fasciculus (UF), cingulum (CB), fornix, splenium, body, and genu of the corpus callosum (CC), and the anterior thalamic radiations (ATR). Across the whole sample, WMH overlap scores were highest in the ATR and IFOF. There were significant across-group differences in overlap scores for nine tracts (all ANCOVAs apart from the UF $p<.05$) with largest effect sizes found in the splenium and body of the CC (η^2_p=0.09 and 0.06 respectively), the IFOF (η^2_p=0.06), and ATR (η^2_p=0.05), covarying for age, sex, and total intracranial volume. Polynomial trend analyses revealed overlap scores increased linearly with greater AD risk in all tested tracts ($p<.05$). Our findings highlight that WMH burden within multiple WM tracts, notably the CC, IFOF and ATR increases with the degree of clinical impairment in groups at-risk of AD, supporting location-based approaches to studying WMHs.

5.4

A novel 0.7 T ultra-compact brain MRI scanner

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MRI scanners are used widely in both clinical and research settings for their gold standard soft tissue contrast. Historically, access to MRI has been limited by the cost and complexity of modern scanners. As part of a process to improve access to clinical quality MRI, we have designed and manufactured an ultra-compact 0.7 T brain MRI scanner. The scanner was substantially funded by a USD 11M grant from National Institutes of Health (USA) and completed by a consortium led by University of Minnesota in 2024.The scanner uses a 0.7 T high-temperature cryogen-free superconducting magnet. The magnet is approximately 900 mm diameter and 450 mm long. The patient is seated upright in the scanner, with their shoulders completely excluded from the scanner, and able to see through the side of the scanner. These three features improve patient experience and minimise the scanner footprint. To achieve this, we have deliberately targeted an imaging volume with +/- 10 proton-kHz B0 variation. In turn, this means we must choose pulse sequences with high tolerance to large B0 variation. In this presentation, the design and manufacture process for the scanner will be briefly outlined including pulse sequence selection. Integration, commissioning and initial imaging results will then be presented. At the time of writing, approval is granted for human imaging and, if available, it is intended to present some preliminary human imaging results. The combination of energy efficient, small footprint scanners producing high-quality images paves the way for broader uptake of MRI beyond conventional settings.

5.5

Better than a hole in the head: a computational model of intracranial hypertension

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Intracranial hypertension (IH) is a serious condition in which brain pressure increases abnormally, common in neurosurgical and neurological practice. If left untreated, it can lead to brain injury, blindness, seizures, coma, stroke, or death. The clinical management of IH is hampered by the lack of a reliable and non-invasive technique to determine if the pressure is increased. Currently, a suspected diagnosis of IH can only be confidently confirmed by invasive measurement (i.e., placement of a pressure catheter via a burr hole or performing spinal tap). In this work, I developed a novel non-invasive technique using an MRI-informed computational model to estimate brain pressure level safely and accurately. The model combines information about brain motion and fluid flow inside the cranium to simulate how pressure builds up. After verifying the technique with in-silico data, it was applied to cases suspected of IH who underwent spinal tap. The results showed 100% sensitivity and specificity in stratifying high- and low-pressure cases. Further validation with more cases is ongoing in an extended clinical trial. Preliminary results suggest this safe, cheap, and non-invasive technique could contribute to the clinical diagnosis of individuals with IH.

5.6

Imaging mild Traumatic Brain Injury: what is the role of iron and inflammation?

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Mild Traumatic Brain Injury (mTBI) is common, and it can be burdensome for the affected individual and is linked to adverse long-term outcomes. Yet, we do not have reliable markers (brain or biomarkers) to determine the diagnosis and prognosis of mTBI. In this talk, I will outline recent evidence of brain changes in acute mTBI. We will highlight a series of experiments from our lab showing elevated cortical iron markers and inflammation after injury in human brains. This is enabled by methodological advances in MRI, specifically column-based quantitative susceptibility mapping and T2-relaxometry, where we compare 40 acutely injured athletes (16-30 years) to an equally sized control population. I also show that brain changes occur in young adults, within two weeks after injury, and correlate with symptom load. The similarities and differences of individual versus group analyses will be discussed. Taken together, this evidence suggests that we can 'image' the acute brain injury, and future directions are discussed, including long-term risks associated with these markers.

5.7

Validation of Ultra High Contrast Neuroinflammatory MRI changes using immunohistochemistry

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Neuroinflammation is the ubiquitous response of the brain to insults and disease processes. While late-stage white matter inflammatory changes can be identified with T2-FLAIR, there are no MRI techniques available that can be used to identify or measure early neuroinflammatory changes. Without early-stage detection, the window for administering disease-altering treatment may be missed. A novel approach for MR imaging in acute inflammation is UHC (Divided, Subtracted, Inversion Recovery), which has been recently developed by Graeme and Mark Bydder at Mātai Medical Research Institute. UHC increases the contrast produced by small changes in T1, by a factor 10 compared with conventional inversion recovery sequences. As a result, white matter which appears normal on T2-FLAIR can show extensive high contrast changes on UHC images, allowing unequivocal identification of previously unrecognised disease. These changes are seen in what we believe is early neuroinflammation, including mild traumatic brain injury, ischaemia, multiple sclerosis and even methamphetamine use. The underlying cellular and biochemical underpinning of UHC changes remain unknown. Our current study is to systematically validate the source of the UHC changes using immunohistochemistry in ovine models, and in particular determine if they are indeed due to neuroinflammation. This MRI technique once validated has the potential to change how we track early disease progression and treatment response in patients in a way that has not previously been possible.

5.8

Multi-parametric MRI mapping of brain changes in early-abstinent methamphetamine users

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Methamphetamine misuse inflicts widespread brain injury, spanning macro-structural shrinkage, micro-tissue disruption, and cerebrovascular stress. Yet most human imaging studies still interrogate single MRI contrasts, leaving the full breadth of damage in methamphetamine-use disorder (MUD) under-characterised. Our pilot study therefore integrated six complementary MRI sequences to build a multi-layer picture of early abstinence. Fifteen recently abstinent (< 30 days) MUD participants and 15 age-, sex-, and ethnicity-matched healthy controls underwent multiple MRI sequences including T1-weighted, diffusion MRI, 4D-flow, myelin-sensitive, ultra-high-contrast, and amplified MRI. Each dataset was processed with sequence-specific pipelines; group differences were tested with general linear models, and individual deviations were mapped as z-scores relative to control distributions. Across diffusion, flow, myelin, susceptibility, and amplified images no significant group effects emerge. Only the T1-weighted analysis revealed lower cortical volume in the right superior-frontal cortex ($p = 0.005$) and lingual cortex ($p = 0.018$) in MUD. Longer lifetime use correlated negatively with cortical volume across attention-related regions ($\rho \approx -0.53$ to -0.75), underscoring cumulative toxicity. Subject-specific z-maps in the non-significant modalities repeatedly identified the same MUD participants as extreme outliers, mirroring the structural deficits seen on T1. These findings illustrate both the subtle early effects of meth and the challenge of detecting group-level changes in small, heterogeneous cohorts whose drug histories, comorbid conditions, injuries, and childhood-trauma profiles vary widely. Multi-parametric MRI coupled with personalised analytics may therefore be essential for capturing the uneven anatomical footprint of methamphetamine and guiding tailored rehabilitation in clinics and communities worldwide.

5.9

From data to discovery in mTBI: FAIR and CARE-aligned multimodal MRI pipelines and federated analysis

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Mild traumatic brain injury (mTBI) presents a trans-disciplinary challenge, requiring integrated approaches across multiple disciplines. This complexity makes it an ideal context to showcase our approach to operationalising multimodal MRI research, combining advanced imaging protocols—both widely used and novel—with tissue testing, immunohistochemistry, video analysis, and impact biomechanics from instrumented mouthguards. Using local and international data, our team is developing open processing workflows aligned with FAIR (Findable, Accessible, Interoperable, Reusable) principles, while maintaining ethical considerations in line with CARE (Collective Benefit, Authority to Control, Responsibility, Ethics) principles. These processing complement widely used infrastructures such as Neurodesk and NiPoppy, and are designed to lower barriers to entry and training requirements while supporting reproducible and scalable workflows across teams with diverse expertise. We are also developing analysis plans for our novel MRI sequences—amplified MRI (aMRI) and ultra-high-contrast (UHC) protocols—to enable the extraction of meaningful imaging measures. These include bespoke region-of-interest analyses, optimisation of automated segmentation methods, and the development of scoring and evaluation matrices. Finally, federated analysis approaches for both our workflows and novel analyses will be introduced to facilitate cross-institutional research while respecting New Zealand data sovereignty and regulatory constraints. We are actively seeking collaborators with aligned interests in neuroimaging research to help advance this work.

7.1

Horizon Europe – Brain health partnership in New Zealand

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The Horizon Europe–Brain Health Partnership is a new partnership in Horizon Europe, pillar II, cluster 1 (health). The Partnership has been under development since 2023. It includes most countries in the European Union, and 8 associated countries, including New Zealand. New Zealand joined the Partnership late in 2024, has subsequently influenced the work plan, and will contribute to the work that will be delivered over the next 10 years. Neurological and mental health disorders are leading causes of disability and mortality in Europe and globally. The Partnership's vision is improved brain health for all, which is essential for healthcare systems to deliver sustainable outcomes, now and in the future, so that national economies can grow. The Partnership will support multi- and inter-disciplinary research teams to conduct research at the forefront of brain health research on the global stage. Come along to hear about the Partnership, what you can do now to prepare for opportunities, expected activity in the next year, how to stay connected for updates, and to have your questions answered.

8.1

Harnessing multimodal MRI for cognitive functioning: Unpacking between-individual differences and longitudinal change

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Cognitive neuroscientists aim to explain variations in cognitive functioning using brain data. While machine learning has successfully generated MRI-based markers for predicting cognitive functioning, particularly when integrating multiple MRI modalities, it remains unclear how much these markers capture between-individual differences versus within-individual changes over time, largely due to the common use of cross-sectional data. To address this, we leveraged longitudinal multimodal MRI data from the Dallas Lifespan Brain Study (DLBS, n=451, aged 21-90, up to three sessions five years apart). We developed machine learning models to predict cognitive function from 37 neuroimaging phenotypes across five MRI modalities: structural (sMRI), task-based functional (tfMRI), diffusion-weighted (DWI), functional connectivity (FC), and arterial spin labeling (ASL). Our models created MRI-based markers from individual and combined phenotypes, both within and across modalities, using stacking techniques. We then applied linear mixed models to decompose the variance of these markers into within-individual and between-individual components. DWI-based and sMRI-based markers showed the strongest predictive performance ($r \approx 0.57$-0.64). Combining all neuroimaging phenotypes into "all-MRI stacked markers" further improved performance ($r = 0.72$). Linear mixed models revealed that these all-MRI stacked markers explained 54% of the total variance in cognitive function, capturing 59.9% of between-individual variance and 7.7% of within-individual variance. Furthermore, the all-MRI stacked markers, particularly their between-individual component, significantly explained age-related cognitive functioning. This indicates 77.3% overlapping with age. Our findings suggest that MRI-based markers predominantly capture age-related between-individual differences in cognitive functioning.

8.2

Effect of head acceleration events on microstructural organisation of brain cortical and deep grey matter: a diffusion MRI investigation

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Head acceleration events(HAE) are direct or indirect impacts to the head without clinical symptom manifestation yet induce neurological effects. Diffusion MRI(dMRI) enables in-vivo investigation of brain microstructural changes. While most HAE studies have focused on white matter regions, this study investigates the effects of repetitive HAE on cortical and subcortical grey matter(GM) using dMRI in rugby players, comparing scans across the season and controls, and examining correlation with symptoms. Thirty-three male high school rugby players underwent MRI (T1-BRAVO and multi-shell dMRI) scans at early-, mid-, and post-season using a 3.0T scanner. Twenty matched non-collision athlete-controls underwent a single-timepoint scan. Mean diffusivity (MD), kurtosis (MK), and kurtosis tensor (MKT) metrics were extracted. T1-weighted images were segmented using Freesurfer. Cortical diffusion metrics were surface-vertex-wise analysed, while deep GM regions were compared using linear models. Symptom assessment was administered at each timepoint and correlated with diffusion changes. In rugby players, MD significantly increased ($p<0.05$) in the left lateral-occipital sulcus from early- to mid-season, with greater spatial extent post-season. Compared to controls, early-season players showed higher MKT in the left lateral orbitofrontal region. ROI analysis revealed a decrease in left amygdala MD from early- to mid-season, and elevated MK and MKT in the right amygdala across timepoints. MK and MKT in the left occipital sulcus positively correlated ($p<0.05$) with changes in symptom scores. Findings highlight HAE-induced GM microstructural alteration and relevance for analysis, given its involvement in sensory integration, emotion regulation, and cognition. This warrants further investigation alongside impact kinematics and developmental factors.

8.3

Neurobehavioral effects of cannabidiol (CBD) in individuals with Alcohol Use Disorder: A double-blind, randomised control trial

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This study aims to investigate this novel pharmacotherapy with a particular focus on neurobiological and physiological indicators of craving. In this double-blind, randomised, cross-over study, 22 non-treatment seekers were allocated to three days of CBD (800 mg/day) or placebo, with an 18-day washout period. Functional magnetic resonance imaging (fMRI) cue reactivity tasks and magnetic resonance spectroscopy (MRS) scans were conducted on day two while psychophysiological cue reactivity tasks were conducted on day three. Outcomes included: i) regional activity during a functional magnetic resonance imaging (fMRI) cue reactivity task, ii) heart rate variability (HRV) and skin conductance levels (SCL) as a proxy for psychophysiological responses to alcohol stimuli, iii) neurometabolite levels (GABA+, NAA, Glx, Cho and GSH) within the dorsal anterior cingulate cortex (dACC) using MRS. Region of interest analyses of the fMRI cue reactivity task demonstrated non-significant treatment effects in dorsolateral and ventromedial prefrontal cortex or caudate. However, exploratory whole-brain analysis indicated a significant treatment effect in the precuneus, independent of cue specificity. Throughout the psychophysiological cue reactivity task CBD vs placebo was associated with elevated HRV and greater reductions in self-report anxiety and alcohol craving from exposure to cue recovery periods. While no main treatment effects were identified across neurometabolites, post-hoc analyses indicated that CBD vs placebo sessions were associated with significantly higher GSH, GLX, and GABA levels in participants who consumed alcohol the previous day compared to those who were abstinent. These findings suggest CBD administration modulates key dysregulated neural and autonomic pathways in AUD.

9.1

Eye saccades align optic flow with intended heading during object pursuit in freely moving mammals

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During pursuit, predatory animals, such as ferrets, simultaneously track fleeing prey and navigate their environment avoiding obstacles. How eye movements, such as saccades, are used to achieve this is unknown. Here, we measured head and eye rotations in freely running ferrets during pursuit behavior. A rendering of the arena and simultaneous tracking of the target allowed us to fully reconstruct the animal's visual fields during pursuit and relate the positions of target and environmental features to retinal structures. Coordinated eye saccades and head rotations were observed as the animal made curved trajectories but were not seen during straight trajectories. The saccades did not fixate the moving target with the high acuity retinal region, the area centralis, but instead aligned the area centralis with the intended direction of travel. This also aligned the area centralis with features of the optic flow pattern, such as flow direction and focus of expansion, used for navigation by many species. The saccades were followed by eye rotations which compensated the rotation of the head to reduce image blur and limit information loss across the visual field during head-turns. The same coordinated head and eye rotations were also measured in freely moving tree shrews, rats and mice, suggesting that these saccades and counter-rotations are a generalized mechanism enabling mammals to navigate complex environments while running. We further suggest that saccades in ferrets, rather than fixating the target, instead recover optic flow patterns useful for navigation.

9.2

Anti-CD14 improved functional outcomes, reduced neuroinflammation and seizures in a mouse model of severe traumatic brain injury

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Traumatic Brain Injury (TBI) is a major cause of disability and mortality, with 74 million people being diagnosed with TBI globally every year [1]. Post-traumatic epilepsy (PTE) is one of the major consequence of TBI and there is still no preventative treatment for it [2]. TBI leads to dysregulated neuroinflammation and neuronal damage [3]. CD14 is a co-receptor, which acts as a bottleneck target as it is a ligand for multiple danger-associated molecular patterns (DAMPs) released after TBI, and it regulates the signalling of multiple Toll-like receptors (TLRs) [4]. Anti-CD14 monoclonal antibody (mAb) was shown to be tolerable and safe in Phase 1 clinical trials [5, 6]. In a porcine polytrauma model, anti-CD14 mAb limited organ dysfunction and inflammation[7]. We therefore evaluated the effect of anti-CD14 mAb in a mouse preclinical TBI model. CD1 mice were subjected to a unilateral cortical contusion by compressing the cortex to a depth of 2 mm at velocity of 5 m/s for 100 ms duration (TBI-0310, PSI, Fairfax, VA). Mice were allocated to treatment groups: 1. Sham + vehicle, 2. Sham + anti-CD14, 3. TBI + vehicle, 4. TBI + anti-CD14. Rotarod, neurological severity score, behavioural and histological tests and pentylenetetrazol (PTZ) test, were performed. Anti-CD14 reduced the neurological severity score, improved rotarod and memory performance, and reduced neuroinflammation. Furthermore, anti-CD14 decreased seizures and was neuroprotective. Anti-CD14 mAb had a profound effect on TBI sequelae, making it a future candidate for clinical translation.

9.3

EEG/LFP waveform shape asymmetry as a future biomarker for Parkinson's disease or levodopa-induced dyskinesia disease states

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Parkinson's disease (PD) alters single-cell and population-level neural activity along the basal ganglia-thalamocortical motor pathway, including the motor thalamus (Mthal) and cortex (MCx). Recent studies identified that MCx EEG (Cole & Voytek, 2017) and Mthal local field potential (LFP; Parr-Brownlie, Itoga, Walters, & Underwood, 2022) oscillatory activities have non-sinusoidal waveform asymmetries that correlate with disease severity and respond to PD treatments, suggesting potential application as biomarkers. This study investigated whether waveform shape asymmetry is present in levodopa-induced dyskinesia (LID) and in the basal ganglia nucleus, substantia nigra reticulata (SNpr). In the Mthal, baseline waveform asymmetry was significantly increased in a rat model of PD ($p = 0.0160$) and LID ($p = 0.0066$) compared to control rat because the peak became sharper than the trough. In PD model rats, levodopa treatment significantly increased asymmetry ($p = 0.0078$), but not in LID, possibly reflecting levodopa's therapeutic versus pathological effect on behaviour. In contrast, SNpr waveform sharpness was significantly reduced in PD and LID model rats ($p = 0.0034$ and 0.0109) compared to controls - the trough was sharper than the peak, likely reflecting GABAergic SNpr neuron population. Levodopa significantly increased waveform sharpness in PD ($p = 0.003$), but not LID ($p = 0.0673$), rats towards control levels. These findings demonstrate waveform asymmetries are present in both PD and LID states, and in basal ganglia nuclei. Additionally, waveform asymmetry is modulated when levodopa effect is therapeutic but not pathological, supporting its potential utility as an accessible biomarker of disease states in PD.

9.4

Do people with Parkinson's disease have increased perception of pareidolia?

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Pareidolia is a psychological phenomenon where meaningful patterns are perceived in random or ambiguous stimuli. It is a natural human tendency, non-pathological, and often visual (e.g., seeing faces in cloud formations). In Parkinson's disease, hallucinations, misperceptions and changes in visual functioning are common. We examined the association between pareidolia, hallucinations and visual function in 62 Parkinson's (mean age: 69 years; 68% male) and 30 age-, sex- and education-similar control participants, to determine whether people with Parkinson's, particularly those who experience hallucinations, experience more pareidolia. The Noise Pareidolia Test was used to evoke and measure face pareidolia. The computerized Freiburg Vision Test (FrACT10) was used to measure visual acuity and contrast sensitivity, and the Psychosis and Hallucinations Questionnaire in Parkinson's Disease (PsycH-Q) was used to measure hallucinations (47 with hallucinations; 15 without). We found that Parkinson's participants had more pareidolia ($p = 0.003$) and poorer visual acuity and contrast sensitivity ($p < 0.0001$) than controls. Multiple regression models showed that pareidolia increased with worse visual acuity and contrast sensitivity, independently ($p < 0.0001$). When group terms were added to these models, however, we did not find a difference in pareidolia frequency between Parkinson's (as a whole, or when divided by hallucination status) and controls. A limitation was that controls had a narrower range of visual functioning than Parkinson's participants; future studies should include controls with the full range of visual ability. Our results indicate that pareidolia is more common in Parkinson's and in general in people with worse visual function.

9.5

Treatment-Refractory Anxiety Disorders: Altered activity and connectivity with emotional stimuli

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Anxiety disorders are the most common mental health conditions, with a lifetime prevalence of 24.9% in Aotearoa. Many individuals do not respond to first-line treatments, however the underlying basis of treatment-refractory anxiety (TRA) remains unclear and effective treatments are lacking. Functional magnetic resonance imaging (fMRI) can be used to investigate neural activity and 'functional connectivity' (i.e., communication) of brain areas. Critically, the amygdala is a region strongly implicated in anxiety with its involvement in signalling emotionally salient events, fear processing and emotional regulation. This study aimed to investigate differences in brain regional activity and amygdala functional connectivity between TRA ($n = 23$) and healthy controls ($n = 17$) in response to passive perception of emotional faces (fearful, happy, or neutral expressions), using scans collected on a 3 Tesla MRI scanner. Following image preprocessing with fMRIPrep, task-based activity and psychophysiological interaction analyses were performed with the Oxford Centre for Functional Magnetic Resonance of the Brain Software Library. Compared to healthy controls, TRA displayed greater activity in left superior parietal lobule and left postcentral gyrus with neutral faces and reduced right amygdala connectivity with the same regions with fearful faces. These findings provide preliminary insights into potential neural alterations associated with TRA, with altered responses in regions involved in sensory integration. They will also be used to support further analyses assessing alterations at rest and the effects of a possible novel ketamine treatment option for TRA on these neural profiles.

9.6

Characteristics of Stuttered Disfluencies in Parkinson's Disease

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This study aimed to establish the prevalence, characteristics, impact, and longitudinal changes of acquired neurogenic stuttering in people with Parkinson's disease (pwPD). For cross-sectional analyses, frequency of stuttered disfluencies (%SD) during conversation, picture description, and reading was analysed in 100 pwPD and 25 controls. %SD was also compared with neuropsychological, motor functioning, and Communicative Participation Item Bank results. Results showed pwPD presented with 2.2 ± 1.8 %SD during conversation, twice the occurrence identified in controls (1.2 ± 1.2 %SD; $p < .01$), with 21% of pwPD meeting the clinical cut-off for stuttering. Speech task significantly affected %SD ($p < .01$), with the highest frequency occurring during conversation. The frequency of stuttered disfluencies in pwPD was associated with longer time since disease onset ($p < .01$), higher levodopa dosage ($p < .01$), and lower cognitive ($p < .01$) and motor scores ($p < .01$). Additionally, a high %SD was significantly associated with poorer communicative participation ($p < .01$). For longitudinal analyses, changes in %SD over an average 3-year period were examined in 46 pwPD. %SD during conversation (0.17 increase per year; CI 0.03–0.31) and picture description (0.18 increase per year; CI 0.02–0.35) increased over 3 years. To conclude, one in five pwPD presented with acquired neurogenic stuttering, with prevalence increasing over time. Additionally, a higher %SD negatively impacted communicative participation. Associations between stuttered disfluencies and cognition, motor functioning, and levodopa suggest a multifactorial origin. Findings indicate that individualized and holistic speech disfluency assessment, monitoring, and intervention are needed for pwPD.

11.1

Age-related meningeal extracellular matrix remodelling compromises CNS lymphatic function

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Efficient clearance of central nervous system (CNS) waste proteins and appropriate immune surveillance is essential for brain health. These processes are facilitated by lymphatic networks present in the meninges that drain cerebrospinal fluid (CSF). Age-related impairments to meningeal lymphatic drainage contribute to CNS waste accumulation and immune dysfunction, yet the underlying mechanisms remain poorly understood. Here, we identify extracellular matrix (ECM) remodelling in the aged dura as a key driver of CSF clearance deficits, demonstrating that peri-lymphatic collagen accumulation disrupts lymphatic function. Exploring immune-derived factors contributing to this ECM remodelling, we identify transforming growth factor beta 1 (TGFβ1) as a major regulator using primary human dural fibroblasts. Using a novel mouse model with constitutively active TGFβ receptor 1 (TGFβR1) signalling in dural fibroblasts, we show that excessive peri-lymphatic collagen deposition impairs meningeal lymphatic drainage and alters meningeal immunity. Mechanistically, we reveal that ECM-associated matrix stiffness disrupts lymphatic junction integrity and impairs lymphangiogenesis in human lymphatic endothelial cells. These findings establish dural immune cell and fibroblast-mediated ECM remodeling as a critical regulator of CSF clearance and highlight it as a potential therapeutic target for restoring brain waste clearance in aging.

11.2

A Case for Vagus Nerve Stimulation in Modern Medicine

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The Vagus Nerve (VN) is a deeply interconnected bidirectional communication pathway between the brain and body. In recent years, the VN has been significantly implicated in the control of immune function via the cholinergic anti-inflammatory pathway (CAP). By releasing acetylcholine, the VN systemically reduces inflammation by stimulating a7-nicotinic acetylcholine receptors (a7nAChRs) in tissue-resident macrophages such as microglia. The VN connects to the locus coeruleus (LC) via the nucleus tractus solitarius (NTS), and the LC projects to the nucleus basalis of Meynert (NBM) which is the primary source of cholinergic innervation to the cerebral cortex. Therefore, optimal VN function is essential for the control of chronically activated microglia in neurological (particularly neurodegenerative) and psychiatric conditions. In addition, the VN exerts anti-inflammatory effects throughout the body via the CAP. Because of this, the VN also plays an important role in conditions such as asthma, irritable bowel syndrome, rheumatoid arthritis, and more. It is therefore no surprise that non-invasive vagus nerve stimulation (nVNS) has shown promise for such a wide variety of conditions and should be strongly considered for the adoption into standard of care. As such, I reviewed the literature from Google Scholar and PubMed for clinical evidence of nVNS across conditions using the search terms “non-invasive vagus nerve stimulation”, “clinical trial”, “psychiatric”, “neurological”, “neurodegenerative”, and “inflammatory.” From 1310 articles identified, 12 are included for further review (ongoing). Despite the heterogeneity of studies, the evidence is compelling for nVNS as an efficacious intervention for a multitude of conditions affected by chronic inflammation.

11.3

From signals to symptoms: infraslow triple-network brain dysconnectivity linked to pain in chronic knee osteoarthritis

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The triple network model (TNM) has been hypothesised in recent literature to provide a more cumulative explanation for chronic pain. Effective connectivity (EC; directional communication) between TNM (Default mode network: DMN; Salience network: SN; Central executive network: CEN) brain regions could provide key insights into this hypothesis. This study aimed to investigate electroencephalogram (EEG)-based EC within the TNM in individuals with knee osteoarthritis (KOA) compared to healthy controls (HC), and to explore the relationship between EC and clinical pain outcomes. Resting-state EEG and clinical pain outcomes from 59 individuals with KOA and matched HC were analysed. EEG data was decomposed into seven frequency bands (Infraslow to Gamma) for 14 proxies of the TNM, and EC was assessed using Granger causality. Between-group statistical comparisons were performed using the Wilcoxon Signed-Rank test. Spearman's correlation analysis was conducted to explore the relationship between EC and clinical pain outcomes. Bonferroni correction was applied for multiple comparisons. Predominant EC changes were observed within the regions of DMN, with KOA consistently exhibiting reduced connectivity compared to the HC group in the Infraslow and Slow oscillations. These connections demonstrated significant relationships with clinical pain outcomes. Specifically, the EC between the right dorsolateral prefrontal cortex (CEN) and DMN regions was positively correlated with pain interference in the Infraslow oscillation. These connections, along with their relationship to clinical pain outcomes, suggest that triple network EC may play a role in pain modulation. Therefore, they warrant further investigation as potential targets for neuromodulation in pain management.

11.4

The therapeutic evaluation of trehalose in sheep models of Batten disease

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Trehalose, an FDA-approved food additive, has been investigated for its ability to stimulate autophagy and promote lysosomal clearance. Anecdotal caregiver reports suggest that daily oral trehalose may slow disease progression in children with Batten disease, a fatal, inherited neurodegenerative lysosomal storage disorder with no known cure. A recent clinical trial in affected children confirmed the safety of oral trehalose but reported no significant clinical benefit, despite perceived improvements by caregivers. In the current study, two naturally occurring forms of CLN5 and CLN6 Batten disease in sheep were used to further test the therapeutic potential of trehalose. Six nine-month-old sheep (n = 3 CLN5-/- and n = 3 CLN6-/-) received weekly intravenous trehalose infusions (0.5 g/kg; average 21 g/week) for three months. Treated animals were compared to age-matched historical and concurrent healthy and untreated affected controls. Clinical progression was monitored using established scoring systems, and brain pathology was assessed by CT imaging and post-mortem neuropathology. Trehalose treatment produced no significant therapeutic effect in CLN5-/- sheep. In contrast, treated CLN6-/- sheep exhibited improved clinical scores, increased weight gain, and slower intracranial volume loss on CT imaging. Post-mortem analysis revealed increased cortical thickness, reduced microglial activation in the primary visual and parieto-occipital cortices, and a significant reduction in lysosomal storage in the visual cortex ($p = 0.0002$). Astrocytosis remained unchanged. These findings support further investigation of trehalose as a potential adjunct therapy for CLN6 Batten disease. We acknowledge the Batten Disease Support & Research Association and Beyond Batten Disease Foundation for providing intravenous trehalose.

11.5

Ketamine effects on EEG and their links to therapy differ across treatment-resistant major depression, post-traumatic stress disorder, and obsessive-compulsive disorder

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Should psychiatry lump or split or both? Neurotic disorders – major depressive disorder (MDD), panic disorder, social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and specific phobia – have differing pharmaceutical profiles. But all, even when resistant to conventional treatment (TR), respond quickly to low dose ketamine. We explore the similarities and differences in the neural effects of ketamine across its treatments of TR-MDD, TR-PTSD and TR-OCD. We recorded 10-minutes' resting frontal activity, and diagnosis-related scale measures, before and 2 hours after fentanyl (50mcg) or ketamine (0.5 or 1.0 mg/kg, I.M.) counterbalanced across three sessions at least a week apart. Average power spectra were calculated for delta, theta, alpha1, alpha2, beta and gamma bands. ANOVA compared TR-PTSD (20♀, 2♂) with TR-MDD (12♀, 13♂). Preliminary TR-OCD (5♀, 2♂) data were also obtained. Power variation across ketamine dose, band frequency, and electrode position differed significantly between TR-MDD and TR-PTSD, with TR-OCD qualitatively different from both. The correlation of power change with scale score change was maximal for different bands and electrodes across the Impact of Events Scale-Revised, Montgomery-Asberg Depression Rating Scale, Hospital Anxiety and Depression Scales, Hamilton Anxiety Scale, Fear Questionnaire and Yale-Brown Obsessive-Compulsive Scale. Ketamine effects and their therapeutic links both vary in band and site with DSM diagnosis – consistent with TR anxiety results and with our double-hit model of neurotic disorders. On this view, a ketamine-sensitive factor generally and indirectly changes the disorder-specific systems that conventional treatments target selectively and directly.

11.6

Cerebrospinal fluid and dural accumulation of alpha synuclein impairs CNS clearance in Parkinson's disease

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Parkinson's disease (PD) is characterised by the build-up of α-synuclein (α-syn) in the brain where it drives neurodegeneration. Importantly, aggregated α-synuclein also accumulates in the cerebrospinal fluid (CSF) of PD patients and while increasingly used for diagnosis, its pathological role remains poorly understood. Here, we demonstrate that α-syn accumulation in central nervous system (CNS) borders promotes CNS clearance deficits—as observed in PD patients. We find that aggregated α-syn accumulates not only in the CSF, but also the dura mater of individuals with PD, and using acute and chronic mouse models, show that α-syn deposition in these sites induces immune alterations in CNS borders and disrupts CNS clearance. Mechanistically, we reveal that α-syn at CNS borders elevates CSF tumour necrosis factor (TNF) and demonstrate both TNF and α-syn aggregates themselves impair lymphatic function. These findings delineate a pathological role for α-syn in the CNS border tissues and position meningeal immunity as a contributor to CNS clearance deficits in PD pathogenesis.

11.7

Development of patient-derived tumour organoids as a drug discovery model

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Brain tumours, though rare, have high mortality rates, with only 12% of patients surviving beyond 5 years post-diagnosis. Treatment development has been hindered by the limitations of conventional 2D models. Patient-derived tumour organoids (PDTOs) offer promise for testing disease modifying treatments due to their ability to mimic the complex cellular heterogeneity of tumours. We aimed to establish a biobank of PDTOs that recapitulate the in vivo tumour microenvironment for use in studying brain tumour mechanisms and as drug screening tools. Specimens were obtained from consented patients undergoing surgical resection of brain tumours, predominantly glioblastoma and meningioma, at Auckland City Hospital. Tissue was dissected into organoid-sized segments and cultured in an optimised medium. PDTOs were generated within 2-4 weeks and passaged when greater than 1 mm in diameter. To characterise the cellular heterogeneity and microenvironment, immunohistochemistry and flow cytometry were utilised. To induce inflammatory responses organoid media was spiked with inflammatory molecules for 72 hours. Meningioma PDTOs showed distinct CD45 surface expression, while Platelet-Derived Growth Factor Receptor-β occupied a subsurface niche with minimal staining at the centre. Surface marker analysis quantified expression levels observed by immunohistochemistry. Lectin staining identified the formation of vascular-like structures akin to in vivo tumours. Inflammatory treatments increased adhesion molecules at the surface layer. This project has demonstrated the ability to procure a biobank of PDTOs that capture the cellular heterogeneity of brain tumours. The model can serve as a robust tool for researching the mechanisms of brain cancer, facilitating drug discovery, and advancing personalised medicine.

11.8

Multimodal MRI marker of cognition explains the association between cognition and mental health in UK Biobank

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Cognitive dysfunction is transdiagnostically related to psychopathology. Using UK Biobank (n>14000), we examine the extent to which the cognition-mental health relationship can be attributed to the neurobiology of cognition reflected in multimodal neuroimaging. We build machine-learning models to predict general cognition (a) from 133 mental health variables and (b) from 72 neuroimaging phenotypes based on three modalities: diffusion-weighted MRI (dwMRI), resting-state fMRI (rsMRI) and structural MRI (sMRI). Our machine-learning technique, called stacking, enabled us to combine different neuroimaging phenotypes within and across MRI modalities, creating neuromarkers of cognition. We then applied commonality analyses to quantify the proportion of the shared variance between cognition and mental health attributed to these neuromarkers. The cross-modal neuromarkers of cognition explained nearly half (48%) of the shared variance between cognition and mental health, while dwMRI, rsMRI, and sMRI captured 25.5%, 29.8%, and 31.6%, respectively. The contributions of sMRI and dwMRI were primarily driven by the volumetric characteristics and white matter connectivity of subcortical structures, particularly limbic structures, caudal anterior cingulate, and putamen. For rsMRI, functional connectivity among 55 resting-state networks, mainly the limbic, frontoparietal, default mode, and dorsal and ventral attention networks, was the most predictive of cognition and captured the highest proportion of cognition-mental health overlap. Importantly, we observed a strong positive association between the predictive accuracy of MRI-based models for cognition and their ability to capture cognition-mental health covariation. These findings support the utility of MRI-derived neuromarkers of cognition in advancing our understanding of the transdiagnostic link between cognitive function and mental health.

11.9

Diabetes, insulin, and Parkinson's disease risk: findings from two complementary population-based cohort studies

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Diabetes has been associated with an increased risk of Parkinson's disease (PD), with impaired insulin signalling implicated in PD pathogenesis. Additionally, insulin neuroprotection has been demonstrated in animal models of PD, suggesting that targeting insulin signalling may have therapeutic potential in PD. We conducted two complementary population-based cohort studies within the Integrated Data Infrastructure, examining diabetes and insulin use in relation to PD risk. Both studies employed inverse probability of treatment weighting methods to address confounding, including a range of demographic, clinical, and healthcare-related variables. Diabetes was associated with an increased PD risk in a cohort of 1,168,470 individuals, after adjustment for baseline confounding (HR 1.18 95% CI 1.13, 1.23), which was attenuated but remained statistically significant after accounting for time-dependent confounding (HR 1.07 95% CI 1.02, 1.12). Among 34,314 individuals with diabetes who initiated insulin or an oral antihyperglycaemic after two previous therapies, insulin use was associated with a reduced risk of PD (HR 0.70 95% CI 0.53, 0.93). While some estimates lacked precision, the direction of effect was consistent across sensitivity analyses. Together, these findings support that diabetes is associated with an increased risk of PD and raise the possibility that insulin may have a protective role. Further investigation is warranted into the role and therapeutic potential of insulin signalling pathways in PD.

11.10

Effort, motivation and the medial prefrontal cortex: A neuropsychological study of brain tumour patients

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Damage to the dorsomedial prefrontal cortex (dmPFC) has been associated with a range of cognitive and behavioural impairments, particularly on tasks requiring sustained effort. One proposal is that this region regulates parasympathetic arousal according to the perceived difficulty of an upcoming task, and the potential reward associated with performing well on it. This project will assess behavioural and psychophysiological responses to manipulations of incentive and effort in a novel Go/No-Go paradigm. The primary focus is on ultra-short term heart rate variability measures (HF-Power and RMSSD) that may indicate parasympathetic activity. Healthy participants and patients with tumours infiltrating the dmPFC completed: 1) a simple reaction time task; 2) a standard Go/No-Go task, and 3) an incentivised Go-No Go task (where participants earn rewards for accurate performance). Preliminary results from healthy controls show a clear pattern of decreased HF-Power as the task became more challenging and/or rewarding, consistent with upregulation of parasympathetic activity. We hypothesise that this effect will be attenuated in individuals with dmPFC damage. Investigating the link between dmPFC damage, autonomic arousal, and goal-directed behaviour serves two purposes: understanding what the dmPFC is critical for, and informing more sensitive clinical assessments of dmPFC damage.

11.11

Investigating the effects of allopregnanolone and estradiol on cortical excitation using visually induced long-term potentiation

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Catamenial epilepsy (CE) is an increase in seizure frequency or intensity at specific menstrual cycle phases. It affects 40% of women with pre-existing epilepsy and is often resistant to treatment. The most common subtype is perimenstrual CE (C1). Visually inducing long-term potentiation (LTP) can be used as a measure of neural plasticity and excitation and inhibition through visually evoked potentials in the brain. LTP is suppressed by the inhibitory progesterone metabolite, allopregnanolone, and enhanced by excitatory estradiol via neurotransmitters GABA and glutamate, respectively. Previous research has identified changes in visual LTP over the menstrual cycle in epilepsy. This study aims to understand the underlying physiology of C1 by using visual LTP to measure cortical changes in excitation versus inhibition following administration of synthetic progesterone or estradiol. In this within-subject, repeated-measures, counterbalanced, experimental design, healthy females aged 18–40 (n=50) completed one intervention and baseline session in their follicular phase (days 5–8). Two hundred milligrams of micronized progesterone (n=25) or 0.5–2 mg estradiol (n=25) were administered and assessed in blood samples. LTP was induced using high-frequency presentation of circular sine gratings and recorded using a 64-channel EEG. To date, progesterone (n=11) baseline and interventional levels were 0.39 nmol and 68.39 nmol ($p=0.002$), respectively. In contrast, estradiol (n=21) baseline and interventional levels were 167 pmol and 2590.14 pmol ($p<0.001$), respectively. EEG analysis and further recruitment are underway. Progesterone and estradiol levels following the intervention exceeded baseline and peak mid-luteal levels. Analysis of visual LTP changes and cortical excitability may improve understanding of the underlying physiology of CE.

11.12

Noradrenergic modulation of thalamocortical interactions in decision-making

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Cognitive flexibility involves switching thoughts and responses rapidly when encountering different task demands. The medial prefrontal cortex (mPFC) is densely innervated with noradrenaline, with both important for cognitive flexibility. Noradrenergic innervation is dysfunctional in various neurological conditions with cognitive deficits, e.g., schizophrenia, Alzheimer's disease, and Parkinson's disease. These conditions also disrupt thalamocortical interactions between the mPFC and thalamus. However, it remains unclear whether noradrenergic modulation can restore cognitive flexibility following thalamic dysfunction. Here, in rats, we first assessed whether bilateral excitotoxic lesions to the mediodorsal thalamus (MD) or thalamic nucleus reuniens (RE) disrupted cognitive flexibility as assessed in an attentional set-shifting task. The task measures the ability to attend to an odour or tactile stimulus dimension that reliably predicts reward (intra-dimensional shift; ID) for three consecutive ID subtasks, followed by a shift to the other previously ignored dimension when reward contingencies change (extradimensional shift). We found RE lesion rats made more errors learning the first ID, although they acquired a stable attentional set response similar to Sham and MD-lesion rats for ID subtasks 2 and 3. In contrast, MD lesion rats were impaired on the extradimensional shift. Next, we found systemic injections of noradrenaline given 30 minutes prior to re-running the task using novel stimulus pairings reduced these shift deficits and overall errors in both lesion groups. This indicates both MD and RE are involved in cognitive flexibility, and suggests noradrenaline be used as a potential treatment for patients with cognitive deficits linked to thalamocortical dysfunctions.

11.13

Electroencephalographic brain adaptations in individuals with chronic patellofemoral pain: Protocol for a source-localised neuroimaging investigation

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Patellofemoral pain (PFP) is a prevalent musculoskeletal condition characterised by diffuse anterior knee pain aggravated by activities that load the patellofemoral joint. In over half of cases, symptoms persist more than five years post-treatment, imposing a significant physical and psychological burden. Although both peripheral and central sensitisation are implicated in PFP, the associated brain changes and their relationship to pain experience remain poorly understood. This study aims to characterise resting-state brain activity and connectivity differences in individuals with chronic PFP using source-localised electroencephalography (EEG), and to examine associations with clinical symptoms (such as pain), sensory processing, and physical function. In this cross-sectional study—designed in accordance with the CONSORT guidelines—12 individuals with chronic PFP and 12 demographically-matched healthy controls will undergo 10-minute resting-state EEG recordings. EEG source localisation and full-band activity/connectivity analyses will be performed using exact low-resolution electromagnetic tomography (eLORETA). Participants will also complete quantitative sensory testing (QST), physical function testing, and self-reported clinical outcome assessments. Appropriate statistical modelling will assess within- and between-group differences for all outcomes, and a correlation analysis will examine associations between EEG and clinical/QST measures. This will be the first study to directly evaluate resting-state EEG alterations in chronic PFP, contributing novel neurophysiological evidence to the field of chronic musculoskeletal pain. Identifying brain changes in chronic PFP may provide critical insights into the neural mechanisms of chronic pain and support the development of targeted, non-invasive neuromodulatory interventions. Results will inform future trials on brain-based interventions such as neurofeedback for chronic pain management.

11.14

Function of cohesin in brain development

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The cohesin complex plays a crucial role in 3D genome organisation and regulation of gene expression, which are essential processes for brain development and function. Recent evidence suggests that alterations to chromatin organisation cause neurodegenerative and neuropsychiatry disorders. Cohesin is an important chromatin protein that is made up of four subunits SMC1A, SMC3, RAD21, and either STAG1 or STAG2. Mutations in cohesin cause a range of developmental syndromes collectively called cohesinopathies, which often present with neurological symptoms. The main objective of this research is to link cohesin-dependent molecular organisation of neuronal DNA with holistic, real-time changes in brain function using zebrafish as a model. We found that stag1b and stag1a/stag1b double mutants exhibit smaller head and inner eye widths. Immunohistochemistry for neuronal activity (pERK:tERK) showed that stag1 mutants have altered forebrain structure and decreased baseline activity. Bulk RNA sequencing of stag1b, and stag1a/stag1b mutants revealed gene expression changes affecting multiple neuronal pathways including behaviour, neuron, and brain development pathways. We are currently investigating where in the brain cohesin subunits Stag1, Stag2, and Rad21 are expressed. Using genetically encoded affinity reagents, zebrafish lines with short epitope tags knocked into the cohesin genes are being generated. Once established this will allow for in vivo visualisation of endogenous cohesin proteins. Additionally, in situ hybridisation and histological sections from larvae are being used to assess the spatial expression of cohesin subunits and identify associated morphological changes. This research will help determine where and how cohesin functions in the brain and may reveal novel molecular mechanisms underlying cohesinopathies and other neurological disorders.

11.15

Enrichment, episodic-like memory, and neuronal immediate-early gene expression

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Enriched housing, which provides social, sensory, and physically stimulating environments, often produces better learning and memory in laboratory rats. There is, however, little evidence whether enrichment improves episodic memory recall and its correlated neuronal activity. Here, young- (YA) and middle-aged (MA) male rats who lived in enriched (EE) or standard housing (SH) ran in an object-based exploration task in which the integrated recall of object (what), place (where), and context was assessed and compared to behavioural controls that ran in a non-episodic object-based task. Clear evidence of episodic-like memory recall was found in rats irrespective of housing condition or age. Zif268 immediate early gene (IEG) neuronal expression was examined post-mortem in hippocampal CA1 and CA3, lateral entorhinal cortex (LEC), and retrosplenial cortex (RSC). By comparison to behavioural controls, we found no clear evidence of Zif268 expression levels in neurons in these structures specific to the episodic-like memory task. However, there were higher Zif268 levels in SH compared to EE rats in CA1, RSC, and LEC, while YA compared to MA rats had higher expression in CA1 and RSC. For rats that ran in the episodic-like memory task or behavioural controls, Zif268 expression was higher in CA3, RSC, LEC compared to home cage control rats, who experienced no task prior to perfusion. These findings suggest Zif268 may be activated by running in object-based tasks. Additional neuronal markers of episodic-like memory could be examined along with IEG expression levels in prefrontal cortex and other hippocampal system regions.

11.16

GLP-1 Receptor Agonism Modulates Local Field Potential in Lateral Septum and Alters Motivated Behavior in Rats

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Here we report the effects of liraglutide, a GLP-1 agonist, on behaviour in the progressive ratio (PR) and differential reinforcement of low rates (DRL-15) tasks. GLP-1 receptor agonists, such as liraglutide, are increasingly recognised for their effects on motivated and consummatory behaviours, however, their behavioural impacts on effort and impulsivity remain unclear. This study aimed to investigate how systemic GLP-1 receptor agonism alters operant responding for palatable food in female rats. Animals (n=12) were tested under two behavioural paradigms: the PR task to assess motivation and animals' willingness to work, and the DRL-15 task to assess response inhibition and timing control. After establishing stable, high accuracy baseline performance, rats received liraglutide (0.06 mg/kg, s.c.) or saline in a counterbalanced within-subjects design. GLP-1 agonism modulated behaviour in these operant tasks. This study adds to a growing body of literature which implicates GLP-1 receptor agonism in motivation/the effort animals are willing to expend to obtain reward, and the tendency to respond impulsively, supporting the role of GLP-1 signalling in modulating multiple components of motivated behaviour. This work also supports the growing theory that GLP-1 receptor agonists may have therapeutic relevance for psychiatric conditions characterised by dysregulated motivation, such as substance use disorders and binge eating. Here we also contribute to addressing the sex gap in preclinical research by focusing exclusively on female animals.

11.17

Cardiolipin and Batten disease: Investigating phospholipid alterations in ovine models

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Batten disease is a group of lysosomal storage disorders associated with mutations in 13 CLN genes causing neurodegeneration, brain atrophy, and juvenile mortality. Within the last decade considerable strides have been made in understanding CLN cellular biochemistry. Select CLN mutations result in lysosomal loss-of-function by inhibiting bis (monoacylglycerol) phosphate (BMP) synthesis. Recent research may have advanced our understanding of CLN-associated lysosomal dysfunction – particularly as it relates to inhibition of BMP synthesis – yet little is known how this may affect extra-lysosomal phospholipids. Given established phospholipid trafficking between the lysosomes, endoplasmic reticulum, and mitochondria, lysosomal perturbations may alter phospholipid metabolism in these organelles. We aim to characterise expression of mitochondrial phospholipid cardiolipin in ovine CLN5/CLN6 mutants to investigate whether disrupted BMP synthesis alters cardiolipin synthesis via their shared precursor, phosphatidyl glycerol. Phospholipid profiles of control and affected sheep will be examined by thin layer chromatographic and hyphenated mass spectrometric techniques to quantify the cardiolipin and related species. We hypothesise that CLN mutations generate excess phosphatidyl glycerol in the ER and mitochondria, causing an oversupply to the functional cardiolipin biosynthetic pathway. The resulting accumulation of cardiolipin in mitochondrial membranes may cause hallmark mitochondrial subunit c (SCMAS) accumulation in Batten disease. Validating this hypothesis would provide the first mechanistic description of SCMAS accumulation in Batten disease, linking lysosomal dysfunction with observed mitochondrial abnormalities, and offering new insight into the biochemistry of neurodegeneration for this disease.

11.18

Increased sleep disturbances in a New Zealand Parkinson's cohort

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Sleep disturbances are common in Parkinson's. Participants in the New Zealand Parkinson's Environment and Genes Study (NZPEGS) completed questionnaires assessing sleep, allowing us to describe the extent of sleep disturbances in the New Zealand Parkinson's population. To date, 456 people with Parkinson's and 462 age and sex matched control participants have completed the Epworth Sleepiness Scale and REM sleep behavior disorder (RBD) questionnaire (RBDQ-HK). Participants also self-reported RBD via the RBDQ1. Bayesian linear models, with predictors of participant group, RBD, age, and sex, were used to examine how sleepiness and sleep behaviour is impacted in Parkinson's. RBD was self-reported by 47 control participants (10%) and 207 people with Parkinson's (45%). The mean sleepiness score in the control group was 10.0, and increased by 2.2 in the Parkinson's group (probability of being higher than the control group, P, > 99.99%). There was no evidence that RBD had an impact on sleepiness as measured by the Epworth Sleepiness Scale. The mean RBDQ-HK for controls with no RBD was 4.9, and increased by 0.3 in the Parkinson's group (P = 98%). The RBDQ-HK score was higher by 3.1 in controls with RBD (P > 99.99%) and there was a further increase of 1.0 (P > 99.99%) in Parkinson's with. RBD and sleep disturbances are more common in those with Parkinson's. Overall, RBD was not associated with increased sleepiness. Future work will investigate, within Parkinson's, if sleep disturbances are associated with genetic risk.

11.19

Increased frequency of head injury in New Zealand Parkinson's disease cohort

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Head injuries can have debilitating effects long after initial recovery is complete. Studies have associated head injuries and later onset of Parkinson's. The New Zealand Parkinson's Environment and Genes Study (NZPEGS) is investigating potential genetic and environmental factors that contribute to Parkinson's within the New Zealand context. The NZPEGS survey captures history of injuries, including any head injury that has required medical attention. The presence of loss of consciousness is also captured. As of June 2025, 454 Parkinson's and 455 age and sex matched control participants completed the medical history questionnaire, with 118 Parkinson's (26%) and 78 control participants (17%) reporting that they have had at least one head injury that required medical attention. A Bayesian Bernoulli model was used to examine the frequency of head injury with predictors of subject group, sex, and age.There was a higher frequency of head injuries in the Parkinson's group (Probability P > 99.99%) as well as in males (P > 99.99%). Similar results were found when restricting to head injuries associated with loss of consciousness. We have found a modest relationship between a history of head injuries requiring medical attention and development of Parkinson's in NZ. Further work will investigate if head injury exposure interacts with genetic risk in the development of Parkinson's.

11.20

Investigating the role of microglial dysfunction in Alzheimer's disease: Regulation of GPNMB expression

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Alzheimer's Disease (AD) is a neurodegenerative disorder characterised by cognitive and memory impairments. Although AD research has historically been neuro-centric, increasing evidence supports the importance of microglia in AD. Microglia are the resident immune cells of the brain, and their dysfunction contributes to AD pathogenesis and progression. Previous transcriptomic studies revealed glycoprotein NMB (GPNMB) as a gene highly upregulated in human AD microglia, but its precise function and how its expression is regulated are unknown. Microphthalmia-associated transcription factor (MITF) has been hypothesised to regulate GPNMB expression in response to cytokines, nutrient status, and AD pathology. This study investigated the relationship between MITF and GPNMB and their potential roles in AD microglia. Fluorescent immunohistochemistry was used in human brain biopsy tissue to validate MITF protein expression for the first time in the human brain. iPSC-derived microglia were exposed to conditions hypothesised to alter MITF transcriptional activity: nutrient depletion and amyloid beta protein. MITF and GPNMB expressions were highly correlated across all treatments and increased in response to nutrient depletion and amyloid beta. This was seen with increases in autophagy and cellular senescence markers, which are processes thought to be important in AD microglia. This indicates that MITF may be responsible for regulating GPNMB expression in human microglia in response to disease-related stimuli, which may lead to increased autophagy and microglial senescence. Understanding the expression and function of GPNMB may provide novel targets for rationalised therapeutic intervention in AD.

11.21

The effect of an impaired blood-brain barrier on microglial phenotype in Alzheimer's Disease

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Microglia are key regulators of inflammation in Alzheimer's disease (AD). Blood-brain barrier (BBB) breakdown, a key pathology in AD, allows blood-derived molecules, such as fibrinogen, to enter the brain and interact with microglia. Microglial activation is complex and only partially understood. Glycoprotein NMB (GPNMB) and secreted phosphoprotein 1 (SPP1) are upregulated transcripts in microglia in AD, but protein level changes and functional roles are unclear. Our study objectives were to investigate fibrinogen deposition in the AD cortex and microglial responses of GPNMB and SPP1 expression to fibrinogen and pro-inflammatory stimuli. Fluorescence immunohistochemistry was used to investigate fibrinogen, GPNMB and SPP1 expression in AD human brain tissue. Human iPSC-derived microglia were treated with fibrinogen and inflammatory cytokines and GPNMB and SPP1 expression assessed by immunocytochemistry. ELISAs, proteome profilers and cytometric bead arrays were performed to investigate microglial secretion of GPNMB and SPP1. : Fibrinogen deposition was significantly elevated in the AD cortex, and GPNMB and SPP1 were expressed in activated microglia near leaky vessels. GPNMB and SPP1 increased both intracellularly and extracellularly in response to fibrinogen and this was accompanied by morphological changes towards an activated state. These findings suggest that GPNMB and SPP1 are elevated in microglia in response to fibrinogen deposition in the AD brain, warranting further investigation into their functional implications. Understanding microglial phenotypes associated with AD could reveal therapeutic strategies to mitigate chronic inflammation in neurodegenerative diseases.

11.22

Dominantly Inherited Alzheimer Network (DIAN) in New Zealand

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The Dominantly Inherited Alzheimer Network (DIAN) is an international research initiative investigating autosomal dominant Alzheimer's Disease (ADAD), a rare, early-onset form of Alzheimer's disease caused by mutations in APP, PSEN1, or PSEN2. DIAN comprises both a longitudinal observational study (DIAN-Obs), aimed at understanding disease progression, and an interventional trials platform (DIAN-TU), to evaluate disease-modifying therapies. Based at Washington University in St. Louis, the DIAN-TU includes 39 sites across 17 countries. In early 2024, New Zealand's first DIAN-TU site was established in Christchurch. Based at the University of Otago, Christchurch and the New Zealand Brain Research Institute, and led by Principal Investigator Campbell Le Heron, the site has active participants in the DIAN-TU E2814 trial. This study targets tau pathology with the monoclonal antibody etalanetug, alongside open-label administration of the anti-amyloid therapy lecanemab. This combined approach addresses both hallmark proteins implicated in Alzheimer's disease. All participants carry a known pathogenic mutation and are either asymptomatic or in the early symptomatic phase, and within ten years of their affected parent's age at symptom onset. After six months of anti-amyloid treatment, symptomatic patients have shown a 20-centiloid reduction on amyloid (PiB) PET, in line with reductions predicted by models based on data from trials in sporadic Alzheimer's disease (Bateman, 2025). The establishment of the Christchurch DIAN-TU site enables local participation in high-impact, globally coordinated Alzheimer's prevention trials and strengthens New Zealand's contribution to global efforts to develop effective disease-modifying therapies for Alzheimer's disease.

11.23

Exploring tear fluid as a source of diagnostic biomarkers for Parkinson's disease

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The growing interest in accessible, minimally-invasive biomarkers has led to the investigation of tear fluid as a promising medium of biomarkers for neurodegenerative diseases including Parkinson's disease (PD). We present a review of the current evidence on the relevance of tear-based biological markers of PD. A systematic search was conducted in major databases like PubMed, Web of Science and Scopus using the advanced search- (TITLE-ABS-KEY ("Parkinson Disease" OR "Parkinson's disease" OR Parkinsonism)) AND (TITLE-ABS-KEY ("tears" OR "tear film" OR "tear fluid")) adapted to each database. This review was conducted in accordance with PRISMA 2020 guidelines. A total of 246 articles were retrieved from 2015 to 2025, of which 11 were selected based on examination of biological markers in tear fluid from human PD and control participants. PD tear studies reported elevated oligomeric (2 studies) and total α-synuclein (5), NfL (1), and catecholamines (2). Proteomic studies reveals altered immune response (Tumour Necrosis Factor alpha), lysosomal pathways, lipid metabolism and oxidative stress suggesting systemic involvement. While protein-based tear markers show promise for non-invasive PD diagnostics there remains significant gaps in the literature. One gap concerns microRNA, because blood plasma reveal biologically meaningful changes in PD patients and some evidence suggests microRNA changes in tears from Alzheimer patients. Our team is examining these possibilities through collaborative research across Christchurch, Dunedin, and Auckland, aiming to validate tear biomarkers as an inexpensive tool for early diagnosis, disease monitoring, and PD subtype differentiation.

11.24

BDNF as a Biomarker of neuroplasticity in LSD microdosing for Major Depressive Disorder

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Major depressive disorder (MDD) is a leading cause of disability globally, characterised by physical and cognitive symptoms that substantially impair quality of life. Current MDD therapeutics are inadequate for many patients, and psychedelics such as lysergic acid diethylamide (LSD) have gained attention for their potential as novel MDD therapies. One proposed mechanism of action is enhanced neuroplasticity mediated by brain-derived neurotrophic factor (BDNF). However, the validity of BDNF as a biomarker of treatment response remains unclear, particularly given variation across different blood fractions, such as serum, plasma, and platelet-poor plasma. This study aims to investigate the potential of LSD microdosing as a treatment for MDD and examine peripheral BDNF as a biomarker of treatment response. Nineteen participants (15 male) completed an open-label 8-week LSD microdosing regimen, receiving twice-weekly doses titrated between 4–20 µg. Depression severity was assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS). Blood samples were collected at baseline, week 4, and week 8, and BDNF levels in serum, plasma, and platelet-poor plasma were quantified via enzyme-linked immunosorbent assays (ELISAs). LSD microdosing was well tolerated, and no serious adverse events were reported. Participants showed a mean 60% reduction in MADRS scores, sustained at three-month follow-up, suggesting potential therapeutic benefit. BDNF ELISA analyses are currently underway. Preliminary findings support the therapeutic potential of LSD microdosing to alleviate depressive symptoms. Ongoing BDNF analysis will help clarify its validity as a biomarker, informing future psychedelic research in MDD.

11.25

The mechanisms by which cholinesterase inhibitors improve apathy in dementia

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Cholinesterase inhibitors are a clinically recognised option for managing the symptoms of apathy in dementia. While it is well-established that cholinesterase inhibitors enhance acetylcholine levels in the brain, the mechanism by which they improve motivation remains unclear. One validated approach to understand changes in motivation is to investigate the way individuals weigh up effort and reward information, a process commonly altered in neurodegenerative apathy. To understand how enhancement of the cholinergic system improves motivation, we investigated the effect of cholinesterase inhibitors (CIs) on effort-based decision-making (EBDM) using the Apple gathering task (AGT). Patients starting CIs were recruited from an early-onset dementia clinic, assessed at baseline before commencing treatment, and again after 6 weeks of therapy. Non-treatment clinic patients and healthy controls were tested twice across the same timeframe. We measured AGT acceptance rates and decision times, and motivation using the apathy evaluation scale (AES). To date, 25 participants have completed both sessions, including 2 from the CI treatment group. Patient 1 showed a significant increase in offer acceptance, from 48.5% at baseline to 74.0% ($p < 0.01$), and a significant decrease in mean decision time from 2.80s to 1.69 s ($p < 0.01$). Patient 2 showed no significant change in offer acceptance (83%, 80%, $p = 0.587$) or mean decision time (2.11s, 2.23s, $p = 0.174$). Self-rated apathy scores (AES) improved in both individuals (+5, +3 points). Our preliminary findings suggest that CIs improve apathy, with one patient showing an increased willingness to exert effort for reward. Further data collection will determine whether changes exist at a group-level.

11.26

Development of a fluorescence-based assay to screen novel synthetic cathinones

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Over 200,000 kiwis used 3,4-methylenedioxymethamphetamine (MDMA) in 2023. Synthetic cathinones are family of novel psychoactive substances which are often sold as MDMA. Over 50 synthetic cathinones were detected between 2014-2020, with increasingly diverse chemical structures. The harms of novel synthetic cathinones are difficult to predict based on chemical structure. MDMA, cathinones, amphetamines, and first-line antidepressants all share a similar molecular mechanism of action, inhibiting the transporters of dopamine (DAT), serotonin (SERT), and norepinephrine (NET), with greater harm associated with high DAT /SERT inhibition ratios. Establishing inhibitory profiles of novel cathinones at DAT, SERT, and NET can serve to predict their in vivo effects, including potential harm. Radiotracer transporter assays, the current gold standard approach to characterise transporters, is limited by the resource intensive nature of the assay. Recently, several novel biosensors that detect extracellular dopamine, serotonin, and norepinephrine have become available. Our project aims to use these biosensors to develop a high throughput, streamlined method for screening novel synthetic cathinones in vitro. Early development and optimisation has yielded promising results – HEK293 cells transfected with the dopamine GRAB sensor (rDA3m) are sensitive to DAT-mediated changes in extracellular dopamine, with a favourable signal-to-noise ratio for detecting DAT inhibition. The optimised transfection and experimental conditions are now being applied to detect SERT and NET inhibition. Rank order of potency of known compounds, relative to novel recently detected cathinones at DAT, SERT, and NERT will then be characterised. Rapid access to such data on detection of novel agents will inform harm reduction strategies.

11.27

Effects of an intravenously administered sAPPα gene therapy on neuropathology in the 5xFAD mouse model of Alzheimer's disease

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This study investigates the therapeutic potential of soluble amyloid precursor protein-alpha (sAPPα) gene therapy in the 5xFAD mouse model of Alzheimer's disease (AD). We also aim to validate peripheral intravenous delivery of the human sAPPα transgene, via the AAV.CAP-B10 vector. Development of effective disease modifying treatments for AD is critical as AD is the majority cause of dementia cases and prevalence is rising as the global population ages. The 5xFAD transgenic mouse model expresses five genetic mutations associated with familial AD. Using adeno-associated viral vector (AAV.CAP-B10) to deliver the sAPPα transgene, we aim to assess its efficacy in preventing AD neuropathology - including amyloid-β plaque load and glial cell activation. The study involved 40 wild-type and 40 5xFAD transgenic mice. Twenty mice of each genotype were administered 1x10^11 vectors at two months of age by lateral tail-vein injection. Further AAV.CAP-B10 vector was prepared carrying the transgene for green fluorescent protein, to allow for visualisation of neural transduction, and was administered to all 80 animals in the study. Animals were euthanised 7-8 months after treatment for post-mortem analyses. Neural tissue from 40 of these animals is being analysed with immunofluorescence techniques for effects on amyloid plaque load and activation of astrocytes and microglia. It is hypothesised that sAPPα treatment will reduce Aβ plaque formation and mitigate neuroinflammation. The 5xFAD mice exhibit higher levels of astrocyte reactivity markers, however, preliminary results from 10 animals show no differences in amyloid plaque load between the two groups of transgenic animals. Analysis is on-going.

11.28

AAV serotype-promoter selection and implications for transduction efficiency in diverse human-derived GBM cell cultures

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Glioblastoma Multiforme (GBM) is a highly invasive and deadly brain cancer, with a median survival of 15 months. The current standard of care is aggressive, consisting of maximal surgical resection with concomitant radiotherapy and chemotherapy. However, 70% of patients experience recurrence within one year, and recurrent GBM remains largely untreatable. GBM is challenging to treat due to its diffuse nature, pro-tumoural microenvironment and complex molecular and transcriptomic cell phenotypes. Gene therapy is a promising treatment approach for GBM, with improving gene therapy delivery to residual GBM cells a potential avenue for sensitising GBM to radiotherapy and chemotherapy, thus decreasing recurrence. This study aims to determine the optimal adeno-associated viral (AAV) vector serotype-promoter combination for efficient and cell-specific transduction of diverse human GBM cell cultures. Determine if the incorporation of secretory motifs in therapeutic microRNAs can enhance delivery and prevent GBM cell growth. Plasmids expressing a GFP transgene under control of the GFAP, nestin, CBA or Ef1α promoters were packaged into AAV vector serotypes 1/2, 6 and 6-Y731F/Y705F/T492V. Vectors were applied to patient-derived GBM cell lines, and immunocytochemical analysis of GFP, cell markers including CD44, and EdU to assess cell proliferation was performed. The most efficient vector was selected to express secretory miRNA. GFP expression was observed with all serotypes, with AAV6-Y731F/Y705F/T492V showing superior transduction efficiency. GFP expression levels were variable depending on the promoter used. This research provides evidence for the development of greater specificity and transduction potential of AAVs for central nervous system-based diseases through promoter and serotype selection.

11.29

Literature review on the effects of Yoga Nidra on the nervous system and sleep

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The New Zealand Health Survey shows that 26.8% of the population gets less sleep than recommended, indicating rising sleep issues. Based on the global statistics, insomnia appears to be a growing epidemic, prompting interest in effective treatment options. While pharmacological treatments are available, they often have side effects, may disrupt sleep architecture, and don't always improve insomnia consistently. Non-pharmacological approaches, such as Cognitive Behavioural Therapy for Insomnia (CBTi), offer safer and longer-term outcomes but face challenges with cost, access, motivation, and adherence. Among alternative treatments, relaxation-based methods like Yoga Nidra have gained attention for their therapeutic potential. There are many claims promoting Yoga Nidra as a sleep aid, including a popular statement by its founder that "one hour of Yoga Nidra equals four hours of sleep". However, scientific research on Yoga Nidra's role in aiding sleep or its effects on the nervous system is limited. This literature review explores the effectiveness of Yoga Nidra in managing insomnia and its potential as a sleep substitute. A systematic review was initially conducted but later traditional literature review was adopted due to limited available studies. Findings suggest that sleep and Yoga Nidra state can have similar effects on brain activity and nervous system activity. Evidence shows Yoga Nidra can improve sleep parameters. However, credible studies remain limited. While Yoga Nidra may promote sleep and could be a partial substitute or an interim solution for sleep issues and insomnia, further rigorous research is required to validate its benefits for sleep and nervous system health.

11.30

Maximizing spatial biology - A workflow combining 3D imaging with 2D multiparameter analysis of adult mouse brain

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Spatial biology is an emerging field that studies the spatial organization of cells and molecules within tissue to better understand complex biological processes. Currently available methods may only provide information from thin tissue sections, limiting analysis to rather roughly selected areas. Our workflow combines 3D imaging with multiplex spatial analysis to get an overview of complex large samples, identify target structures within them, and to further analyze a carefully selected region in depth with hundreds of markers – all on the same valuable specimen. In this study, we utilized 3D-immunofluorescence (3D-IF) staining and tissue clearing to prepare mouse brain hemispheres for 3D light sheet imaging with the UltraMicroscope Blaze™. With the full specimen's 3D view, we were able to identify target regions in order to prepare tissue sections that precisely cover these specific parts of the specimen, a process termed light sheet guided histology. The tissue sections were further analyzed with MACSima™ Imaging Cyclic Staining (MICS), providing expression levels of up to hundreds of protein markers from individual cells on a single sample. Remarkably, the fluorochrome conjugates used for 3D-IF staining remained detectable after sectioning, enabling us to verify the location of our target region and markers. Furthermore, the epitopes remained stable throughout the entire process of sample preparation for 3D imaging, 3D imaging itself, and sample preparation for MICS. Thus, we have demonstrated that it is possible to apply our MICS technology to a previously cleared tissue. The ability to obtain both a comprehensive 3D context and detailed information about cellular diversity in a spatial context from a single sample makes our workflow game-changing in spatial biology.

12.1

Translational insights into the aftermath and treatment of brain injuries caused by intimate partner violence

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Intimate partner violence (IPV) is a pervasive global public-health issue that remains underrecognized. While IPV is common in individuals of all genders, women are disproportionally affected, with one in three experiencing IPV during their lifetime. IPV can inflict significant neurobiological harm with lasting consequences.. Physical trauma to the head, face, or neck, exposes survivors to brain injuries (BI) such as concussion and non-fatal strangulation. Living under a prolonged state of threat and stress can also activate neuropathophysiological cascades linked to neurodegeneration and brain dysfunction. Despite its prevalence and severity, the neurological impact of IPV remains poorly characterised and there are major gaps in the clinical care of survivors. In this presentation, Professor Sandy Shultz will share findings from a translational research program spanning clinical and preclinical studies on the pathophysiology, detection, consequences, and treatment of IPV-related neurological conditions. This includes studies into the use of blood biomarkers to improve the acute detection of IPV-BI, neuroimaging and cognitive findings showing the long-term impact of IPV and IPV-BI, and exploration of psilocybin-assisted therapy as a potential intervention to promote recovery.

13.1

Relationship between task-based fMRI activity during working memory task and mTBI-related symptoms in adolescent rugby players: A longitudinal neuroimaging study

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Rugby players experience hundreds of repetitive head impacts (RHI) over a season, often without diagnosed mild traumatic brain injury (mTBI). While attention impairment is a prevalent and persisting consequence following mTBI, the cumulative effects of subclinical RHI on attentional functioning remain poorly understood. We conducted a longitudinal study of adolescent rugby players across one season, combining task-based fMRI (1-back working memory task) with clinical assessments (BIST, SCAT5) at baseline, mid- and post-season. We analysed individual differences and seasonal changes in fMRI activation (1-back vs. rest) during the working memory task in relation to mTBI symptoms. Individual differences in right supplementary motor area (SMA) and frontal/parietal eye fields (FEF/PEF) were positively associated with physical symptoms (hypersensitivity to sound/light, headaches) (β=0.69-0.73, p_FDR<0.03). Left SMA/premotor regions, right superior frontal gyrus, ventral premotor cortex, and ventral intraparietal area were positively associated with undefined feelings ("don't feel right", confusion) and, cognitive/emotional symptoms (concentration difficulties, fogginess, irritability) (β=0.61-0.78, p_FDR<0.04). Seasonal changes in the left inferior temporal gyrus were positively associated with neurobehavioral symptoms (irritability, sleep disturbances, fatigue) (β=0.504, p_FDR=0.01). These findings indicated that higher brain activation during working memory tasks correlated with more severe mTBI-related symptoms. This pattern may reflect a potential compensatory mechanism attempting to maintain cognitive performance despite underlying brain dysfunction or inefficient neural information processing resulting from RHI. Our results demonstrated that cumulative subclinical RHIs produce measurable changes in brain activation patterns and self-reported symptoms. Future research should investigate these neural changes and their relationship to long-term cognitive outcomes in youth athletes.

13.2

Cognitive effects of traumatic brain injury in a New Zealand prison

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Existing research indicates that offending populations report a high prevalence of traumatic brain injury (TBI), often accompanied by numerous risk factors associated with poorer recovery outcomes, such as repeated injuries, alcohol misuse, and substance abuse. As such, forensic populations represent a critical area of study for understanding the long-term effects of TBI within vulnerable and highly exposed groups. This study investigated the cognitive outcomes associated with TBI history in a population of incarcerated men in Aotearoa New Zealand. A volunteer sample (N=63) completed structured interviews to assess lifetime TBI exposure and participated in a bespoke neuropsychological assessment battery evaluating various cognitive domains. Cognitive performance was analysed in relation to TBI severity, frequency, and the presence of pervasive TBI exposure—defined as multiple mild TBIs occurring within a narrow timeframe. Findings revealed that 25.4% of participants reported a history of moderate to severe TBI, 46.0% sustained their first TBI before the age of 13, and 49.2% reported pervasive injury exposure. Notably, individuals with a history of pervasive TBI exhibited significantly lower performance on the Colour-Word Interference Test, a measure of inhibitory control ($p<.01$). No other associations remained statistically significant following correction for multiple comparisons. These findings highlight pervasive TBI exposure as a potentially overlooked factor in understanding longer-term brain health following TBI. These findings also raise critical questions about the appropriateness of current interview-based methods for identifying and classifying historical TBI in forensic populations.

13.3

Multimodal MRI reveals brain structural deficits and executive dysfunction in early methamphetamine abstinence

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Methamphetamine use disorder (MUD) is associated with structural brain changes and cognitive impairments. Understanding these changes during early abstinence is crucial for informing targeted rehabilitation strategies. This study assessed cortical and subcortical volumetric differences and myelin volume in early-abstinent methamphetamine users compared with healthy controls. Thirty participants were included: 15 with MUD in early abstinence (<30 days; 37.4 ± 9 years, 66% female) and 15 age- and sex-matched healthy controls (39.2 ± 11.1 years, 74% female). All underwent MRI (3T GE), including T1-weighted and myelin-sensitive imaging. The Tower of London (TOL) task was used to assess executive functioning. Cortical thickness and volume were extracted using FreeSurfer, controlling for age and sex. Regional and global myelin volume was also quantified. Analysis revealed cortical thinning in the left lateral-occipital and right lingual cortices in the MUD group. Additionally, volumes in the right superior-frontal and right lingual cortices were significantly reduced. Correlation analysis showed a negative relationship between left middle-temporal cortical volume and duration of use. Global myelin volume was slightly lower in the MUD group (166.7 ± 22.5) versus controls (172.1 ± 29.8), though not statistically significant. While overall TOL scores were similar between groups, MUD participants showed significantly longer execution times ($p = 0.01$) and required more attempts ($p = 0.05$). This study found methamphetamine use is linked to cortical structural alterations and executive function deficits during early abstinence. Myelin volume was not significantly reduced, suggesting cortical grey-matter is more vulnerable to meth-induced damage than white-matter.

13.4

The structural integrity of nucleus basalis of Meynert and its association with hallucinations in Parkinson's disease

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Visual hallucinations in Parkinson's disease are common and are associated with increased early institutionalisation and mortality. Treatment options however are limited. Recent work to determine the pathological and functional mechanisms that underlie Parkinson's hallucinations suggest that cholinergic dysfunction may be the driver of this prevalent and often distressing symptom. The Nucleus Basalis of Meynert (NBM) is located within the basal forebrain and consists primarily of cholinergic neurons (90%). We have examined the structural integrity of the NBM using structural and diffusion-weighted MRI and its association with hallucination frequency (measured by the Psychosis and Hallucination Questionnaire in Parkinson's disease) in 74 Parkinson's participants (mean age: 70.1 years [SD: 6.7]); 62% male; mean hallucination frequency score: 4 [SD: 5]; mean disease duration: 8.1 years [SD: 4.8]). Bayesian mixed-effects models including age and sex indicated that increased NBM volume (95% Credible Interval [95%CI] 0.17, 0.42) and being female (95%CI 0.03, 0.59) was associated with higher hallucination frequency scores, but not age. Mean diffusivity within the NBM was not associated with higher hallucination frequency scores. The macrostructural changes observed could be due to gliosis, inflammation or compensatory mechanisms. An increase in NBM volume without detectable microstructural degeneration in the NBM may suggest that hallucinations in Parkinson's disease result because of functional or network-level dysregulation rather than from local structural damage within the basal forebrain. Developing targeted interventions that restore cholinergic network function, rather than compensate for neuronal loss, may be the next step in advancing hallucination treatment in Parkinson's disease.

13.5

Source-Space EEG functional connectivity and prediction of cognition in Parkinson's disease: No added benefit of individualized head models over standard templates

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Parkinson's disease (PD) involves cognitive decline, often progressing to dementia, but we lack reliable biomarkers for this. EEG source-space functional connectivity (EEG-FC) shows promise for cognitive prediction. However, preprocessing choices - such as using standard versus individualized head models - may affect outcomes; the latter choice is presumed more accurate but adds individual MRI costs. This study compared the predictive value of EEG-FC derived from the two head model choices for estimating cognitive function in 136 PD patients and 51 healthy controls recruited from the New Zealand Longitudinal Parkinson's Progression Study. Neuropsychological testing was conducted across five domains – attention/working memory, executive function, visuospatial ability, episodic memory, and language - with a global cognitive score derived from these domains. Resting-state EEG was recorded using a 64-channel cap during a 9-minute eyes-closed session. Preprocessing (MNE-BIDS-Pipeline and custom Python scripts) included filtering, artifact removal, re-referencing, ICA-based artifact correction, and bad epoch and channel interpolation. We performed source reconstruction using both a standard head model (fsaverage) and individualized T1-weighted MRI data. EEG-FC was computed using power (Amplitude Envelope Correlation, AEC) and phase-based measures (debiased weighted Phase Lag Index, dwPLI) for delta, theta, alpha, beta, and gamma frequency bands, parcellated via the Glasser atlas. Multiple machine learning models, including a stacking approach, were applied to predict global cognitive scores from EEG-FC. We found that EEG-FC derived from standard head models performed slightly better, on average, than that from individualized models across multiple frequency bands and connectivity metrics.

13.6

Decision cost hypersensitivity underlies Huntington's disease apathy

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Apathy is a common and disabling syndrome in Huntington's disease (HD). However, the mechanisms underlying it are poorly understood. A fundamental computation underlying motivated, goal-directed behaviour across species is weighing up the costs and rewards associated with actions. Here, we asked whether people with apathy are more sensitive to costs of actions (physical effort and time delay), less sensitive to rewarding outcomes, or both. Genetically confirmed carriers of the expanded Huntingtin gene (n=53) were compared to healthy controls (n = 38). Participants performed a physical effort-based decision-making task (Apple Gathering Task) and a delay discounting task (Money Choice Questionnaire). Choice data was analysed using linear regression and drift diffusion models which incorporated decision time. Apathetic people with HD accepted fewer offers overall on the Apple Gathering Task, specifically driven by increased sensitivity to physical effort costs. Drift diffusion modelling provided further evidence of effort hypersensitivity, with apathy associated with a faster drift rate towards rejecting offers as a function of varying effort. Increased delay sensitivity was also associated with apathy, both when analysing raw choice and drift rate, where there was moderate evidence of HD apathy drifting faster towards the immediately available (low cost) option. Furthermore, the effort and delay sensitivity parameters from these tasks were positively correlated. The results demonstrate a clear mechanism for apathy in HD, cost hypersensitivity, which manifests in both the effort and time costs associated with actions towards rewarding goals. This suggests that HD pathology may cause a domain-general disruption of cost processing.

15.1

Investigating the disruptive role of T-cells in Parkinson's disease

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Parkinson's Disease (PD) is a progressive neurodegenerative disorder marked by the selective degeneration of dopamine neurons in the substantia nigra (SN). The accumulation of pathological alpha-synuclein (a-syn) and activation of pro-inflammatory immune cells are thought to contribute to this loss, but the underlying mechanisms remain poorly understood. Recent works have highlighted neuroimmune communication between peripheral immune cells and neurons via unconventional cytokine signalling. By analysing midbrain single cell RNA-sequencing transcriptomic data in mice we find that dopamine neurons uniquely express receptors for interleukin-13 (IL-13), a cytokine secreted during type 2 immune responses by T cells and others. Notably, peripheral T-cell dysregulation is among the earliest immune alterations observed in PD, suggesting that dopamine neurons may be especially vulnerable to changes in their associated cytokine levels. To explore this, we developed an iPSC-derived dopaminergic neuron model of PD to study the impact of T-cell–derived cytokines on human neuronal function in adeno-associated virus (AAV)-driven a-syn models of PD. Moreover, we reveal that, dopamine neurons in post-mortem human SN tissue reveal the same expression of the IL-13 receptor. Together this details a novel mechanism for communication between neurons and immune cells that utilises cytokines and may be perturbed in PD. Notably, such work may identify therapeutic targets for PD treatment with peripheral drug targets overcoming challenges with drug delivery across the blood brain barrier.

15.2

Adeno-associated virus vector targeting of striatal astrocytes and neurons

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Current clinical trials for adeno-associated viral vector (AAV) gene therapies for central nervous system diseases focus on manipulation of neuronal function. Targeting neuronal and non-neuronal cell types could improve therapeutic efficacy. This study aims to develop and characterise AAV vectors capable of targeting both astrocytes and neurons through capsid selection and expression cassette design. A bicistronic AAV plasmid expressing GFP and mCherry under control of neuronal human synapsin and astrocytic glial fibrillary acidic protein (GFAP) promoters, respectively, was packaged into six AAV serotypes as well monocistronic AAV plasmids expressing GFP under control of aldehyde dehydrogenase 1 family member L1 (ALDH1L1) and GFAP promoters. Mouse primary corticostriatal cultures were transduced with the AAV vector panel and reporter gene expression analysed after seven days. Selected vectors were injected into the 2–3-month-old C57BL6 mouse striatum. Transduction spread and cell specificity were assessed 3-4 weeks later. In primary cells, AAV1 and AAV 6 bicistronic and ALDH1L1 vectors showed highest neuronal and astrocytic transduction. In the mouse striatum, the bicistronic plasmid had greater striatal spread in AAV9 compared to AAV6 (44.47%±3.95 vs 14.69%±8.25, p=0.015). ALDH1L1 in AAV9 (48.54%±14.04) also had higher spread than the bicistronic expression cassette in AAV1 (19.00±3.84, p=0.016) and AAV6 (p=0.003). All vectors showed greater neuronal than astrocytic transduction. This study demonstrates the capacity for bicistronic and ALDH1L1 promoters to drive transgene expression in cultured astrocytes and neurons with efficiency and specificity that is highly dependent on AAV serotype. Future work will compare serotype choice in vivo.

15.3

Relevance of the Kappa Opioid Receptor as a potential dual-regulatory therapeutic for Multiple Sclerosis

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Multiple sclerosis (MS) is a chronic, inflammatory, and neurodegenerative disease that has no cure. Progression of MS treatments is impeded by the multi-faceted pathology of the disease. MS is characterised by maladaptive peripheral immune system attacks on myelin, which current treatments target, but also periods of central neuroinflammation and demyelination. Designing pharmacotherapies that target these central nervous system aspects of MS pathology is critical for future drug development. Agonism of the kappa opioid receptor (KOR) has been shown to have immunomodulatory effects in vivo that synergise with fingolimod, a current MS treatment. In preclinical models, we show that treatment with the KOR agonist, nalfurafine, reduces astrogliosis and drive microglia from a pro-inflammatory (CD74+/CD68+) phenotype towards a phenotype promoting healing and repair (CD206+). We also show that administration of novel KOR agonists in oligodendrocyte precursor cell-containing cultures drives the differentiation of these cells into complex, myelinating oligodendrocytes a favourable effect for remyelination. Limited knowledge exists regarding KOR expression within the human brain, especially its expression on cell-types relevant to neuroinflammation and myelination. Using in situ hybridization and immunohistochemistry, we have characterised human KOR expression on neurons, astrocytes, microglia, and oligodendrocytes. It shows region-dependent expression levels with greatest expression in subcortical structures including the caudate nucleus and medulla. KOR expression is highest on neurons compared to other relevant cell-types, a finding seen in tissue from both healthy and MS-diagnosed donors. The dual-mechanism mode of action, and clinical relevance, of the KOR renders it a viable target for development of MS pharmacotherapies.

15.4

Characterising changes in immune cell populations at the brain borders after traumatic brain injury

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New Zealand has higher rates of mild traumatic brain injuries (mTBIs, or concussions) than the worldwide average, with 790 of 100,000 Kiwis suffering a mTBI annually. Concerningly, mTBI is 23% more common in Māori, presenting an important equity issue for New Zealand. Recent evidence has revealed the membranes that surround the brain termed the meninges—specifically the outermost dura mater—to be a critical site of immunological activity after traumatic injury. Furthermore, direct connections between the dura and skull bone marrow (SBM) through vascular channels in the skull bone, allows the SBM to act as a reservoir of immune cell first-responders following injury. To better understand the role of the dura and SBM after mTBI, we aimed to characterise changes in immune cell populations within the dura and SBM. We applied a closed-skull cortical impact or sham surgery to C57BL/6J mice and collected the SBM and dura for spectral flow cytometry 4, 7, and 14 days after injury. We observed extensive infiltration of diverse immune cells, including macrophages, monocytes, neutrophils, and T cells, into the dura 4 days after mTBI. Fewer neutrophils were observed in the SBM, indicating that the SBM may supply neutrophils to the dura after mTBI. Interestingly, these changes were significantly reduced by day 7-14. These results provide a temporal profile of the immunological processes following mTBI and highlights key immunological players involved, such as neutrophils, monocytes, and macrophages. Modulating the immune activity at the brain borders could hold therapeutic potential for Kiwis who suffer a concussion.

15.5

The kor receptor nalfurafine improves inflammation in a rodent model of spinal cord injury

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Kappa opioid receptors (KOR) have been shown to reduce inflammation, modify the immune response and promote remyelination in models of multiple sclerosis. The KOR nalfurafine has been shown to be more effective than older KORs due to its biased agonism for the G-protein coupled pathway as opposed to the β-arrestin pathway and p38 activation. This pathway is a major contributor to SCI injury and inflammation. Therefore, we are testing the G-protein biased KOR nalfurafine for its ability to improve inflammation, improve remyelination and modify immune cell infiltration after SCI. Sprague Dawley rats were given a moderate (175 kdyne) contusion spinal cord injury at T10 using the Infinite Horizons impactor. Animals were randomly divided into 3 groups (n = 8/group) and received daily i.p injections of vehicle, 0.03 or 0.1 mg/kg nalfurafine for 4 weeks. Animals underwent open field testing to measure hind limb function and co-ordination using the Basso-Beattie-Bresnahan (BBB) rating scale and tissue was collected at the end of the study for immunohistochemical analysis. Treatment with 0.03 mg/kg showed a significant decrease in total and M1 microglia compared to control (one-way ANOVA, Bonferronis post-hoc test, $p < 0.05$). No significant difference in astrocytes or M2 microglia was seen between the groups. Data on the valuation of T cell populations using a cell classification algorithm is currently underway and will be presented. Preliminary analysis suggests different effects of the treatment on different T-helper cell subtypes. Our study suggests that treatment with nalfurafine may potentially modify inflammation after SCI.

15.6

Neuronal α-synuclein toxicity drives degeneration in Multiple System Atrophy

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Multiple system atrophy (MSA) is a rare, rapidly progressing neurodegenerative disorder often misdiagnosed as Parkinson's disease (PD) due to overlapping clinical features. While MSA is defined by α-synuclein (α-Syn) inclusions in oligodendrocytes—known as glial cytoplasmic inclusions (GCIs)—this has led to the misconception that it is primarily a glial disorder. In fact, MSA shows more extensive loss of non-dopaminergic neurons in the nigrostriatal and olivopontocerebellar systems compared to PD, with limited oligodendroglial cell death. Using a combination of an N-terminal α-Syn antibody that enhances the detection of α-Syn pathology and super-resolution imaging, we identified α-Syn fibrils in MSA neurons extending from the cytoplasm into the nucleus. This nuclear invasion causes envelope breakdown, loss of Lamin integrity, and subsequent neuronal death. While similar cytoplasm-to-nucleus progression occurs in oligodendrocytes, the α-Syn aggregation states differ: neuronal inclusions are more protease-resistant than GCIs and are associated with nuclear destruction. These findings highlight a more direct and toxic role for neuronal α-Syn pathology in MSA progression. The more aggressive neurodegeneration seen in MSA compared to PD may result from this nuclear damage. To better reflect the dual pathology of MSA, we propose reclassifying it as a "Dual-Phase α-Synucleinopathy", recognising the combined but distinct contributions of oligodendroglial and neuronal α-Syn pathology—particularly the destructive nuclear involvement in neurons—as key drivers of disease progression.

16.1

Simultaneous 2- and 3-photon multiplane imaging across cortical layers in freely moving mice

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Head-mounted multiphoton microscopes enable imaging of activity from neuronal populations spread throughout the cortical layers in freely moving mice, but so far have been restricted to recording from one cortical layer at a time. Here, combining 2- and 3-photon based excitation delivered through multiple fibers, we built a head-mounted multiplane microscope enabling near simultaneous imaging (8ns between planes) of neuronal activity from five vertically separated planes, spread across multiple cortical layers. Both excitation pathways had remote focusing mechanisms for fine axial adjustments enabling activity recordings from the same neuronal populations over weeks in freely behaving mice. The lightweight microscope utilized an onboard, 2-channel detection system designed to enable activity recordings from neuronal populations spread across visual-cortex layers in both lit and dark conditions as well as imaging activity across posterior parietal cortex layers during complex gap-crossing behaviors. We show that during gap-crossing tasks, layer 5 and 2/3 neuronal subpopulations in posterior parietal cortex have differential pattern sequences during free decision making.

16.2

Streamlining neurodegenerative imaging: Early-phase amyloid PET as a one-stop modality, comparisons with FDG PET and ASL MRI

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Dual-phase amyloid Positron emission tomography (PET) imaging has emerged as a promising technique to simultaneously assess both protein pathology and cerebral perfusion or metabolism. This modality involves PET images taken immediately after radiotracer injection to mirror perfusion/metabolism, alongside the standard amyloid pathology assessment. The study aimed to evaluate early-phase 18F-Florbetaben (eFBB) PET as a surrogate for Fluorodeoxyglucose (FDG) PET and arterial spin labelling (ASL) MRI in individuals with varying levels of cognitive impairment. Twenty participants underwent dual-phase FBB PET, FDG PET, and ASL MRI, including Alzheimer's disease (AD, n=3), mild cognitive impairment (MCI, n=11), subjective cognitive decline (SCD, n=4), and non-neurodegenerative controls (n=2). They also underwent cognitive assessments (Addenbrooke's Cognitive Examination). eFBB PET demonstrated strong within-subject and regional correlations with FDG PET (median r = 0.85–0.81), supporting its potential as a proxy for cerebral metabolism. In contrast, ASL MRI showed weaker and more variable associations with both PET measures. Voxel-wise analyses revealed significant correlations between eFBB uptake and cognitive performance in temporoparietal regions commonly affected in AD. These associations largely mirrored those observed with FDG PET. Importantly, early-phase and FDG PET outperformed ASL MRI in their associations with cognitive performance. These findings support the growing literature that early-phase amyloid PET is a feasible alternative to FDG PET for assessing hypometabolism in cognitive impairment. This approach may reduce scan time, radiation exposure, and cost, making it attractive for memory clinics and trials of disease-modifying therapies. Early-phase imaging may also improve diagnostic accuracy and participant stratification in clinical research.

16.3

Investigating a potential "viability switch" in a juvenile-onset ATP13A2-associated Parkinson's disease model

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Parkinson's disease (PD)-associated mutations disrupt the cell functions, making dopaminergic neurons in the mid-brain region vulnerable to environmental factors. While most PD cases require decades to demonstrate the pathogenic phenotype, ATP13A2-associated PD has a juvenile age of onset. Long non-coding RNAs (lncRNAs) have a regulatory function in many cellular processes, and one of the specific features of ATP13A2-associated PD is the low expression level of lncRNA NL02, which is associated with cell viability. Here, we investigated the expression of NL02 in ATP13A2-associated PD and whether NL02 inhibition could mimic PD-associated phenotypes in dopaminergic neurons. ATP13A2 knockout (KO) iPSC-derived dopaminergic neurons (iDAs) show a significant increase in α-synuclein (the primary hallmark of PD) expression (149±17.92% KO vs 100±10.34% control, $p < 0.05$) and a drop in mitochondrial membrane potential (48±11.1% KO vs 100±18.9% control, $p < 0.05$) in comparison to the control. In silico analysis shows a significant decrease in NL02 expression specifically for ATP13A2-associated PD (data from GEO analysed with R). Further analysis revealed that in the mid-brain region, multiple NL02 variants are expressed, whose function is unknown. We established that inhibiting NL02 in iDAs shows PD-like phenotypes (significant increase in α-synuclein, 127.96±3.94% NL02-deficient vs 100±2.64% control, $p < 0.05$). We aim to evaluate the NL02 variant expression in two ATP13A2 patient iPSC-derived mutant iDAs. We will confirm the pathology in the ATP13A2 mutant iDAs before testing whether NL02 can rescue PD phenotypes. These studies will guide future work on NL02 variant expression and the potential to rescue ATP13A2-associated PD.

16.4

Mapping Nurr1's functional domains for targeted gene activation and therapeutic use in Parkinson's disease

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We are developing a compact gene regulation system using Nurr1, an endogenous transcription factor essential for the development and survival of dopaminergic neurons as both a therapeutic agent and transcriptional regulator for a gene therapy strategy for Parkinson's disease (PD). Adeno-associated viruses are widely used for gene therapy but are limited by a packaging capacity of ~4.7 kb, so we aimed to develop an optimised, truncated NURR1 switch. We generated six structural variants of Nurr1 with different combinations of the N- and C-terminal regions that contain the putative activation function 1 (AF1) domain, and the DNA-binding domain (DBD). Plasmids expressing these variants were cloned and HEK293 cells were co-transfected with each variant alongside a GFP reporter under the control of a Nurr1-responsive element. Nurr1 expression and activation of the response element were assessed using immunocytochemistry and western blot. In parallel, AAV vectors encoding the variants were used to transduce differentiated SH-SY5Y cells to evaluate their impact on endogenous dopaminergic targets. All six variants activated the reporter to varying degrees. Variants containing only AF1 and DBD showed the lowest activity, while those retaining the C-terminal region and a truncated N-terminus matched the transcriptional activity of the full-length protein, highlighting the importance of these regions in gene expression. In SH-SY5Y cells, Nurr1 transduction increased expression of tyrosine hydroxylase, a key enzyme in dopamine synthesis. These results demonstrate the functional efficiency of shorter Nurr1 variants, which will be further developed to engineer a compact, internally regulated gene therapy system for PD.

16.5

Benchmarking different MRI phenotypes for ethnic bias in cognitive-functioning prediction

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Ethnic bias in machine learning occurs when models show unequal predictive accuracy across demographic groups, often due to under-representation of certain ethnicities in training data. While recent studies have used machine learning to predict cognitive functioning from MRI-based brain phenotypes, it remains unclear which MRI phenotypes are susceptible to ethnic bias. Using the Adolescent Brain Cognitive Development (ABCD) dataset, we trained models to predict cognitive functioning from various MRI phenotypes, including resting-state fMRI (rsfMRI), task-based fMRI (tfMRI), structural MRI (sMRI), diffusion tensor imaging (DTI), and their combinations. Models were trained on three datasets: (a) African American (AA) only, (b) White American (WA) only, and (c) a balanced AA+WA subset. To quantify bias, we calculated the difference in performance between ethnicity-congruent and incongruent training-test pairs. Permutation testing revealed ethnicity-specific biases in test performance, measured by Mean Absolute Error (MAE). WA-trained models significantly underperformed on AA test sets, and vice versa, across all MRI phenotypes. Even models trained on the full or balanced datasets showed persistent underperformance for AA participants. Ethnicity-bias scores ranged from 0.36 to 1.106, with some MRI phenotypes, showing the least bias (e.g., tfMRI from the two-back-minus-zero-back contrast). Combining across MRI phenotypes through multimodal stacking did not consistently reduce bias. We also found a moderate relationship (r=–.57) between predictive accuracy and ethnicity-bias scores, suggesting that improving model performance may help mitigate bias indirectly. These findings highlight the need for bias-mitigation strategies (e.g., focusing on MRI phenotypes less affected by the bias, and using ethnicity-specific models) to ensure fair/equitable cognitive prediction across diverse populations.

16.6

From menarche to menopause: Estradiol and brain aging in women

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The transition to menopause is characterized by declining estradiol levels, which coincides with an increased risk of dementia in women. This temporal overlap suggests estradiol may influence brain aging and age-related neuropathology. We investigated whether reproductive events associated with estradiol exposure—namely, age at menarche and menopause—relate to brain aging. Using a validated machine learning model, we analyzed structural MRI data from 1,006 postmenopausal women. We found that earlier menarche, later menopause, and a longer reproductive span were each associated with less evident brain aging. These findings support the hypothesis that longer cumulative exposure to estradiol may have neuroprotective effects. However, the observed effects were modest, and estradiol levels were not directly measured. Further research is needed to clarify causal mechanisms and to examine the influence of additional factors, including genetic predispositions, lifestyle, and comorbidities. Future work incorporating hormone assays and more diverse samples will be critical for improving our understanding of the relationship between reproductive history, estradiol, and female brain aging.

17.1

The role of plasticity in the central and peripheral nervous systems

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Plasticity is a widespread feature of synapses in both the central and peripheral nervous systems. Research in my lab has focused on Shank3 - a postsynaptic multidomain PSD scaffold protein that is critical for structural stability, synaptic maturation and plasticity. Our early studies showed that zinc is a potent regulator of Shank3 activation and dynamics, and that Autism Spectrum Disorder (ASD)- and Phelan-McDermid Syndrome (PMD)-associated variants of *Shank3* retain zinc sensitivity and zinc-dependent activation of excitatory synaptic transmission. We then advanced this work to ASD and PMD animal models, and found that in vivo dietary zinc supplementation can reverse ASD/PMD-associated behaviours and alter glutamatergic synaptic transmission and plasticity in young adult *Shank3*$^{-/-}$ mice. These data link dietary changes in zinc levels with plasticity in the brain that could be beneficial for treatment strategy for ASD, and we are now testing zinc treatment in human derived neurons. In contrast to the brain, synaptic structure and function in the peripheral nervous system differs significantly. We have recently focussed on plasticity occurring within clusters of neurons localised on the heart surface where they play a critical role in controlling heart rhythm. We conducted the first electrophysiological and structural analysis of these neurons in the human heart, and showed that they exhibit significant structural complexity. Interestingly they also show increased excitability in patients with the common cardiac arrhythmia atrial fibrillation (AF). Therefore, similar to the brain, human heart neurons alter their structure and function with disease. Together these data identify synaptic targets and neural plasticity as a major contributor to the substrate of atrial arrhythmia in a similar fashion to what is observed with neuropathologies in the brain, and also identifies plasticity pathways for peripheral nervous system treatment strategies.