2022

AWCBR

Australasian Winter Conference on Brain Research

AWCBR 2022

Neurological Foundation
A pathway to hope

Aotearoa Brain Project | Kaupapa Roro o Aotearoa

Sunday 28 August 2022

3.30 pm-6.00 pm	REGISTRATION, CROWNE PLAZA HOTEL
6.00 pm	OPENING RECEPTION, CASH BAR AND LIGHT FOOD, Atrium
7.00 pm	OPENING REMARKS

7.15 pm

1. PLENARY LECTURE:

CHAIR: STEPHANIE HUGHES

Margaret Morris, *University of New South Wales, Sydney, Australia*

The modern food environment: how diets high in fat and sugar impair cognition and alter the gut microbiome in rats

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2. Disorders of the Nervous System

CHAIR: IAN KIRK

8.00 pm	2.1	**Caitlin Oyagawa, *University of Auckland, Auckland, New Zealand*** Investigating the mechanisms of cardiac glycosides as modulators of barrier inflammation
8.15 pm	2.2	**Maize Cao, *University of Auckland, Auckland, New Zealand*** Identifying TDP-43 loss-of-function markers in amyotrophic lateral sclerosis
8.30 pm	2.3	**Victor Dieriks, *University of Auckland, Auckland, New Zealand*** Stopping Parkinson's disease. Are 'strains' the solution?
8.45 pm	2.4	**Yuanyuan He, *University of Otago, Dunedin, New Zealand*** Peripheral gene therapy for Alzheimer's disease
9.00 pm	2.5	**Kyla-Louise Horne, *New Zealand Brain Research Institute, Christchurch, New Zealand*** The Wechsler Test of Adult Reading is a stable measure of premorbid IQ in Parkinson's disease

8.15 am COFFEE/TEA

3. Novel Methods and Technology Development

CHAIR: CHRISTOPHER ERB

8.30 am	3.1	**Indranil Basak, *University of Otago, Dunedin, New Zealand*** Loss of Batten disease associated CLN5 leads to neuronal lysosomal defects, altered cell proliferation and ion transport in human neurons
8.45 am	3.2	**Julia Plank, *University of Auckland, Auckland, New Zealand*** Brain temperature as a measure of neuroinflammation: Assessment using whole-brain magnetic resonance spectroscopy
9.00 am	3.3	**Darren Svirskis, *University of Auckland, Auckland, New Zealand*** Neural recordings in freely moving rats using a novel bioelectronic implant positioned and maintained directly on the spinal cord
9.15 am	3.4	**Maryam Tayebi, *Auckland Bioengineering Institute, Auckland, New Zealand*** Microstructural differences in the brain of high school rugby players compared to non-contact sports athletes
9.30 am	3.5	**Sahan Jayatissa, *University of Auckland, Auckland, New Zealand*** A high throughput *in vitro* platform for traumatic brain injury: A stretchy solution

4. Poster Session

MORNING TEA AVAILABLAE

9.45 am-11.45 am

Presenters with odd numbers should put up their posters at 8.00 am and be in attendance from 9.45 am-10.45 am.

Presenters with even numbers should put up their posters at 8.00 am and be in attendance from 10.45 am-11.45 am.

All presenters: Please remove your poster at 1.00 pm to allow the next person to use your board.

4.1 **Abbie Harris, *New Zealand Brain Research Institute, Christchurch, New Zealand***

Parkinson's disease: Neuroanatomical differences and correlates of cognitive impairment

4.2 **Kaaryn Cater, *Whitireia, Wellington, New Zealand***

Environmental sensitivity and its impact on learning for higher education students

4.3 **Aimee Mills, *University of Auckland, Auckland, New Zealand***

Mutant huntingtin aggregates and glial changes in the midcingulate cortex in Huntington's disease

4.4 **Kate Witt, *Victoria University of Wellington, Wellington, New Zealand***

Dopamine D1 receptor and effort-based decision making in rats: The moderating effect of sex

4.5 **Ali Delbaz, *Griffith University, Queensland, Australia***

Streptococcus agalactiae brain invasion via the olfactory and trigeminal nerves

4.6 **Nakhon Thai, *University of Auckland, Auckland, New Zealand***

Characterisation of DARPP-32 within the human basal ganglia in Huntington's and Parkinson's disease

4.7 **Bronwyn Riley, *University of Auckland, Auckland, New Zealand***

Regional differences in striatal dopamine transmission between DAT-KO and wildtype rats

4.8 **Katie Smith, *University of Auckland, Auckland, New Zealand***
Moving beyond response times: A simple solution for capturing response dynamics

4.9 **Bryony Thorne, *Victoria University of Wellington, Wellington, New Zealand***
Mitochondrial abundance and function in the serotonin transporter knockout model: a sexually dimorphic association

4.10 **Kreesan Reddy, *University of Auckland, Auckland, New Zealand***
A strain-specific approach: Identification of therapeutic targets associated with distinct α-Synuclein polymorphs

4.11 **Brad Raos, *University of Auckland, Auckland, New Zealand***
An in vitro model of neural strain injury to investigate the effects of electric fields on promoting axonal repair

4.12 **Kristina Jardine, *University of Otago, Dunedin, New Zealand***
The role of RNF167 in lysosomal regulation within neuronal dendrites

4.13 **Catherine Webb-Robinson, *University of Auckland, Auckland, New Zealand***
Insulin resistance does not change PSA-NCAM load in the rat entorhinal cortex.

4.14 **Olivia Harrison, *University of Otago, Dunedin, New Zealand***
Anxiety is associated with interoceptive insight deficits in women but not men

4.15 **Chelsie Osterman, *University of Auckland, Auckland, New Zealand***
Vasculature and neuroinflammation in chronic traumatic encephalopathy

4.16 **Kyrah Thumbadoo, *University of Auckland, Auckland, New Zealand***
X marks the spot: A neuropathological signature of the X-linked motor neuron disease gene *UBQLN2*

4.17 **Daiana Yedgey, *University of Auckland, Auckland, New Zealand***
Phosphorylated tau and α-synuclein presentation in the human olfactory epithelium.

4.18 **Bhavya Chawdhary**, ***University of Auckland, Auckland, New Zealand***
Tonabersat rescues inflammatory damage in an experimental mouse model of multiple sclerosis through Connexin-43 hemichannel blockade

4.19 **Bronwyn Kivell, *Victoria University of Wellington, Wellington, New Zealand***

Nalfurafine and ethoxymethyl ether Salvinorin B promote recovery and remyelination in CNS demyelination disease models

4.20 **Lee-Anne Morris, *University of Otago, Christchurch, New Zealand***

Altered nucleus accumbens functional connectivity predicts apathy development in Parkinson's disease

4.21 **Delshad Kalantary, *University of Auckland, Auckland, New Zealand***

In vivo fibre photometry in freely behaving mice: a cutting-edge technique to measure activity of hippocampal neurons

4.22 **Panzao Yang, *University of Auckland, Auckland, New Zealand***

Therapeutic hypothermia attenuates cortical interneuron loss after cerebral ischemia in near-term fetal sheep

4.23 **Denise Neumann, *University of Auckland, Auckland, New Zealand***

A longitudinal study of antenatal and perinatal risk factors for executive control and receptive language in early childhood

4.24 **Marion McKinnon, *University of Waikato, Hamilton, New Zealand***

Efficacy of cannabinoids to treat neuropathic pain symptoms in a mouse model of Charcot-Marie-Tooth disease, Type 2A

4.25 **Eryn Kwon, *Mātai Medical Research Institute, Gisborne, New Zealand***

Value of multimodal MRI in analysis and visualisation of physiological changes before and after a mild traumatic brain injury in a large animal model

4.26 **Laura Marriott, *University of Auckland, Auckland, New Zealand***

Identification of primary tauopathy cases in the New Zealand Neurological Foundation Human Brain Bank

4.27 **Emily Gould, *University of Auckland, Auckland, New Zealand***

Regional variation of dopamine transmission in the caudolateral (tail) striatum

4.28 **Remai Parker, *University of Auckland, Auckland, New Zealand***

Preparation of human brain tissue for studies of neurodegenerative diseases

4.29 **Paul Condron, *Mātai Medical Research Institute, Gisborne, New Zealand***

Multiplication, Addition, Subtraction and/or Division of Inversion Recovery (MASDIR) sequences: Theory and practice in MRI of the brain

4.30 **Nidhi Aggarwal, *University of Auckland, Auckland, New Zealand***
Event related potentials during adaptive go/no-go auditory discrimination in sighted and blind human adults

4.31 **Miriam Rodrigues, *Auckland District Health Board, Auckland, New Zealand***
The New Zealand motor neurone disease registry

4.32 **Patricia Lam, *University of Auckland, Auckland, New Zealand***
Investigating the expression of NKCC1 and KCC2 in Alzheimer's disease mouse models

4.33 **Hannah Hawley, *Massey University, Palmerston North, New Zealand***
Focus on the foci: Investigating the role of HDAC4 aggregation in neuronal development in *Drosophila melanogaster*

4.34 **Ruth Monk, *University of Auckland, Auckland, New Zealand***
Development of a human neuronal model for Parkinson's disease drug discovery to test novel compounds targeting α-synuclein and protein degradation machinery

4.35 **Hannah Mein**, ***University of Otago, Dunedin, New Zealand***
Altered polyamine system in the P301S (PS19) tauopathy model

4.36 **Miran Mrkela, *University of Auckland, Auckland, New Zealand***
Genetics of motor neuron disease in New Zealand

4.37 **Henry Liu**, ***University of Auckland, Auckland, New Zealand***
Characterisation of astrocyte and microglia phenotypes in the Alzheimer's disease human brain

4.38 **Rebecca Lee, *New Zealand Brain Research Institute, Christchurch, New Zealand***
Early cannabis use and its impact on the ageing brain: an MRI study of a New Zealand longitudinal birth cohort

4.39 **Florian Kurth, *University of Auckland, Auckland, New Zealand***
Age-related gray matter asymmetry changes

4.40 **Ruben Vergara, *University of Otago, Dunedin, New Zealand***
Role of ryanodine receptor clustering in Alzheimer's disease

4.41 **Huey-Tieng Tan, *University of Otago, Dunedin, New Zealand***
Stimulation-evoked dopamine release in the auditory cortex of anaesthetised rats

4.42 **Samuel Schwarzkopf,** ***University of Auckland, Auckland, New Zealand***
Population receptive field maps of the physiological blind spot in human observers

4.43 **James Wiseman,** ***University of Auckland, Auckland, New Zealand***
N-terminus α-synuclein immunoreactivity reveals novel and distinct α-synuclein aggregate morphologies in Parkinson's disease

4.44 **Shelley Scheepers,** ***University of Auckland, Auckland, New Zealand***
Nanostring nCounter analysis of the neuroinflammatory pathways in the midcingulate cortex in Huntington's disease

4.45 **Kathryn Todd,** ***University of Auckland, Auckland, New Zealand***
Modulation of the substantia nigra pars lateralis by the subthalamic nucleus

4.46 **Sophie Mathiesen,** ***University of Otago, Dunedin, New Zealand***
Peripheral administration of AAV-PHP.eB encoding TFEB causes toxicity in mice

4.47 **Janelle Chong,** ***University of Auckland, Auckland, New Zealand***
The effects of general anaesthesia and light on the mammalian circadian clock

4.48 **William Cook,** ***Auckland District Health Board, Auckland, New Zealand***
Using a rapid adeno-associated virus vector screening method for optimising the development of gene therapy for neurological disease

4.49 **Jerram Sheehan,** ***University of Auckland, Auckland, New Zealand***
Spinal cord injury alters oligodendrocyte specific expression of ADAMTS4, a key modulator of oligodendrocyte maturation and myelination

4.50 **Victoria Low,** ***University of Auckland, Auckland, New Zealand***
Three-dimensional modelling of the human olfactory system and its changes in Parkinson's disease

4.51 **Mayumi Minamisawa,** ***Chiba Institute of Technology, Chiba, Japan***
Treatment of gut and brain leakage by L-arginine and limonoids in Alzheimer's disease

4.52 **Yury Lages,** ***Pontifical Catholic University of Rio de Janeiro, Rio de Janeiro, Brazil***
Anxiolytic effects of CBD are modulated by innate fear-response background in Carioca rat lines

4.53 **Joan Chan,** ***University of Otago, Dunedin, New Zealand***

The effect of benzothiazepine S107, a preventative Ca^{2+} leak drug, on ryanodine type II receptor (RyR2) calcium leak

4.54 **Conor Nelson,** ***University of Auckland, Auckland, New Zealand***

Characterisation of a novel transcription regulation system: optimising gene therapy in the central nervous system

4.55 **Joseph Chen,** ***University of Auckland, Auckland, New Zealand***

Scopolamine's effect on heart rate variability and electroencephalography measures in healthy participants and participants with depression

5. Neural Excitability, Synapses, and Glia: Cellular Mechanisms

CHAIR: LUCIA SCHWEITZER

11.45 am	5.1	**Rabia Bibi,** ***Victoria University of Wellington, Wellington, New Zealand*** Investigating the effects of novel kappa opioid receptor agonists on the differentiation of oligodendrocyte precursor cells *in vitro*
12.00 pm	5.2	**Macarena Pavez,** ***University of Otago, Dunedin, New Zealand*** Uncovering new trafficking routes in axons
12.15 pm	5.3	**Taylor Stevenson,** ***University of Auckland, Auckland, New Zealand*** Pericyte cell death and α-synuclein – a double hit
12.30 pm	5.4	**Emma Deeney,** ***University of Otago, Dunedin, New Zealand*** Voluntary exercise restores motor performance in a mouse model of spinocerebellar ataxia type 1 (SCA1)
12.45 pm	5.5	**Shane Ohline,** ***University of Otago, Dunedin, New Zealand*** Immediate early gene expression and intrinsic excitability are not linked in adult-born hippocampal neurons

1.45-2.15 pm ANNUAL GENERAL MEETING
All conference participants are invited to attend

2.15 pm 6. PLENARY LECTURE:

CHAIR: SIMON O'CARROLL

Peter Mombaerts, ***Max Planck Research Unit for Neurogenetics, Frankfurt, Germany***

Visualizing in deceased COVID-19 patients how SARS-CoV-2 attacks the respiratory and olfactory mucosae but spares the olfactory bulb

7. Poster Session

AFTERNOON TEA AVAILABLE

3.00 pm-5.00 pm

Presenters with odd numbers should put up their posters by 1.15 pm and be in attendance from 3.00 pm-4.00 pm.

Presenters with even numbers should put up their posters by 1.15 pm and be in attendance from 4.00 pm-5.00 pm.

All posters to be removed at 5.00 pm.

7.1 **Alexandra Lister,** ***Victoria University of Wellington, Wellington, New Zealand***

Communicative and hippocampal gene expression changes in the serotonin transporter knockout rat following poly I:C -induced maternal immune activation

7.2 **Katja Brand,** ***University of Otago, Dunedin, New Zealand***

Developing models of dynamic interoceptive learning

7.3 **Alexandra Garton,** ***University of Auckland, Auckland, New Zealand***

Molecular and cellular characterisation of the Parkinson's disease olfactory bulb: An origin of disease pathology

7.4 **Katie Peppercorn,** ***University of Otago, Dunedin, New Zealand***

Secreted amyloid precursor protein alpha has widespread effects on the transcriptome and proteome of human neurons related to memory mechanisms

7.5 **Helen Murray,** ***University of Auckland, Auckland, New Zealand***

Multiplex immunohistochemistry and spatial proteomic analysis of the human olfactory bulb in Alzheimer's and Parkinson's disease

7.6 **Jennifer Hamilton,** ***University of Canterbury, Christchurch, New Zealand***

Non-spatial memory and the anterior thalamic nuclei

7.7 **Alina Tetereva,** ***University of Otago, Dunedin, New Zealand***

Multimodal MRI predictive biomarkers for cognition across the lifespan

7.8 **Kushan Gandhi,** ***University of Otago, Dunedin, New Zealand***
A focused ultrasound-mediated drug delivery system in a hemiparkinsonian rat model

7.9 **Ann Holden,** ***University of Otago, Christchurch, New Zealand***
Development of a visual decision-making task to investigate the mechanisms of visual hallucinations in Parkinson's disease

7.10 **Lance Martinez,** ***University of Auckland, Auckland, New Zealand***
Tau pathology in the Huntington's disease human brain

7.11 **Brigid Ryan,** ***University of Auckland, Auckland, New Zealand***
Sociodemographic and clinical characteristics of 1350 patients with young onset dementia: a comparison with older patients

7.12 **Laura McNamara,** ***University of Auckland, Auckland, New Zealand***
Identifying the cellular mechanisms of Alzheimer's disease (AD) in vivo.

7.13 **Ashleigh Barrett-Young,** ***University of Otago, Dunedin, New Zealand***
Childhood social isolation as a predictor of retinal neuronal thickness in middle age: A lifecourse birth cohort study

7.14 **Lucia Schweitzer,** ***University of Otago, Dunedin, New Zealand***
A bad influence: Do glia with defective lysosomes harm healthy neurons?

7.15 **Ashley Deane,** ***University of Otago, Christchurch, New Zealand***
Parkinson's disease: the role of perivascular spaces in cognitive decline

7.16 **Lenore Tahara-Eckl,** ***University of Auckland, Auckland, New Zealand***
Poorer executive function performance is associated with lower white matter fibre in the superior longitudinal fasciculus in Alzheimer's disease risk groups

7.17 **Bria Pengelly,** ***Victoria University of Wellington, Wellington, New Zealand***
The effects of nalfurafine a kappa opioid receptor agonist on glial cell activation in preclinical models of multiple sclerosis

7.18 **Lysea Haggie,** ***Auckland Bioengineering Institute, Auckland, New Zealand***
A spiking neural network model of motor cortex activity

7.19 **Bruce Harland,** ***University of Auckland, Auckland, New Zealand***
Hippocampal place cells form a multi-scale representation of megaspace

7.20 **Meyrick Kidwell,** ***Victoria University of Wellington, Wellington, New Zealand***
The exploration of depression and anxiety like behaviour using novel techniques in SERT Knockout rats

7.21 **Brittney Black,** ***University of Auckland, Auckland, New Zealand***
Glutamatergic characterisation of the human globus pallidus in Huntington's and Parkinson's disease

7.22 **Molly Swanson,** ***University of Auckland, Auckland, New Zealand***
Increased microglial CD68 expression in human Amyotrophic Lateral Sclerosis is associated with pTDP-43 pathology load

7.23 **Brittany Hazelgrove,** ***University of Auckland, Auckland, New Zealand***
Uncovering neural activity in the spinal cord recorded by a novel bioelectronic implant

7.24 **Mackenzie Ferguson,** ***University of Auckland, Auckland, New Zealand***
Neuroinflammatory pathways in the midcingulate cortex in Huntington's disease.

7.25 **Christine Arasaratnam,** ***University of Auckland, Auckland, New Zealand***
DARPP-32 positive cell proportions in the striosome and matrix compartments of the post-mortem human dorsal striatum

7.26 **Nicky Slater,** ***University of Canterbury, Christchurch, New Zealand***
Cholinergic basal forebrain integrity and cognition in Parkinson's disease

7.27 **Cameron Ryall,** ***University of Auckland, Auckland, New Zealand***
Identifying networks of genes interacting with α-synuclein in pericytes

7.28 **Richard Roxburgh,** ***Auckland City Hospital, Auckland, New Zealand***
Pūnaha Io – the New Zealand NeuroGenetic Registry and Biobank

7.29 **Cassandra Dawson,** ***University of Otago, Dunedin, New Zealand***
Assessing the relationship between intrinsic motivations, personality traits and mental health

7.30 **Oliver Burnett,** ***University of Auckland, Auckland, New Zealand***
Neuropathology of the X-linked dystonia parkinsonism striatum

7.31 **Christopher Erb,** ***University of Auckland, Auckland, New Zealand***
Linking the dynamics of cognitive control to individual differences in working memory capacity: Evidence from reaching behaviour

7.32 **Oliver Wood,** ***University of Auckland, Auckland, New Zealand***
Glutamate transporter expression in the hippocampus, subiculum, entorhinal cortex and superior temporal gyrus in Alzheimer's disease

7.33 **Ernest Cheah,** ***University of Auckland, Auckland, New Zealand***
The development of electrically stimulated release of neurotrophic growth factors

7.34 **Sheryl Tan,** ***University of Auckland, Auckland, New Zealand***
Characterisation of the distribution of calcium binding buffer proteins in the human spinal cord

7.35 **Ethan Marshall,** ***University of Otago, Christchurch, New Zealand***
Artificial intelligence as a novel form of motion tracking in Parkinson's disease

7.36 **Poutasi Urale,** ***University of Auckland, Auckland, New Zealand***
Psychophysical evidence for a relationship between cortical distance and illusion magnitude in the Ebbinghaus and Delboeuf illusions

7.37 **Giovanni Pedone,** ***University of Otago, Dunedin, New Zealand***
Determining the relationship between molecular changes in the amygdala and the emergence of associative learning in the rat

7.38 **Joseph Balfe,** ***University of Otago, Wellington, New Zealand***
Serum levels of S100B are significantly correlated with injury severity

7.39 **Deidre Jansson,** ***University of Auckland, Auckland, New Zealand***
Circadian dysregulation of the choroid plexus with age and amyloid pathology

7.40 **Sophie Cawood,** ***University of Otago, Dunedin, New Zealand***
Investigating the relationship between microRNA expression, brain structure and biochemistry in anxiety disorders and their potential treatment with ketamine

7.41 **Grace Hall-McMaster,** ***University of Otago, Christchurch, New Zealand***
Alterations in normalised EEG power across the cognitive spectrum in Parkinson's disease

7.42 **Timothy Sargeant,** ***South Australian Health and Medical Research Institute, Adelaide, Australia***
Retromer is crucial for autophagy and restrains Alzheimer disease-related pathology in human neurons

7.43 **James Davies,** ***University of Otago, Dunedin, New Zealand***
Reliability of remote gait and balance assessment of people with Parkinson's disease

7.44 **Svenja Meissner,** ***University of Auckland, Auckland, New Zealand***
The development of a hydrogel-based ultrasound-triggered delivery system for neurotrophic growth factors

7.45 **Elodie Kip,** ***University of Otago, Dunedin, New Zealand***
Patterned simulation of the Chrimson opsin in glutamatergic motor thalamus neurons improves forelimb akinesia in a chronic rat model of Parkinson's disease

7.46 **Tapasya Pal,** ***University of Waikato, Hamilton, New Zealand***
Aberrant feeding patterns and gene expression in the valproic acid-induced rat model of autism

7.47 **Aliesha Kemp,** ***University of Otago, Dunedin, New Zealand***
Assessing the relationship between sub-clinical anxiety and resting state functional connectivity

7.48 **Thomas Cawood,** ***University of Otago, Dunedin, New Zealand***
Valproate usage correlates with changes in brain volumes in ultra-treatment-resistant schizophrenia

7.49 **Sarah Wilson,** ***Massey University, Palmerston North, New Zealand***
Investigating the interaction between HDAC4 and Ankyrin2 in *Drosophila melanogaster* neuronal function: It's not just about physical attraction

7.50 **Zohreh Doborjeh,** ***University of Auckland, Auckland, New Zealand***
Prediction of tinnitus therapy success using Artificial Intelligence (AI) decision tool

7.51 **Idrish Ali,** ***Monash University, Melbourne, Australia***
E2730, a GABA transporter-1 inhibitor, suppresses epileptic seizures in a rat model of chronic drug resistant mesial temporal lobe epilepsy

7.52 **William Aye,** ***New Zealand Brain Research Institute, Christchurch, New Zealand***
Early phase amyloid PET as a surrogate marker of brain metabolism in neurodegenerative disorders

7.53 **Julia Newland,** ***University of Auckland, Auckland, New Zealand***
KCC2 expression in the human Alzheimer's disease medial temporal lobe

7.54 **Yihan Wu,** ***University of Auckland, Auckland, New Zealand***
Inducing traumatic brain injury in human pericytes using dielectric elastomer actuators

7.55 **Jennifer Tinston,** ***Monash University, Melbourne, Australia***
40Hz sensory entrainment impedes kindling epileptogenesis

Conference Dinner

Colonel's Homestead Restaurant

Walter Peak

Tickets must be purchased in advance.
The ticket includes return transport to and from the restaurant.

5.45 pm Boarding TSS Earnslaw at Steamer Wharf, Queenstown

6.00 pm Departure

6.45 pm Gourmet BBQ dinner

10.00 pm Arrival back at Steamer Wharf, Queenstown

Cash bar on board the TSS Earnslaw. Wine and beer will be provided during dinner.
Musical entertainment will also be provided.

8.45 am COFFEE/TEA

8. Development
CHAIR: SUSAN SCHENK

9.00 am 8.1 **Evgeniia Golovina, *University of Auckland, Auckland, New Zealand***
Autism spectrum disorder: understanding the impacts of SNPs on biological pathways in the human fetal and adult cortex

9.15 am 8.2 **Hamid Abbasi, *University of Auckland, Auckland, New Zealand***
Deep-learning-based automated infant movement tracking scheme for early diagnosis of neurodevelopmental disorders

9.30 am 8.3 **Molly Abraham, *University of Auckland, Auckland, New Zealand***
Knockdown of specific hyaluronan synthases inhibits neurite development in hippocampal neurons *in vitro*

9.45 am 8.4 **Rashi Karunasinghe, *University of Auckland, Auckland, New Zealand***
The hyaluronan cornerstone: An extracellular matrix molecule that regulates early neurite outgrowth in hippocampal neurons

10.00 am **Peter Thorne and Cliff Abraham**
Update on the Aotearoa Brain Project – Kaupapa Roro o Aotearoa

10.15 am MORNING TEA

9. Sensory and Motor System
CHAIR: VICTOR DIERIKS

10.45 am 9.1 **Christina Buchanan, *Auckland District Health Board, Auckland, New Zealand***
A pathogenic PINK1 gene variant is a common cause of early-onset Parkinson's disease in people of Western Polynesian ethnicities

11.00 am	9.2	**Zahra Laouby,** ***University of Auckland, Auckland, New Zealand*** Development of miniaturised microscope imaging in freely behaving rats to examine cortical plasticity following spinal cord injury
11.15 am	9.3	**Rachael Sumner,** ***University of Auckland, Auckland, New Zealand*** Modelling thalamocortical circuitry shows that visually induced LTP changes laminar connectivity in human visual cortex
11.30 am	9.4	**Jordan Lloyd,** ***University of Auckland, Auckland, New Zealand*** Progress towards developing a novel model of parkinsonism based on the dopamine transporter knockout (DAT-KO) rat

10. Cognition and Behaviour

CHAIR: JENNIFER HAMILTON

11.45 am	10.1	**Narun Pat,** ***University of Otago, Dunedin, New Zealand*** Predicting children's general intelligence through multimodal brain-based models
12.00 pm	10.2	**Rebekah Blakemore,** ***University of Otago, Dunedin, New Zealand*** Volitional suppression of parkinsonian resting tremor: A role for the limbic system in modulating tremor-related activity in the striatopallidal motor circuit
12.15 pm	10.3	**Susan Schenk,** ***University of Otago, Dunedin, New Zealand*** Zebrafish on "P": Behavioural effects of methamphetamine
12.30 pm	10.4	**Sonja Seeger-Armbruster,** ***University of Otago, Dunedin, New Zealand*** Thalamic paraventricular nucleus: Bridging homeostatic and reward pathways in the control of feeding
12.45 pm		CLOSING REMARKS AND PRESENTATION OF PRIZES LIGHT LUNCH, THREESIXTY RESAURANT

Acknowledgements

Acknowledgements

We are very grateful to the Neurological Foundation of New Zealand for its generous financial assistance towards travel and registration for students and early career researchers. We also wish to thank the Aotearoa Brain Project – Kaupapa roro o Aotearoa for their support and sponsorship of the early career researcher prizes for best oral and poster presentations.

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Abstracts in Presentation Order

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1.1

The modern food environment: how diets high in fat and sugar impair cognition and alter the gut microbiome in rats

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Increasing intake of energy dense 'discretionary' food items high in fat and sugar is a key risk factor for obesity. Research in rodents and humans indicates that even short-term consumption of such diets, is associated with metabolic dysfunction and mild cognitive impairment. Increasing evidence implicates changes in the composition of the gut microbiome in such behavioural effects. To model dietary effects on intake, cognition and gut microbiome, our laboratory uses high choice cafeteria-style diet, rich in saturated fat and sugars (Caf), incorporating palatable supermarket foods alongside regular chow, which trebles energy intake compared to chow controls. The hippocampus appears particularly sensitive to poor diet, specifically hippocampal-dependent place recognition memory, and people who report greater consumption of fats and sugars ('junk foods') showed more marked loss of hippocampal volume. In rats, exposure to a Caf diet impairs hippocampal dependent spatial learning within 1 week, prior to significant body weight changes. Purified diets that were enriched in saturated fats or simple sugars had a similar impact, with changes in microbiota composition in the absence of body weight changes. Gut microbial diversity was dramatically decreased by extended consumption of Caf and correlated with hippocampal expression of inflammation-related genes. Understanding how these foods influence the gut-brain axis will allow us to develop strategies to mitigate the effects of unhealthy diet on brain health through dietary and other pre/probiotic approaches.

2.1

Investigating the mechanisms of cardiac glycosides as modulators of barrier inflammation

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Neuroinflammation plays a considerable role in the pathology of numerous neurodegenerative diseases. Recent work has indicated that cardiac glycosides act as inflammatory-modulating drugs in human-derived brain cells of the blood-brain barrier (BBB), though their mechanism of action remains to be determined. In this study, Oleandrin, a BBB-permeable cardiac glycoside with potent anti-inflammatory activity in pericytes, was selected as a candidate drug for mechanistic studies. Human phospho-kinase arrays were performed on vehicle or Oleandrin-treated pericytes as a screening tool, and relevant pathways were followed up via the use of specific pathway inhibitors in combination with immunocytochemistry and/or flow cytometry. As the primary action of cardiac glycosides is $Na^{+/}K^{+}$-ATPase inhibition, patch-clamp experiments and ATPase activity assays were performed to investigate effects on the $Na^{+/}K^{+}$-ATPase in pericytes. Results indicated that the anti-inflammatory phenotype is likely downstream of phosphoinositide 3-kinase (PI3K) signalling, and not mediated by Src kinase activity. Patch-clamping and ATPase activity assays revealed that the anti-inflammatory effects occur at concentrations that also inhibit $Na^{+}K^{+}$-ATPase activity. This study has begun to elucidate the mechanisms underlying the anti-inflammatory effects of cardiac glycosides on human brain-derived pericytes, comprehensive understanding of which may provide novel avenues for targeting neuroinflammation at the BBB.

2.2

Identifying TDP-43 loss-of-function markers in amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is a neurological movement disorder that is fatal within 2-5 years after diagnosis. ALS lacks reliable diagnostics and effective treatment, likely due to the heterogeneity of disease. However, a common pathological signature exists in 97% of ALS cases; the aggregation of TAR-DNA binding protein (TDP-43) in motor neurons. TDP-43 normally resides in the nucleus and interacts with DNA and RNA, therefore has a critical role in regulating gene expression. We generated a TDP-43 loss-of-function model of disease by depleting TDP-43 using siRNA in primary human brain pericytes, and analysed the resulting gene expression and splicing changes with RNA sequencing. Differentially expressed genes (padj <0.05, fold change >2) included *PFKP* and *KIAA1324*. Additionally, TDP-43 knockdown led to the inclusion of 'cryptic exons' in the transcripts of several genes. These included *EXD3* and ALS-associated gene *UNC13A.* These changes were all confirmed by quantitative RT-PCR. To extend these findings, we aimed to evaluate whether these TDP-43 loss-of-function mRNA markers and their cognate proteins can be detected in ALS brain tissue with immunohistochemistry. Understanding whether TDP-43 loss-of-function is pathomechanistic in ALS, and in what cell types it occurs, will inform the development of therapeutic strategies to restore TDP-43 function.

2.3

Stopping Parkinson's disease. Are 'strains' the solution?

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Parkinson's disease (PD) is a progressive, degenerative brain disorder affecting the dopaminergic neurons in the *substantia nigra*. Pathologically, PD is grouped with other synucleinopathies such as Dementia with Lewy bodies and Multiple system atrophy, which are all characterised by the abnormal accumulation of α-synuclein aggregates. We hypothesise that the presence of distinct α-synuclein 3D conformations or 'strains' with differences in structural and phenotypic traits are responsible for the heterogeneous nature of PD. We propose that the variability in these synucleinopathies can be stratified based on the α-synuclein strains and that effective treatment requires a strain-specific approach. For this study, we used human brain pericytes. These perivascular cells play an essential role in neuroinflammation and are decreased in PD. Pericytes in situ contain α-synuclein aggregates and in vitro data indicates they can phagocyte and degrade α-synuclein aggregates. Using RNAseq, we identified 622 significantly modified genes after treating pericytes with different α-synuclein strains (Fibrils, Ribbons, fibrils65, fibrils91, and fibrils110). The top 100 proteins will now be validated on human brain sections and in vitro on pericytes. We will select those hits potentially involved in decreasing α-synuclein strain-specific aggregates and subsequently identify the potential therapeutic targets that would enable more efficient α-synuclein degradation.

2.4

Peripheral gene therapy for Alzheimer's disease

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There is no effective treatment for Alzheimer's disease (AD). Soluble amyloid precursor protein-alpha (sAPPα) has promising therapeutic potential. However, E1, a small peptide fragment of sAPPα, may hold even stronger translational potential, particularly if coupled to a cell-penetrating chaperone. AAV-PHP.eB, which readily crosses the blood-brain barrier in C57/BL6 mice, may be a useful vector for delivering E1 to the brain. Accordingly, this project aimed to test AAV-PHP.eB-mediated expression of HA-HA-sAPPα or chaperone-HA-HA-E1 as a peripheral gene therapy in the APPswe/PS1dE9 mouse model of AD. First, to understand the functionality of different peptides, LTP persistence was tested in area CA1 of hippocampal slices from 16-23-month-old female wild-type (WT) and transgenic (Tg) mice. LTP persistence was significantly enhanced by 1 nM E1 and HA-HA-E1 in WT mice, and by chaperone-HA-HA-E1 in both genotypes. To test the therapeutic effects of AAV-PHP.eB-HA-HA-sAPPα versus AAV-PHP.eB-chaperone-HA-HA-E1, 6-month-old WT or Tg mice were given a single tail vein injection and tested 3 months later. Results showed that both HA-HA-sAPPα and chaperone-HA-HA-E1 completely rescued LTP in the Tg mice. Moreover, both treatments dramatically reduced the amyloid plaque load in the hippocampus and frontal cortex. These findings provide a promising novel peripheral gene therapy approach for reducing AD severity.

2.5

The Wechsler Test of Adult Reading is a stable measure of premorbid IQ in Parkinson's disease

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In Parkinson's disease, the Wechsler Test of Adult Reading (WTAR) is recommended as a measure of premorbid intelligence and a reference against which to assess current cognition. We examined if WTAR scores were stable in Parkinson's. Latent class trajectory modelling was used to examine 252 Parkinson's and 57 Control participants with at least two WTAR assessments over up to nine years. Participants were classified into data-driven clusters based on longitudinal trajectories. WTAR scores were above average when adjusted for age-and-education (Control: M=112.6[9.5]; Parkinson's: M=108.9[9.3]). Two trajectories were identified. The first we labelled 'Typical', capturing 78% of participants (81% Parkinson's; 65% Control). In this class, the WTAR-estimated score for a person at the mean age of assessment (70.7 years) was 107.6[105.9, 109.2]. Scores then gently declined at -1.2[-1.9, -0.6] per decade. The remaining participants were captured by the second class, labelled 'High-Performers'. This class had an intercept of 121.0[118.9, 123.1] and a slope of -0.2[-1.2, 0.8] per decade (effectively flat). WTAR scores remained stable over time, even for those who developed dementia. The overestimation of premorbid IQ may make the WTAR unsuitable to establish an individual's decline in cognition. However, the stable performance of the WTAR validates it as a group-level measure of premorbid function in Parkinson's.

3.1

Loss of Batten disease associated CLN5 leads to neuronal lysosomal defects, altered cell proliferation and ion transport in human neurons

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Batten disease is a group of fatal childhood neurodegenerative diseases caused by mutations in one of at least thirteen genes. One of the late-infantile disease forms is caused by mutations in *CLN5* and there is no cure or treatment for this disease. To investigate the underlying neuronal pathologies in CLN5 Batten disease, CLN5 was inhibited (CLN5i) using CRISPR interference (CRISPRi) in an induced pluripotent stem cell-derived human neuronal model (i^3Ns). CLN5i i^3Ns were tested for lysosomal, mitochondrial, and autophagy function followed by multi-omics analysis to understand the mechanism behind neuronal pathology in CLN5 Batten disease. Deficiency of CLN5 in the i^3Ns resulted in compromised lysosomal function, and movement, compromised mitochondrial health, and impaired autophagy. Transcriptomic analysis revealed cell proliferation as an over-represented pathway, whereas ion transport was downregulated in the CLN5i i^3Ns compared to healthy i^3Ns. Proteomic analysis confirmed the downregulation of several transport pathways in CLN5i i^3Ns, including ion transport and protein targeting pathways. The impaired lysosomal function and trafficking due to the loss of CLN5 could lead to improper waste clearance leading to neuronal dysfunction. Furthermore, defects in the transport mechanisms due to the loss of CLN5 could be secondary effects leading to neurodegeneration in CLN5 Batten disease.

3.2

Brain temperature as a measure of neuroinflammation: assessment using whole-brain magnetic resonance spectroscopy

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Studies suggest a pathogenic role of neuroinflammation in psychiatric disorders; however, there are no accepted methods that can reliably measure these inflammatory processes in patients. Magnetic resonance spectroscopic imaging (MRSI) is a non-invasive technique that demonstrates sensitivity to neuroinflammation. Using MRSI in conjunction with echo-planar spectroscopic imaging (EPSI), we aimed to measure brain metabolites to derive estimations of whole-brain and regional brain temperature, which may increase during neuroinflammation. Typhoid vaccine, a safe experimental model of human neuroinflammation, was administered to twenty healthy volunteers in a double-blind, placebo-controlled crossover study including MRSI/EPSI scans before and after treatment administration. Mood, assessed using the Profile of Mood States, was measured hourly up to four hours post-treatment administration. A mixed model analysis of variance tested for treatment effects. A significant proportion of brain regions (44/47) increased in temperature post-vaccine compared to post-placebo ($p<0.0001$). For temperature change in the brain as a whole, no significant treatment effect was observed. Significant correlations were observed between mood scores and post-treatment whole brain and regional temperatures. Results indicate that regional, rather than whole, brain temperature may be a more sensitive measure of neuroinflammation. Future application of these neuroimaging techniques to patient populations would be of clinical interest.

3.3

Neural recordings in freely moving rats using a novel bioelectronic implant positioned and maintained directly on the spinal cord

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Bioelectronic implants are promising neural interfaces for treating central nervous system disorders as they are capable of combining multiple functionalities within the same interface. Here, we present the development and characterization of a thin flexible bioelectronic implant designed to be placed in the subdural space above a spinal cord injury to monitor changes in neural activity. We show the implant can be inserted over the thoracic spinal cord in rats without negative impact on hind-limb functionality. Seven days after implantation of the devices, there was a slight reduction in spinal cord volume and an increased foreign body response of astrocytes and microglia in spinal tissue. To facilitate neural recordings with the bioelectronic implant, we house the external connector in a 3-D printed backpack, attached to the back muscle via sutures and surgical mesh. The bioelectronic implant and backpack assemblies were maintained in rats for a period of 3 months. We present neural recordings taken with the bioelectronic implant, which to our knowledge constitute the first recordings of spinal cord activity in freely moving animals. In the future, this implant will facilitate the identification of biomarkers in spinal cord injury and recovery, while facilitating the delivery of electroceutical and chemical treatments.

3.4

Microstructural differences in the brain of high school rugby players compared to non-contact sports athletes

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Contact sports athletes experience repeated head impacts during their games and practices. Such repeated exposures might lead to subtle changes in their brain, especially in the structure of WM fibre tracts. We conducted a diffusion MRI study on high school rugby players and non-contact sports athletes to investigate the microstructural differences in the brain of these two groups. Thirty-seven male high school rugby players and 11 healthy non-contact sports athletes were recruited. Using a 3T MRI scanner, a multi-shell dMRI sequence was acquired on the brains of all participants (two times for rugby players; pre and post-season). Diffusion images were processed using FSL, and diffusion metrics including fractional anisotropy, mean, axial and radial diffusivity were analysed with a TBSS tool. In multiple white matter tracts, the MD and AD were found to be significantly lower in the brain of rugby players (pre-season scan) compared with the control group. A statistically significant two-fold difference of MD and AD was observed in the brain of rugby players post-season compared with the healthy controls. While such changes may suggest axonal damage or edema, further work is required to factor in changes such as growth, and better filtration of other 'ground truth' comparative measures.

3.5

A high throughput *in vitro* platform for traumatic brain injury: A stretchy solution

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Mild Traumatic Brain Injury (mTBI) is a leading neurological injuries worldwide, and New Zealand has one of the highest rates among developed countries. While the immediate injury is considered 'mild', the results can include persistent neurological dysfunction and long-term neurodegeneration. The nature of mTBI makes it difficult to study in human patients; hence, an *in vitro* mechanical assay has been explored as a potential way to study mTBI. We present a high throughput platform (HTP) that utilises an Dielectric Elastomer Actuator (DEA) as a deformable cell culture substrate to provide high strain with fast response times, recapitulating the characteristic strains experienced during an mTBI event. Our HTP conforms to a standard 12-well plate, allowing it to be used in a variety of pre-existing biological apparatus. We conducted experiments using cultured human brain cells isolated directly from patient biopsy specimens to validate the platform. We characterised the strain homogeneity of a culture well by mapping the strain levels induced onto the cells using a registration algorithm with sub-pixel resolution. Our HTP is capable of applying controlled amounts of mechanical insults directly to human brain cells in a high-throughput manner, making it an attractive device for drug and biomarker researcher for TBI.

Poster 4.1

Parkinson's disease: neuroanatomical differences and correlates of cognitive impairment

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Cognitive impairment is an almost inevitable symptom of PD, although individual trajectory is highly variable, and the key neural changes remain uncertain. T1 structural magnetic resonance imaging and level-II neuropsychological testing was conducted in 115 participants with PD (male=72) and 40 controls (male=18). Whole-brain grey matter (GM) volumes were assessed between groups and associations between global cognitive scores were evaluated. Compared to controls, PD patients showed significantly smaller GM volume in temporal and occipital cortices (corrected P <.05). A global cognitive score was positively correlated with GM volume in widespread areas of temporal and occipital regions, including the medial temporal lobe (corrected P <.05). Longitudinal research will determine whether these GM regions are predictive of cognitive decline in PD. This evidence may improve risk profiling for cognitive decline in PD.

Poster 4.2

Environmental sensitivity and its impact on learning for higher education students

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People differ in their levels of sensitivity to internal, external, social, and emotional stimuli and this is underpinned by genetic, physiological, and personality/temperamental factors. Environmental sensitivity exists on a continuum of low, medium, and high and the phenotypic expression of high sensitivity is Sensory Processing Sensitivity as measured by the Highly Sensitive Person Scale. The historical deficit notion of sensitivity is being challenged empirically, and the recent framework of Vantage Sensitivity holds that highly sensitive people may disproportionately benefit from positive environments than less sensitive individuals. Further, high sensitivity is associated with deep cognitive processing, heightened emotional reactivity, creativity, memory, divergent thinking, giftedness, and metacognitive monitoring. This study (n=365) explored the associations between levels of sensitivity as measured by the Highly Sensitive Person Scale-12 and success-promoting attitudes and strategies as measured by the Perceived Success in Study Survey for postsecondary students. Correlational, descriptive, independent T-tests and ANOVA statistics were used to analyse the data. The results found that high sensitivity is positively associated with increased success-promoting attitudes and strategies. This is one of the first studies investigating the impact that environmental sensitivity has on learning and highlights interesting educational implications for learners at both ends of the sensitivity spectrum.

Poster 4.3

Mutant huntingtin aggregates and glial changes in the midcingulate cortex in Huntington's disease

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Huntington's disease (HD) is a neurodegenerative disorder that can cause motor, mood and cognitive symptoms. Neuronal death in the cingulate cortex correlates with mood symptomatology. Neuronal loss is also linked to accumulation of mutant huntingtin protein (mHTT), a known trigger of neuroinflammation. Neuroinflammation involves protein and morphology changes in microglia and astrocytes. However, the contribution of these glial changes to HD pathology is not well understood. Using immunohistochemistry, post-mortem midcingulate cortex (MCC) tissue from HD and control cases were stained with fluorescent markers for mHTT, microglia (Iba-1), and astrocyte proteins: Connexin 43 (Cx43) and excitatory amino acid transporter 2 (EAAT2). Glial marker and mHTT density, alongside microglia morphology were quantified. The results show microglia do not proliferate in HD, but transition from ramified states into activated morphologies in HD compared to controls ($p=0.001$). Activated microglia display close contacts with mHTT aggregates and the proportion of activated microglia positively correlate with mHTT burden ($p=0.001$). Astrocytes labelled with EAAT2 show decreased density ($p=0.0012$), size ($p=0.0054$), and percent area coverage ($p=0.0015$) in HD cases, particularly those associated with mood symptoms. This data demonstrates the presence of glial changes and their association with mHTT burden in the MCC in HD.

Poster 4.4

Dopamine D1 receptor and effort-based decision making in rats: The moderating effect of sex

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Dopamine is a modulating factor in effort-based decision-making, and emerging evidence from pharmacological research suggests that the D1 receptor is the primary regulator. Given the limited selectivity of pharmacological tools, to explore this hypothesis we used dopamine D1 mutant (DAD1$^{-/-}$) rats which have a genetic reduction in D1 receptors. Adult male and female DAD1$^{-/-}$ rats and wild type controls were trained to press a lever for a reinforcer. Subjects then completed multiple fixed-ratio, progressive ratio, and operant effort-choice experiments. As predicted, DAD1$^{-/-}$ rats (regardless of sex) pressed the lever significantly less than controls and had lower breakpoints. Interestingly, there was a sex * genotype interaction for acquisition of lever pressing and change in breakpoints with free food available. Only 31% of DAD1$^{-/-}$ males acquired lever pressing while 73% of DAD1$^{-/-}$ females acquired. Additionally, DAD1$^{-/-}$ males had significantly larger percentage change in breakpoints with free food available. These findings extend the pharmacological research suggesting that the dopamine D1 receptor modulates decisions based on effort, which has implications for the development of treatment targeting amotivation in neuropsychiatric disorders. The sex * genotype interaction highlights the importance of examining both sexes, especially when there are sex differences in neuropsychiatric disorder incidences and severity.

Poster 4.5

***Streptococcus agalactiae* brain invasion via the olfactory and trigeminal nerves**

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S. agalactiae causes neonatal meningitis and can also infect the adult central nervous system (CNS) crossing the blood-brain barrier and other paths. Preterm birth is associated with increased risk of infection which dwell in the nasogastric tubes, also used in adults, causing nasal injuries, and increasing contamination. In this study we determine whether bacteria could invade the CNS after intranasal inoculation in mice and subsequent glial responses to the bacteria. We investigated the role of bacterial brain infection via the olfactory and/or trigeminal nerves after intranasal inoculation with and without nasal epithelial injury. As the ability to infect glia is important for bacterial invasion of both cranial nerves, we investigated how the glial cells of those nerves responded to bacteria. To understand the immune responses of glia to bacteria we also analysed secretion of cytokines. Bacteria rapidly infected the olfactory nerve and brain. Epithelial injury led to increased bacterial load in these tissues. Bacteria infected and survived in cultured glia, resulting in cytokine production, with some differences between glial types. This study shows that *S. agalactiae* can infect the CNS via the nose-to-brain path with increased load after epithelial injury, and that the bacteria can survive in glia.

Poster 4.6

Characterisation of DARPP-32 within the human basal ganglia in Huntington's and Parkinson's disease

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The basal ganglia (BG) regulate motor, emotional and cognitive function; consisting of the striatum connected to the output structures, the globus pallidus (GP) and the substantia nigra (SN). BG circuitry dysfunction is associated with Huntington's disease (HD) and Parkinson's disease (PD). In HD, medium spiny neurons (MSNs) are lost in the striatum causing mood and motor changes. PD pathology consists of the loss of dopamine in the striatum. Dopamine-and-cAMP-regulated-neuronal-phosphoprotein-of-32kDa (DARPP-32) is an MSN marker in the human striatum. This study aims to determine whether DARPP-32 expression is changed in HD and PD within one of the main BG structure outputs, the SN. A 66% decrease of DARPP-32 immunoreactivity in the HD SN compared to controls was observed using immunohistochemical techniques in post-mortem human brain tissue. This finding links HD neuropathology and the loss of DARPP-32 immunoreactivity. There was also a trending increase in DARPP-32 immunoreactivity in the human PD SN. DARPP-32 is observed to possess low co-labelling with well-established BG MSNs via double-labelling immunofluorescent techniques, implying the existence of separate neuronal populations of DARPP-32 and other MSN groups. This finding in the DARPP-32 striatonigral pathway has important implications for the BG circuitry in health and disease.

Poster 4.7

Regional differences in striatal dopamine transmission between DAT-KO and wildtype rats

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The caudolateral (tail) striatum (TS) is a region of growing interest and distinct from the dorsolateral striatum (DLS). Whereas dopamine transmission has been well-characterised in the DLS, it remains poorly understood in the TS. Our previous pilot study identified that evoked dopamine release was considerably smaller in the TS, compared to the DLS, but surprisingly, was significantly larger in animals lacking the dopamine transporter (DAT-KO). Anatomical differences between the DLS and TS have also been identified: D1 and D2 dopamine receptors are distributed evenly across the DLS, whereas they are segregated in the ventral-lateral (D1-poor) and ventral-medial (D2-poor) TS. We studied dopamine transmission in three TS regions (ventral-lateral, ventral-medial, dorsal) and compared them to the DLS using fast-scan cyclic-voltammetry to measure electrically evoked dopamine release from coronal rat brain slices (P28±2; 300µm) containing either the DLS or TS from wildtype and DAT-KO rats. Evoked dopamine release was greater in amplitude, prolonged and slower to reach peak amplitude in all regions in DAT-KO relative to wildtype. Interestingly, the amplitude difference was greatest in the dorsal and ventral-lateral TS (~6.1x), contrasted with the ~3x increase in the DLS and ventral-medial TS. The mechanisms underlying this regional variance in the role of DAT in dopamine transmission require further investigation.

Poster 4.8

Moving beyond response times: A simple solution for capturing response dynamics

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Response Times (RTs) have long served a central role in psychological research. However, RTs provide limited insight into processing over time. To address this limitation, researchers have used hand-tracking techniques to investigate how cognitive processes unfold over the course of a response. Despite the efficacy of these techniques, widespread adoption is hindered by a range of factors, including equipment costs and the use of specialized software. Here, we demonstrate that the behavioural dynamics previously observed with specialized motion-tracking equipment can be captured with an affordable, portable, and easy-to-assemble response box. Six- to 8-year-olds and adults (N = 90) completed a computerized version of the flanker task by pressing and holding a central button until a stimulus array appeared. Participants then responded by releasing the central button and reaching to press one of two response buttons. This method allowed RT to be separated into *initiation time* (IT; when the central button was released) and *movement time* (MT; when a response button was pressed). Consistent with previous research using specialized motion-tracking techniques, ITs and MTs revealed distinct patterns of effects across trials and between age groups, indicating that our method presents a simple solution for researchers looking to move beyond RTs.

Poster 4.9

Mitochondrial abundance and function in the serotonin transporter knockout model: A sexually dimorphic association

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Neuropsychiatric and neurodevelopmental disorders such as major depressive disorder (MDD) and autism spectrum disorder (ASD) are complex conditions attributed to both genetic and environmental factors. Both serotonergic signalling and mitochondrial function are implicated in the pathophysiology of these disorders, and there is growing evidence showing that these factors may be linked as signalling through serotonin receptors has been shown to regulate mitochondrial biogenesis. The serotonin transporter (SERT) is important in these disorders as it regulates synaptic serotonin levels as well as being a target for major classes of antidepressants. Human allelic variants of the serotonin transporter-linked polymorphic region (5-HTTLPR) are associated with reduced SERT expression and increased susceptibility for developing neuropsychiatric disorders. Using a rat model that is haploinsufficient for SERT expression to mimic naturally occurring human variants, we demonstrate that reduced SERT expression modulates mitochondrial biogenesis and respiratory chain activity in the brain in a sex-dependent manner. These findings suggest that serotonergic signalling may have a role in regulating mitochondrial biogenesis in the brain, and that this may contribute to sex differences in the incidence and presentation of disorders such as MDD and ASD.

Poster 4.10

A strain-specific approach: Identification of therapeutic targets associated with distinct α-Synuclein polymorphs

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Parkinson's disease (PD), Dementia with Lewy body disease and Multiple system atrophy are defined by aggregated α-Synuclein (α-Syn). Recent evidence suggests α-Syn forms conformationally distinct polymorphs which may be disease-specific. In this study, we treated human brain-derived pericytes with distinct a-Syn polymorphs. Subsequent RNAseq analysis revealed polymorph specific changes in gene expression. Here we validated some of the changes seen at the gene transcript level using fluorescent immunohistochemistry. We optimised and validated 39 antibodies specific for 29 proteins, a subset of the differentially expressed transcripts, on middle temporal gyrus tissue from normal and PD brains. Middle temporal gyrus tissue microarrays were then used to determine the differential expression of proteins in normal and PD cases. In addition, we detected proteins in normal and PD human-derived pericytes treated with distinct α-Syn polymorphs. Ten proteins were successfully detected immunolabeling human brain, while eight were detected in cultured human brain-derived pericytes. One protein was differentially expressed in human brain and pericytes. SAT1 displayed decreased nuclear (p= 0.0101) and vascular (p=0.0093) protein expression in PD tissue. Whereas GMNN expression was upregulated (p=0.039) in treated control vs PD pericytes but downregulated in PD brain tissue (p=0.0424). Further investigation will unravel their relationship with α-Syn polymorphs.

Poster 4.11

An in vitro model of neural strain injury to investigate the effects of electric fields on promoting axonal repair

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Traumatic spinal cord injuries damage axons that carry electrical signals from the brain to the rest of the body, severely impacting sensory and motor function. Recent evidence has suggested that exogenous electrical fields can promote axonal growth. By promoting axonal growth it may be possible to reconnect electrical pathways and restore lost function to patients. In this work we develop an *in vitro* model of axonal strain for testing the effects of electric fields on axonal regeneration. Traditional cell culture setups are made from rigid substrates such as polystyrene and glass. These materials cannot support the large strains that are necessary for investigating the effects of mechanical strain on cells. Data will be presented on the development of a stretchable microchannel device that is capable of supporting mechanical strain injury in a neuronal culture. We demonstrate that human cortical neurons, differentiated from induced pluripotent stem cells, extend axonal projections through long microchannels. Spatial distancing of axons from the soma allows strain injury to be limited to the axon. The severity of axonal damage is characterised in relation to the applied strain and preliminary data is presented on the effects of electric fields promoting axonal repair.

Poster 4.12

The Role of RNF167 in lysosomal regulation within neuronal dendrites

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RING Finger Protein 167 (RNF167), an E3 ubiquitin ligase, is a key regulator of lysosomal trafficking. Dysfunctional lysosomes are associated with neurodegenerative disorders including Alzheimer's, Parkinson's disease, and lysosomal storage diseases; thus, it is essential to understand how lysosomal trafficking is regulated. Previous research determined that RNF167 ubiquitinates adaptor proteins and targets them for proteasomal degradation, causing lysosomes to become unloaded from microtubules. However, there is little research surrounding how RNF167 and a newly identified isoform, RNF167B, regulate lysosomes in neuronal dendrites. The main aim of this project is to investigate the roles of RNF167 isoforms in lysosomal regulation within dendrites. This will be investigated by identifying RNF167 interacting proteins using a proximity-dependent biotinylation-based technique (BioID), determining the localization of RNF167A and B within neurons, and by testing how each isoform impacts lysosomal function and trafficking. We have shown that knockdown of both RNF167 isoforms results in a net movement of lysosomes into dendrites. To differentiate the localization of the novel B isoform in neurons, we have cloned RNF167 isoforms as fusions with neon green. Finally, using BioID we showed that RNF167 interacts with LAMTOR1 and DVL2/3. The significance of this finding is currently being investigated.

Poster 4.13

Insulin resistance does not change PSA-NCAM load in the rat entorhinal cortex.

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Insulin resistance (IR) is a major risk factor in Alzheimer's disease. Insulin regulates structural plasticity of cells *in-vitro* by preventing down-regulation of polysialylated neural cell adhesion molecule (PSA-NCAM). Previous work demonstrated that PSA-NCAM, a cell-surface molecule that enables neuritic remodelling, is reduced in the human entorhinal cortex in Alzheimer's disease. Since the entorhinal cortex is a highly plastic region and key to memory formation, a deficit in neuritic remodelling here would likely exacerbate dementia symptoms. To investigate whether insulin signalling modulates PSA-NCAM *in vivo,* we induced IR in rats by feeding a high fat diet. IR was validated by measuring HOMA-IR values. The brain tissue was immunolabelled and the confocal images were analysed using a novel method of unbiased image segmentation. There was no difference in PSA-NCAM load in the entorhinal cortex as a result of IR. There was also no difference in the density of cells expressing insulin receptors. Thus, IR in rats is not responsible for the loss of PSA-NCAM in the entorhinal cortex. Furthermore, we conclude IR cannot be detected in tissue by immunolabelling insulin receptors. Instead, the molecular changes must occur at the level of phosphorylation or downstream effector expression, rather than total receptor protein.

Poster 4.14

Anxiety is associated with interoceptive insight deficits in women but not men

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Anxiety is one of the most common mental health disorders, with often debilitating symptoms. Many of anxiety's physical symptoms present themselves in our body (e.g. racing heart or shortness of breath). Recent theories have proposed that a mis-communication exists between brain and body when perceiving and interpreting these sensations (termed 'interoception') in conditions such as anxiety. Beyond simple perception, interoceptive insight (or 'metacognition') describes the ability to judge one's own performance when perceiving these body signals. We created a novel interoceptive task focussed on breathing, whereby participants reported whether they perceived a small change in breathing resistance, and reflected on their decision via a confidence score. We pooled data across four study sites (n=175) to clarify previous conflicting findings about interoceptive metacognition with anxiety. Here we observed that elevated anxiety was only related to decreased interoceptive insight ('metacognitive performance'; coherence between confidence scores and correct/incorrect decisions) in women (n=89) but not men (n=86). In comparison, anxiety was strongly related to reduced overall confidence in interoceptive decisions ('metacognitive bias') in both men and women. These findings help to clarify the relationship between interoceptive insight and anxiety, providing the first evidence that the relationship between anxiety and interoception may differ with gender.

Poster 4.15

Vasculature and neuroinflammation in chronic traumatic encephalopathy

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Chronic Traumatic Encephalopathy (CTE) is a neurodegenerative disease associated with repetitive head injury and is characterised by the perivascular accumulation of phosphorylated tau at the depths of the cortical sulci. Most research on CTE neuropathology has focused on phosphorylated tau, while other pathological processes such as vascular damage and neuroinflammation are still largely unexplored. Therefore, we aim to identify and characterise the relationship between vasculature, neuroinflammation, and tau pathology in CTE and how it compares to another tauopathy, Alzheimer's disease (AD). To achieve this, we are using multiplex fluorescent immunohistochemistry to label frontal cortex tissue sections from neurologically normal, CTE, and AD cases with up to 50 antibodies relevant to astrogliosis, microgliosis and vascular injury. We have performed preliminary qualitative multiplex labelling analysis of a subset of antibodies against microglia (CD68, HLADR, L-ferritin and Iba1), astrocytes (GFAP, aquaporin IV), blood vessels (collagen IV, UEA-lectin) and tau on frontal cortex tissue from two CTE, two control and two AD cases. This analysis shows evidence of reactive gliosis and blood vessel abnormalities in CTE and AD cases compared to controls. Overall, our results demonstrate the spatial relationships and interactions between proteins and cells involved in vascular dysfunction and neuroinflammation in CTE.

Poster 4.16

X marks the spot: A neuropathological signature of the X-linked motor neuron disease gene *UBQLN2*

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Amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative disorder, affecting upper motor neurons of the motor cortex, and lower motor neurons of the brain stem and spinal cord. Progressive neuronal damage leads to muscle atrophy and eventual paralysis in patients, resulting in death 2-4 years after symptom onset. The cause of ALS in a significant majority of patients is unknown, while ~15% can be linked to a variety of genes encoding diverse protein functions. One such gene is *UBQLN2*, encoding ubiquilin 2, a triage protein involved in intracellular protein quality control. A large family across New Zealand and Australia carrying the UBQLN2 p.T487I variant was identified previously, and all individuals harbouring this variant had diagnosed ALS. However, the pathogenicity of this variant in ALS is currently inconclusive. Using multiplex immunohistochemistry, deposition of ALS-relevant aggregates (ubiquilin 2 itself, phosphorylated TDP-43 (pTDP-43), dipeptide repeat proteins polyGA and polyGP, and p62) were examined in a cohort of ALS (n=35) and neurologically normal (n=5) control hippocampal sections. Our co-labelling of these ALS-linked markers reveals a predictable and unique neuropathological signature within cases with confirmed pathogenic variants in *UBQLN2*, which was also seen in UBQLN2 p.T487I cases but not in other genotypes, confirming UBQLN2 p.T487I variant pathogenicity.

Poster 4.17

Phosphorylated Tau and α-synuclein presentation in the human olfactory epithelium.

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Olfactory dysfunction and pathological protein aggregations occur in the olfactory bulb (OB) six to ten years before clinical symptoms of dementia, Alzheimer's or Parkinson's disease (PD) are evident. Additionally, glomeruli, the functional units of olfaction, are reduced in volume in the OB of PD patients. To reach the OB, olfactory sensory neurons (OSNs) in the olfactory mucosa send signals through axons that project into the OB and coalesce to form glomeruli and are the only neurons in direct contact with the external environment putting them at risk of exposure to toxins, viruses and bacteria. In this study we investigated the presence of phosphorylated tau and α-synuclein in human olfactory epithelium (OE) and its association with OSNs and dementia using immunofluorescence and sections through the human olfactory mucosa and bulb. We developed an analysis method that allows for preservation of anatomical distribution of phosphorylated tau and α-synuclein proteins in OE. Pathological aggregations were present in every case, and furthermore, there was no single location of elevated accumulation of pathology. Instead, pathology is heterogeneously distributed throughout the mucosa, varying in each case. Understanding patterns of pathological aggregations in the OE might help with early diagnosis and even early treatment delivery.

Poster 4.18

Tonabersat rescues inflammatory damage in an experimental mouse model of multiple sclerosis through connexin-43 hemichannel blockade

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Multiple sclerosis (MS) is a neurodegenerative disease marked by the chronic inflammation of the central nervous system. Connexin 43 (Cx43) hemichannel blockade has been shown to prevent inflammasome activation and secretion of disease-driving inflammatory cytokines. Here, we show that the Cx43 hemichannel blocking drug, Tonabersat, reduces inflammation in various regions of the mouse brain in an Experimental Autoimmune Encephalomyelitis (EAE) mouse model of MS. Paraffin-embedded mouse brain tissue sections were immunolabelled for Iba1 (microglia marker) and GFAP (astrocyte marker) to characterize the level of inflammation. We observed prominent expression of the markers across the corpus callosum, motor cortex, and striatum region of the mouse brains in EAE mice. The integrated density of Iba1 and GFAP, and the number of activated microglia and astrocytes, were significantly increased in EAE mice while EAE-Tonabersat treated mice showed an inflammatory profile similar to naïve control mice. Behavioural analysis showed a significant improvement in the behavioural scores of the EAE-Tonabersat treated mice compared with the EAE mice as a possible consequence of reduced inflammation. These data demonstrate that Cx43 hemichannel blockade reduces inflammation in the EAE mouse model, suggesting that Tonabersat may be a potential pharmacological candidate for the treatment of MS.

Poster 4.19

Nalfurafine and ethoxymethyl ether Salvinorin B promote recovery and remyelination in CNS demyelination disease models

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Multiple sclerosis (MS) is a neuroinflammatory and demyelinating disease that affects the central nervous system. There is no cure for MS, and pharmacotherapies that enhance recovery are urgently needed. Activation of kappa opioid receptor (KOR) was recently shown to promote functional recovery and remyelination preclinically. However, traditional KOR agonists, like U50, 488 have side effects that limit clinical use. The KORs agonists nalfurafine and the salvinorin A analog, ethoxymethyl ether Salvinorin B (EOM), have fewer side effects, and nalfurafine is the only clinically approved KOR agonist. In experimental autoimmune encephalomyelitis, a model that mimics immune driven demyelination, we revealed that nalfurafine and EOM reduced disease scores (paralysis), increased recovery rate, and reduced number of relapses in a KOR-dependent manner, and their therapeutic effects were better than U50,488. In the cuprizone toxin-induced demyelination model, a model that recapitulates more progressive forms of MS, both nalfurafine and EOM increased the number of myelinated axons, myelin thickness and the number of mature oligodendrocytes in the corpus callosum. Taken together, nalfurafine and EOM effectively drive remyelination and recovery in preclinical models of MS by promoting OPC differentiation into mature myelinating oligodendrocytes. This study confirms KOR agonists are a promising target for the development of remyelination therapies.

Poster 4.20

Altered nucleus accumbens functional connectivity predicts apathy development in Parkinson's disease

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Converging behavioural and physiological evidence points to altered reward processing underpinning apathy in PD. Whilst cross-sectional neural correlates of apathy in PD include key nodes of the reward network, it remains unknown whether changes in this network precede development of apathy in PD. Multimodal MRI data (T1w, diffusion, resting state) and apathy status were obtained at baseline, in 199 PD patients. Apathy status was determined again at 2 year clinical follow up, and baseline no-apathy patients were classified as either converters or non-converters to apathy. We performed voxel-based morphometry, tract-based spatial statistics and seed-based functional connectivity analyses on baseline MRI data to look for neural predictors of later conversion to apathy. The presence of apathy at baseline was associated with nucleus accumbens atrophy, whereas in those without apathy at baseline, there were no significant structural differences between later converters and non-converters. In contrast, functional connectivity between nucleus accumbens and left dorsal anterior cingulate cortex at baseline was increased in converters compared to non-converters. Altered functional connectivity between nucleus accumbens and other key nodes of the reward network predicts the subsequent development of apathy in people with PD without motivational impairment.

Poster 4.21

***In vivo* fibre photometry in freely behaving mice: A cutting-edge technique to measure activity of hippocampal neurons**

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Fibre photometry is a powerful technique that has enabled neuroscientists to record changes in fluorescent signals as a measure of neural activity dynamics of a particular population of neurons in the brains of freely living animals. It employs optical fibre(s) implanted at the targeted brain region of interest delivering excitation light to the specific cell or fibre population expressing genetically encoded calcium indicators (GECIs) and collecting overall calcium activity-induced fluorescence during certain behaviour. Importantly, fibre photometry is compatible with optogenetics which allows control of the activity of a specific cell population using genetics and light stimulation. Despite the wide use of this versatile tool, the lack of a structural protocol for its construction and interpretation of data has limited its progress. Here, we introduced a detailed protocol of fibre photometry covering a comprehensive structural set-up, implantation surgery, virus injection, data collection, and analysis. Furthermore, we applied this protocol to explore the neuronal activity of GABAergic interneurons in the CA1 hippocampal subregion. The successful virus-based GECI expression in CA1 and the recorded neuronal activity indicates that this custom-made fibre photometry device is reliable and effective for neuronal activity detection by fibre photometry, which will help neuroscientists carry out functional and behavioural studies in the future.

Poster 4.22

Therapeutic hypothermia attenuates cortical interneuron loss after cerebral ischemia in near-term fetal sheep

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Perinatal hypoxia-ischemia is associated with loss of cortical gamma-aminobutyric acid (GABA)ergic interneurons, which may contribute to persisting neurological deficits. In this study, we tested the hypothesis that 72h is the most effective hypothermia duration for promoting the survival of cortical interneurons after perinatal hypoxia-ischemia. Term-equivalent fetal sheep received 30min of bilateral carotid artery occlusion, recovery for 3h, followed by normothermia or 48h, 72h or 120h cerebral hypothermia. Brain tissues were stained for interneuron markers including glutamic acid decarboxylase, parvalbumin and calbindin. Cerebral ischemia was associated with loss of cortical interneurons. While the 72h hypothermia prevented loss of all interneuron subpopulations in the cortex, the 48h hypothermia showed insufficient protection for all interneuron subpopulations, and the 120h hypothermia failed to prevent the loss of calbindin-expressing interneurons. The densities of cortical glutamic acid decarboxylase- and parvalbumin-expressing interneurons were positively correlated with average electroencephalography power. The data suggest that perinatal hypoxia-ischemia in fetal sheep leads to loss of cortical interneurons. The 72h hypothermia treatment may be an effective strategy to improve cortical interneuron survival and long-term neurological outcomes after perinatal hypoxia-ischemia.

Poster 4.23

A longitudinal study of antenatal and perinatal risk factors for executive control and receptive language in early childhood

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Maternal mental and physical health issues and disadvantageous exposures during pregnancy as well as unfavourable perinatal events are associated with adverse trajectories in offspring cognitive functioning. We examined the longitudinal associations between antenatal maternal, perinatal and maternal health characteristics and early childhood executive control and receptive language. Analyses comprised interview and observational data from 4587 children and their mothers enrolled in the longitudinal *Growing Up in New Zealand* birth cohort study. At age 4.5 years, children's receptive language was observed using the Peabody Picture Vocabulary Test and executive control was assessed with the Luria hand clap task. Multivariate logistic regression analyses were conducted with several antenatal and perinatal characteristics as predictors for preschool executive control and perceptive language, controlling for a range of sociodemographic confounders. Results demonstrate that smoking pre-pregnancy, antenatal anxiety and no folate intake during first trimester of pregnancy increased the likelihood of poorer receptive language ability in preschool children. Smoking pre- and during pregnancy, no folate intake during first trimester and low birth weight were associated with poorer executive control. Improving maternal support during pregnancy may help to reduce the potential deleterious impact of adverse antenatal and perinatal conditions on children's early cognitive development.

Poster 4.24

Efficacy of cannabinoids to treat neuropathic pain symptoms in a mouse model of Charcot-Marie-Tooth Disease, Type 2A

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Charcot-Marie-Tooth disease type 2A (CMT2A) is a debilitating disease that causes a progressive, distal to proximal peripheral neuropathy and neuropathic pain. This study determined the efficacy of cannabinoids in alleviating neuropathic pain symptoms in a pre-clinical mouse model of CMT2A, which, like human patients, display peripheral neuropathy, including mechanical allodynia and thermal hyperalgesia symptoms. A range of cannabidiol (CBD) doses (6.25 mg/kg up to 100 mg/kg) were given orally and testing occurred at set time points post-administration to determine changes to mechanical allodynia and thermal hyperalgesia. CBD efficacy was compared to vehicle control (olive oil) and gabapentin (40 mg/kg orally: a current neuropathic pain treatment). Lower doses of CBD were more efficacious, with greatest improvement in pain symptoms seen with 12.5 mg/kg of CBD. This dose equalled gabapentin for efficacy in improving thermal hyperalgesia across four hours of testing. Comparisons were also performed with high CBD whole extract and CBD:THC mix. The high CBD whole extract showed greater efficacy in improving neuropathic pain symptoms than CBD alone, suggesting another compound(s) in cannabis might have improved therapeutic efficacy or the presence of an entourage effect. This pre-clinical efficacy indicates further investigation into cannabis compounds for treatment of neuropathic pain symptoms.

Poster 4.25

Value of multimodal MRI in analysis and visualisation of physiological changes before and after a mild traumatic brain injury in a large animal model

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The majority of traumatic brain injuries that require medical attention are mild (mTBI). Diagnosis and prognosis in mTBI relies heavily on clinical evaluation of self-reported symptoms, influencing the objectivity of the assessment causing over- or under-diagnosis. Here we used three advanced MRI sequences in conjunction to characterize the physiological changes associated with acute mTBI. Using a large animal model (ovine, n=3), a controlled impact was delivered to the frontal area of the head and MRI sequences were acquired pre- and post-injury using a 3T MAGNETOM Skyra system (Siemens) and 32-channel head coil. The three MRI sequences were: 1) amplified MRI (aMRI), a motion detection and visualization technique used to amplify pulsatile brain motion; 2) 4D flow MRI, a sequence utilised to analyse and visualise blood flow; and 3) diffusion MRI (dMRI) to delineate features of tissue microstructure. We found that mTBI is associated with increased parenchymal micro-displacements within the brain (aMRI), altered blood flow profile in the brain vasculature and carotid arteries (4D flow), and changes in the diffusion parameters (dMRI). We show that using multiple sequences to obtain a more comprehensive overview of these subtle brain changes lends itself to a more objective marker of mTBI than single-modal MRI.

Poster 4.26

Identification of primary tauopathy cases in the New Zealand Neurological Foundation Human Brain Bank

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Primary tauopathies are a heterogeneous group of neurodegenerative diseases characterised by pathological aggregation of tau protein within neurons and/or glia. Examples include progressive supranuclear palsy (PSP) and frontotemporal dementia (FTD). The New Zealand Neurological Foundation Human Brain Bank (NZ Brain Bank) is a tissue repository that collects post-mortem central nervous system tissue from people who have died from neurological disease, and from neurologically normal controls. Studies of post-mortem human brain tissue are critical to elucidate the mechanisms underlying tau pathology. The aim of this work was to identify and characterise all cases of primary tauopathy in the NZ Brain Bank, to enable their use in future studies. Neuropathology reports of all possible primary tauopathy cases in the NZ Brain Bank were reviewed using updated neuropathological criteria. All available demographic, clinical, processing, and storage data were collected. We identified 15 cases of primary tauopathy in the NZ Brain Bank (PSP=7; FTD=6; primary age-related tauopathy (PART) =1; argyrophilic grain disease (AGD) =1). Mean age at death was 76 (range: 64-96). Five cases were female; 10 were male. Mean post-mortem delay was 16h (range: 3.5-48h). The primary tauopathy cases identified in the NZ Brain Bank will be further studied to elucidate the mechanisms underlying tau pathology.

Poster 4.27

Regional variation of dopamine transmission in the caudolateral (tail) striatum

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The caudolateral (tail) striatum is a region of growing interest but is poorly understood compared to the dorsolateral striatum (DLS) which is implicated in Parkinson's disease. Our previous work has suggested that dopamine transmission in the tail striatum is different in amplitude and kinetics, compared to the DLS. Recent studies show the tail striatum having discrete regions of dopamine receptor D1- and D2-poor zones located ventral-laterally (VLT) and ventral-medially (VMT), respectively. The aim is to regionally examine dopamine transmission in the tail striatum (VLT, VMT, dorsal), and compare to the DLS. Fast-scan cyclic voltammetry (FSCV) was used to measure electrically evoked dopamine release from DLS and tail striatum regions in coronal rat brain slices (Wistar; P28±2; 300 µm). Recordings showed that evoked dopamine release in the DLS (596±73 nM) was almost double that of any tail striatum region (VMT: 322±85nM; VLT: 275±49 nM; dorsal: 221±83 nM). These are the first measurements of dopamine transmission investigating regional differences in the tail striatum. Further study will determine the mechanisms underlying these differences.

Poster 4.28

Preparation of human brain tissue for studies of neurodegenerative diseases

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The prevalence of neurodegenerative disease is increasing in New Zealand due to the ageing population, highlighting the importance of research in this field. The Neurological Foundation Human Brain Bank was formed in 1993 to facilitate research into a wide range of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and Huntington's disease. Unique protocols have been developed by Brain Bank personnel for the optimal preservation of human brain tissue, while maintaining high safety standards. This tissue is carefully processed to generate high quality unfixed, formalin-fixed and paraffin-embedded tissue, allowing for the use of a wide range of research techniques. Following pathological examination, this tissue is made available to researchers, both within New Zealand and internationally. The success of the Brain Bank relies on the close relationship with donors, families and community groups. We are continuously exploring new ways to optimise the use of already banked human brain tissue, using techniques such as whole genome sequencing and tissue microarrays, to maximise the information we may learn from these invaluable donations.

Poster 4.29

Multiplication, Addition, Subtraction and/or Division of Inversion Recovery (MASDIR) sequences: Theory and practice in MRI of the brain

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The main pulse sequences used in clinical neuro-MRI are utilised with a basic understanding of how to generate T1 and T2 contrast and have not changed significantly over the past 30 years. We have developed a new framework for describing the contrast between different tissues on MRI which provides better understanding of contrast and creation of new sequences such as Multiplication, Addition, Subtraction and Division of conventional Inversion Recovery (i.e., MASDIR). MASDIR sequences contrast can be increased by using a single tissue property twice or more synergistically using two or more tissue properties for the same purpose demonstrating a 5-10-fold increase in contrast compared with current IR sequences. This makes detection of subtle changes due to disease far easier. A single multiple sclerosis patient was scanned with 3D FLAIR and dual echo white and grey matter suppressed inversion recovery images from which MASDIR sequences were created. The MASDIR sequences depicted significant underlying white matter changes not identified using the gold standard FLAIR. This work highlights the opportunities that arise from a more precise understating of how tissue contrast is generated in MRI. These sequences can be obtained on any MRI scanner and have potential applications in a wide range of diseases in the nervous system and other organs.

Poster 4.30

Event related potentials during adaptive go/no-go auditory discrimination in sighted and blind human adults

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Research in cortical plasticity in visually-impaired individuals has focused on understanding the mechanism and functional relevance of the involvement of occipital cortex in blind individuals during a variety of tactile and auditory tasks. However, the focus has been on understanding "where the plasticity occurred?" We aim to understand the time course of this plasticity. We investigated difference in event related potentials between blind and sighted adults during a go/no-go auditory discrimination task. Participants heard 3 tones varying in pitch (lowest, standard, highest) randomly. In one condition, participants were asked to respond to the lowest pitch tone and give no response for other two tones, and for other condition, participants responded to the highest pitch tone. The standard tone was 1000Hz and other two tones were decided for each participant based on 3-down-1-up adaptive staircase method. We found high N1 and P2 amplitude for blind compared to sighted. Also, P2 was more frontal in blind and centrally distributed in sighted. The findings demonstrate both spatial and temporal cortical response is different in blind.

Poster 4.31

The New Zealand Motor Neurone Disease Registry

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Motor neurone disease (MND) is a rare, terminal, neuromuscular disease with limited treatments. However, globally there is considerable research and drug discovery underway. Patient registries play an important role in the therapy development pathway e.g. identifying participants for clinical research, and supporting specific research questions. The New Zealand (NZ) MND Registry aims to provide New Zealanders the opportunity to participate in research. This opt-in longitudinal registry collects demographic and clinical data on people with MND, carriers of MND disease-causing genes, and those at risk of inheriting such a gene. Since its inception in 2017, 341 participants have enrolled. Gender distribution reflects that reported worldwide. 86% of participants identify as NZ European, and 6% Māori. Participants have sporadic MND (85%) or familial MND (5%). The remainder haven't been diagnosed but 6% have a positive result for an MND-causing genetic mutation. Most participants are within the higher range of the ALSFRS-R disability scale. The Registry has facilitated entry of participants into twelve studies. Genetic data is important given the increasing number of clinical trials for specific disease-causing variants. The NZMND Registry has accelerated MND research in NZ and demonstrates clear utility at every point along the pathway of research and drug discovery.

Poster 4.32

Investigating the expression of NKCC1 and KCC2 in Alzheimer's disease mouse models

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Alzheimer's disease (AD) is a neurodegenerative disorder. The γ-aminobutyric acid (GABA) neurotransmitter system undergoes remodelling in AD, thus disrupting the excitatory and inhibitory (E/I) balance in the brain. The cation chloride-cotransporters, K-Cl-2 (KCC2) and N-K-Cl-1 (NKCC1), have been implicated in several neurological disorders as they affect GABA signalling polarity, but have not been explored in AD. This study examined the potential neuroprotective effects of bumetanide, an NKCC1 inhibitor, in an AD mouse model. Primary mouse hippocampal cultures were treated with beta-amyloid ($A\beta_{1-42}$) and bumetanide (1µM, 10µM, 100µM, 1mM) to investigate the effect of bumetanide on cell viability. $A\beta_{1-42}$ produced 53% cell death after 5 days, which did not improve with bumetanide treatment. Bumetanide at 1µM alone, and at higher concentrations, lead to 61.5% cell death after 5 days, suggesting bumetanide is neurotoxic. No change in KCC2 and NKCC1 expression was observed in the in vitro AD model, however localized NKCC1 upregulation and KCC2 downregulation was apparent in the CA1 subregion of the hippocampus in an in vivo AD mouse model. This research is questioning bumetanide's suitability for AD therapy and suggests that further investigations are required to examine whether targeting KCC2 and NKCC1 might offer a therapeutic approach for AD.

Poster 4.33

Focus on the foci: Investigating the role of HDAC4 aggregation in neuronal development in *Drosophila melanogaster*

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Dysregulation of histone deacetylase 4 (HDAC4) expression and subcellular distribution has been observed in a number of neurodevelopmental and neurodegenerative diseases, and in our *Drosophila melanogaster* model, *HDAC4* overexpression impairs neuronal development and long-term memory. Interestingly, this is associated with minimal transcriptional changes. Upon increased abundance in nuclei, we observe HDAC4 aggregation into punctate foci, and therefore hypothesise that neuronal dysfunction mediated by HDAC4 overexpression is a result of aggregate formation. The glutamine-rich N-terminus of HDAC4 forms an alpha helix which assembles into an unstable tetramer. To investigate whether HDAC4 aggregates contribute to neurodevelopmental deficits, transgenic *Drosophila* were generated which express HDAC4 mutants harbouring structure-guided substitutions of key amino acids important in mediating tetramerisation. Expression of these mutant HDAC4 constructs significantly reduced aggregate formation in neuronal nuclei (ANOVA, $p < 0.01$), and this correlated with a significant reduction in defects in axon morphogenesis (Fisher's exact, $p < 0.01$) and photoreceptor development (ANOVA, $p < 0.01$), as compared to wild-type HDAC4. These data suggest HDAC4 aggregation is at least in part responsible for neurodevelopmental and neurodegenerative disease in which HDAC4 is aberrantly expressed, and warrants further studies into the composition of these aggregates as well as strategies to mitigate their formation.

Poster 4.34

Development of a human neuronal model for Parkinson's disease drug discovery to test novel compounds targeting α-synuclein and protein degradation machinery

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Parkinson's disease (PD) is the second most common neurodegenerative disorder in New Zealand and worldwide. PD is identified neuropathologically by the build-up of α-synuclein aggregation coinciding with and the subsequent loss of dopaminergic neurons in the substantia nigra, causing bradykinesia. Impairments in protein processing and degradation machinery in PD may cause α-synuclein-related pathogenesis in PD. Most *in vitro* PD drug discovery research has been conducted in undifferentiated SH-SY5Y neuroblastoma cells under conditions of acute cell stress or after genetic modification. These features are unlikely to reflect the effects of α-synuclein in the PD brain. In this study, we optimised the protocols for the generation of functionally mature dopaminergic neurons from SH-SY5Ys. We also investigated the uptake and degradation of pre-formed recombinant human α-synuclein fibrils on differentiated SH-SY5Y neurons to establish a model of α-synuclein activity in neurons. Finally, we studied the effects of proteolysis targeting chimeras (PROTACs) on reducing α-synuclein expression and aggregation in SH-SY5Ys. Thus, we have established a human neuronal platform for PD drug discovery upon which we will test novel compounds specifically targeted towards α-synuclein and protein degradation machinery.

Poster 4.35

Altered polyamine system in the P301S (PS19) tauopathy model

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Tauopathies are progressive neurodegenerative disorders, including Alzheimer's disease and Frontotemporal dementia, characterised by hyperphosphorylated and aggregated microtubule associated protein tau (MAPT) accumulation in the brain. Physiological levels of polyamines (putrescine, spermidine and spermine) are essential in maintaining normal cellular functions and microtubule stabilization and assembly, while the highest order polyamine, spermine, blocks MAPT aggregation. Using transgenic PS19 mice expressing the human *MAPT* P301S mutation, we systematically investigated how polyamine levels and their synthetic and catabolic enzymes changed in the hippocampus and parahippocampal region at 2-12 months of age (prodromal to severe disease-like states). We employed high-performance liquid chromatography and liquid chromatography/mass spectrometry to measure the polyamine concentrations, and quantitative reverse transcription-polymerase chain reaction for the polyamine enzymes gene expression. PS19 mice displayed early and sustained increases in putrescine and spermidine, but reduced levels of spermine at later age-points, relative to their age-matched littermates. Moreover, there were upregulated polyamine *de novo* synthetic enzymes for putrescine and spermidine and polyamine retro-conversion from spermine in the PS19 mice. These results demonstrate that the polyamine system is abnormally upregulated, however fails to produce more spermine, in PS19 mice. Such a sustained polyamine stress response may have significant implications in the pathogenesis of tauopathies.

Poster 4.36

Genetics of Motor Neuron Disease in New Zealand

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Incidence and mortality of motor neuron disease (MND) in New Zealand are among the highest in the world. We sought to understand this high rate of MND by characterising its genetic aetiology. Participants had sporadic or familial MND, or were relatives of familial MND cases. DNA was tested by *C9ORF72* repeat-primed-PCR; Sanger sequencing (*SOD1*, *TARDBP*, *FUS*, and *UNC13A*); genome-wide screening array for MND-associated variation in 17 other genes, and identity-by-descent (IBD) analysis. Familial, young-onset MND cases, or those related (IBD) to another MND case, were also sequenced for a commercial panel of 42 genes (Invitae). Pathogenic variants were validated clinically and reported back to participants with MND. We identified pathogenic variants in 16/103 participants (16%): 2/79 sporadic (2.5%), 4/9 familial (44%), and 10/15 unaffected relatives (67%). These were *C9ORF72* repeat expansions and *SOD1* p.Glu101Gly and p.Ile114Thr variants. A *SOD1* p.Ile114Thr-positive individual was related to a cluster of >50 individuals from Australia and the UK with the same variant. We also found a likely pathogenic variant: *SQSTM1* p.Pro392Leu in a sporadic participant (1/79 - 1.3%).The genetics of MND in New Zealand resemble those of Australia and the UK. Unaffected relatives of familial cases harboured the majority of the identified pathogenic variants, representing an urgent need for pre-symptomatic interventions.

Poster 4.37

Characterisation of astrocyte and microglia phenotypes in the Alzheimer's disease human brain

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Alzheimer's disease (AD) is the most common neurodegenerative disease with no existing cure. Previous *in vitro* and human transcriptomic studies have implicated key molecular pathways associated with astrocytes and microglia in AD progression. This project characterized these alterations at the protein level in the post-mortem AD human middle temporal gyrus on human brain tissue microarrays (TMAs) - a technique that utilizes up to 60 tissue core samples from control and AD cases. Immunohistochemistry was used to investigate astrocytic (Kir4.1, AQP-4, and GLT-1) and microglial (ATG7 and MYO1E) protein expression in the TMAs. Image acquisition was conducted using the V-slide automated scanning microscope, and the software MetaMorph was used for quantitative analysis. Increased protein expression of Kir4.1, AQP-4, GLT-1, ATG7, and MYO1E was observed in the AD human brain compared to controls. Apart from GLT-1, all changes were more strongly correlated with tau compared to amyloid-beta pathology. A re-distribution of Kir4.1 from astrocytic cell bodies to processes also occurred in AD. Using TMAs, this study advances our understanding of novel astrocytic and microglial proteins and their potential associations with the hallmarks of AD neuropathology. Co-localisation studies are on-going to further investigate the redistribution of Kir4.1 and the specificity of the microglial changes.

Poster 4.38

Early cannabis use and its impact on the ageing brain:
An MRI study of a New Zealand longitudinal birth cohort

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Cannabis is the most widely used illicit drug in New Zealand, and is known to impact learning, attention, and memory. Past studies have also suggested cannabis-related structural and functional changes in the brain. In a subset of the Christchurch Health and Development Study's (CHDS) longitudinal birth cohort, now in their 40's, we explored the impacts of past heavy cannabis exposure on brain structure using MRI, with particular focus on brain atrophy, cerebral perfusion, and white matter structure. Between cannabis users (n=35) and non-using controls (n=35, matched for sex and tobacco use), we identified significant atrophy in *a priori* regions of interest, including the hippocampus and amygdala. Whilst it is evident that brain changes occur naturally through ageing, how cannabis abuse interacts and impacts these age-related changes currently remain ambiguous. For a clearer picture, it will be vital to continue this longitudinal study and follow the participants' brain changes over time.

Poster 4.39

Age-related gray matter asymmetry changes

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Previous research suggests that aging processes might affect the brain asymmetrically, with one hemisphere experiencing an earlier or more pronounced tissue loss than the other. This was postulated to be of particular interest in neurodegenerative diseases, when a study on Alzheimer's disease observed an accelerated tissue loss in the left hemisphere. However, it remains unclear whether asymmetric tissue loss may already be observed during healthy aging. Here, we set out to investigate such a potential age-related asymmetric tissue loss in a large sample of 485 healthy adults (286 females, 199 males) aged 42 – 97 years. We applied a customized state-of-the-art processing workflow to map and examine age-related changes in grey matter asymmetries across the whole brain. We observed an increasing rightward asymmetry with increasing age in the hippocampus, the amygdala, the basal insula, and the supramarginal gyrus. In all cases, this association between age and rightward asymmetry was due to a more pronounced tissue loss in the left hemisphere. The present results suggest that a more pronounced tissue loss in left-hemispheric regions involved in memory, attention, and emotion processing compared to their right-hemispheric counterparts might be observed already in healthy aging.

Poster 4.40

Role of ryanodine receptor clustering in Alzheimer's disease

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Alzheimer's disease (AD) is the most common form of dementia. A growing body of evidence associates the intracellular calcium release channel, ryanodine receptor (RyR2), with AD progression. In the heart, RyR2 function is regulated through its ultrastructural arrangement, with RyR2 forming discrete clusters. These clusters' arrangement impacts the activity of RyR2-mediated intracellular calcium release. Whether clustering of RyR2 occurs in neurons, and whether changes in clustering underlies the altered calcium release in AD, has never been examined. Super-resolution microscopy (dSTORM) was used to analyse the structure of RyR2 clusters in the soma of hippocampal CA1 neurons from 9-month-old wild type and AD model (APPswe/PS1ΔE9) female mouse brains. The results show a clear formation of RyR2 clusters in CA1 neurons. More excitingly, the data indicate that RyR2 clusters become smaller in the APPswe/PS1ΔE9 mice with no significant difference in channel packing, indicating overall fewer RyR2 channels in a cluster. We also found an increase in inter-cluster distance and a reduction of individual clusters in a functional calcium release unit (CRU). These changes in RyR2 clustering ultrastructural arrangement may underlie changes in calcium release known to underpin various symptoms of AD. Supported by the Health Research Council (20/370) and Neurological Foundation Grant 2011 PRG

Poster 4.41

Stimulation-evoked dopamine release in the auditory cortex of anaesthetised rats

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Dopaminergic neurotransmission in the primary auditory cortex (A1) is associated with auditory perceptual learning and memory functions. Dopaminergic innervation and receptor distribution within the A1 show layer-dependent organisation, suggesting specific functions in the cortical circuitry. Phasic dopamine is known to modulate dynamic activity of cortical neurons; however, little is known about the characteristics of phasic dopamine release in the A1. Here, stimulation-evoked dopamine transmission within the A1 of anaesthetised rats was characterised, for the first time, using fast-scan cyclic voltammetry with carbon-fiber microelectrodes. The carbon-fiber recording electrode was placed in the dopamine-rich cortical layer of the A1 and the concentric bipolar stimulating electrode was placed in the ventral tegmental area. Stimulation-evoked dopamine release in the A1 was characterised using dopamine and noradrenaline reuptake inhibitors and compared to that obtained in the nucleus accumbens (NAcc). In the A1, both stimulation-evoked dopamine release (4.31±0.52 nM) and uptake activity were lower than in the NAcc (111.79±37.86 nM). The findings suggest that the regulation of phasic dopamine is different within limbic and cortical regions, with the former being more concentrated and exhibiting a more rapid time course, while the latter being more limited in concentration but longer-lasting.

Poster 4.42

Population receptive field maps of the physiological blind spot in human observers

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The physiological blind spot is a naturally occurring scotoma corresponding to the optic disc, the region of the retina where the optic nerve leaves the eyeball. Even during monocular viewing, observers are usually oblivious to the blind spot because the visual system extrapolates information from the surrounding area. Unfortunately, studying this visual field region with neuroimaging has proven difficult because it occupies only a small part of the retinotopic cortex. Here we used functional magnetic resonance imaging (fMRI) to reconstruct retinotopic maps in and around the blind spot. Specifically, we presented traversing bar stimuli within a confined region of interest (radius: 5.3 degrees of visual angle) centred on the observer's blind spot defined via a behavioural localiser. We then used a data-driven method for measuring population receptive fields (pRF) and projected measured fMRI responses from area V1 back into visual space. Our findings show very precise reconstructions of the extent of the observer's blind spot, far more precise than can be achieved with conventional model-based pRF analysis. Thus, our method has exciting potential for studying plasticity of receptive fields after visual field loss (e.g. in stroke or glaucoma) and investigating the neural mechanisms underlying perceptual filling-in in human observers.

Poster 4.43

N-terminus α-synuclein immunoreactivity reveals novel and distinct α-synuclein aggregate morphologies in Parkinson's disease

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α-synuclein antibodies are routinely used to detect and quantify α-synuclein in the human brain for both diagnostic and research purposes. Currently, most commercially available α-synuclein antibodies target epitopes within the C-terminus. Due to the truncational and conformational heterogeneity of α-synuclein, C-terminus α-synuclein antibodies may fail to capture the full cohort of α-synuclein variants present in the human brain. With diagnostic and research efforts relying heavily on α-synuclein detection using antibodies, it is critical to consider the specific epitopes these antibodies detect in the context of α-synuclein's inherently complex structure. Four epitope-specific α-synuclein antibodies, mapping the three structural domains and serine 129 phosphorylation status of α-synuclein, were used to immunohistochemically interrogate the differential epitope-specific detection of α-synuclein aggregates across pathologically significant regions of the human Parkinson's disease brain. Distinct epitope-specific α-synuclein immunoreactivities were demonstrated for all antibodies in Lewy neurite and Lewy body aggregate morphologies across all interrogated regions/cases. We identified novel and distinct populations of α-synuclein aggregates that exhibit exclusive N-terminus immunoreactivity and are localised within glial cells and neuronal lysosomes. For the first time, a multiplex epitope-specific immunohistochemical approach was used to capture the N-terminus fragment of α-synuclein within the human Parkinson's disease brain.

Poster 4.44

Nanostring nCounter analysis of the neuroinflammatory pathways in the midcingulate cortex in Huntington's disease

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Huntington's disease (HD) is a genetic neurodegenerative disorder. Cell loss is putatively associated with chronic neuroinflammation. HD symptom profiles include mood, motor, and cognitive changes. Cell loss and inflammation in the anterior cingulate cortex is associated with mood symptomology. In this validation study on post-mortem human cases, Nanostring nCounter analysis was conducted on 50 inflammatory related mRNA transcripts found to have differential expression through previous mRNA sequencing (RNAseq) in the midcingulate cortex. Of these, 36 were in accordance with the RNAseq changes seen between HD and control cases, validating 24 of the upregulated and 12 downregulated inflammatory related markers. Differential expression in controls compared to mood, motor, and mixed symptom HD profiles showed 17 symptom specific transcript changes, with six genes validating the symptom changes found in the RNAseq. These transcripts included SPP1, CD44, CCL4, NGFR, CD8B2, and AQP4; all upregulated in motor symptom cases. Some of the most significant HD vs control expression changes included upregulation of TMIGD3, SIGLEC8, and S100A9, and the downregulation of GPR85 and EGR1. This study highlights the importance of validation of RNAseq data. Importantly, the findings further corroborate the complex mRNA expression changes found in the inflammatory pathway that contribute to HD pathology.

Poster 4.45

Modulation of the substantia nigra pars lateralis by the subthalamic nucleus

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Our recent work has identified a novel dopamine pathway originating in the substantia nigra pars lateralis (SNL) and terminating in the tail (caudolateral) striatum. We also showed that the subthalamic nucleus (STN), which is implicated in Parkinson's disease and the target for therapeutic deep brain stimulation (DBS), selectively modulates dopamine release from SNL neurons. Here, we characterised the effect of STN stimulation on the electrophysiological activity of SNL dopamine neurons compared to neurons of the substantia nigra pars compacta (SNc; dopamine) and pars reticulata (SNr; GABA). A multielectrode array (32 channels) was used to measure extracellular activity in anaesthetised rats (Wistar; 290g). Electrical stimulation of the STN differentially modulated the activity of SNL neurons compared to SNc and SNr neurons in a frequency-dependent manner. DBS-like stimulation (130Hz, 100µs pulses) excited SNL neurons (1.9x increased firing), inhibited SNr neurons (23% of baseline) and caused no change in SNc neurons. This differential response highlights the unique role of the STN in selectively modulating SNL dopamine neurons and not the SNc. Further work will investigate the modulatory role of the STN on the activity of SNL dopamine neurons and dopamine release in the tail striatum in a Parkinson's rat model.

Poster 4.46

Peripheral administration of AAV-PHP.eB encoding TFEB causes toxicity in mice

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Adeno-associated viral (AAV) vector AAV-PHP.eB has enhanced ability to cross the blood-brain barrier, and shows promise for neurological gene therapy applications. Autophagic dysfunction likely contributes to the accumulation of toxic proteins such as β-amyloid in Alzheimer's disease (AD). Here, our aim was to overexpress a master regulator of autophagy, transcription factor EB (TFEB) in the brain using AAV-PHP.eB to investigate its impact on AD pathology in the APP/PS1 AD mouse model. Male 13-month-old (n = 8) and 10-month-old (n = 4) APP/PS1 mice were injected with AAV-PHP.eB encoding a TFEB transgene, and 13-month-old APP/PS1 (n = 4) and C57BL/6 mice (n = 7) were injected with AAV-PHP.eB encoding a reporter protein, tdTomato, via tail-vein injection. Unexpectedly, mice injected with the TFEB vector began to lose bodyweight soon after injection and required euthanasia due to reaching ethical weight loss limits. All mice that received the tdTomato vector retained their weight throughout the study. Pathological analysis of peripheral organ tissue (liver, spleen, and kidney) indicated that an unexpected immunological reaction involving splenic macrophage destruction of erythrocytes may be responsible for the adverse TFEB treatment effects. TFEB gene therapy for AD may be limited to methods that produce overexpression only in the brain.

Poster 4.47

The effects of general anaesthesia and light on the mammalian circadian clock

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General anaesthesia (GA) affects the circadian clock, however, whether this occurs through a direct effect on clock genes or via neurotransmitters such as GABA is less understood. Here we investigated the effects of light and GA on behaviour and $GABA_A$ receptor ($GABA_AR$) expression in the SCN. Behavioural studies on C57BL/6 mice examined time-dependent effects of light and GA (isoflurane) on wheel-running activity at different circadian times (CT) over a 24-hour period (n=60). Analysis of α1, β3, and γ2 $GABA_AR$ subunit expression in the SCN was quantified in mice exposed to light and GA at the same CTs (by immunohistochemical analysis) (n=20). Behavioural phase shifts persisted in anaesthetized mice exposed to light, suggesting that either: (1) isoflurane exerts its own phase shifts on the clock while blocking light-induced shifting or (2) isoflurane does not entirely block light-induced phase shifts. In the SCN, γ2 subunit expression was increased following light and GA treatment compared to light-alone, while α1 subunit expression was increased at times of large behavioural phase delays. We conclude that there is a time-dependent relationship between light and GA on the clock and that $GABA_AR$ activity may mediate behavioural phase shifts with these agents.

Poster 4.48

Using a rapid adeno-associated virus vector screening method for optimising the development of gene therapy for neurological disease

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Adeno-associated virus vectors (AAVs) are the gene delivery vehicle of choice for gene therapy of the central nervous system. Successful clinical translation of gene therapy relies on the selection of efficient vectors for human use, but although multiple AAV serotypes and promoters exist, few have been directly compared. We have developed a rapid AAV screening method that could be used to aid the selection of optimal AAVs for the delivery of transgenes to mouse and human brain cells. In proof-of-concept studies, primary mouse hippocampal neurons or human glioblastoma (GBM) cells cultured from biopsy tissue were treated with a panel of AAV serotypes expressing a green fluorescent protein (GFP). Cells were fixed at specific time points, and high content imaging was performed. AAV serotypes varied in their ability to transduce these cell types. AAVs under the control of human synapsin promoter mediated strong GFP expression in mouse neurons. AAV serotypes 1 and 1/2 demonstrated the highest tropism for mouse neurons, 80% and 90%, respectively. In contrast, AAV2 and 6.2 were the strongest transducers of human GBM cell cultures, transducing 50% of cells. Our data suggest the utility of this approach to select AAV vectors for further development of gene therapy strategies.

Poster 4.49

Spinal cord injury alters oligodendrocyte specific expression of ADAMTS4, a key modulator of oligodendrocyte maturation and myelination

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Spinal injuries induce oligodendrocyte loss and demyelination alongside hyper-deposition of chondroitin sulfate proteoglycans (CSPGs), which chronically inhibit cellular regeneration and remyelination. Research investigating the proteinase a disintegrin and metalloproteinase with thrombospondin motif 4 (ADAMTS4) highlights it as a promising therapeutic intervention for spinal injuries as it can degrade CSPGs and promote functional recovery. The endogenous expression of ADAMTS4 in the spinal cord is associated with oligodendrocytes and is important for maturation and myelination. However, ADAMTS4 expression post-spinal cord injury (SC) is relatively unknown. Immunohistochemistry was performed on injured rodent spinal cord tissue and demonstrated for the first time that perilesional mature oligodendrocytes have a loss of ADAMTS4 at 1- and 7-days post-injury. *In vitro* primary cell cultures investigated the mechanistic changes in ADAMTS4 expression in SCI conditions. Transforming growth factor-beta (TGF-β), an essential cytokine in SCI progression, does not influence ADAMTS4 in oligodendrocytes at the mRNA level. However, preliminary immunocytochemistry results suggest TGF-β does downregulate ADAMTS4 at the protein level. Understanding the impact of SCI pathophysiology on oligodendrocyte expressed ADAMTS4 and the mechanisms involved will inform future research focused on targeting endogenous ADAMTS4 expression to aid oligodendrocyte-specific and overall cellular regeneration as a treatment for SCI.

Poster 4.50

Three-dimensional modelling of the human olfactory system and its changes in Parkinson's disease

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Our sense of smell (olfaction) is important for social communication, harm avoidance, and evaluating food. Olfactory dysfunction significantly impacts quality of life, is a predictor of mortality risk, and is prevalent in ageing/dementia diseases long before clinical symptoms. Olfactory sensory neurons directly sample the chemical composition of the external environment and their axons coalesce into glomeruli in the olfactory bulb. The olfactory bulb is one of the first neural structures to show pathological load and anatomical changes in Parkinson's disease. However, anatomical, and histological characterisation of the normal human olfactory system is surprisingly lacking yet is critical to substantiate extrapolation of studies from rodents to humans. Here, we have combined histological studies of the human olfactory system with advanced imaging processing techniques and have visualised the human olfactory system with detailed anatomical structures in its native three-dimensional arrangement. The resulting model is a graphical representation of the distribution of olfactory sensory neurons in the nasal epithelium and visualises their axon coalescence as they cross the cribriform plate and innervate the olfactory bulb. Applying this workflow will allow us to understand the earliest changes in the olfactory system in ageing and common neurodegenerative diseases such as Parkinson's disease.

Poster 4.51

Treatment of gut and brain leakage by L-arginine and limonoids in Alzheimer's disease

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We observed the interaction between the brain and intestine in a mouse model of Alzheimer's disease (AD), and attempting to inhibit disease progression through the dietary supplementation of L-arginine and limonoids. Neurodegeneration of the brain, destruction of intestinal epithelial cells, abnormalities in the gut microbiota, and bacterial translocation to organs throughout the body, including the brain, were observed in the no-treatment AD mice (AC mice). Considering bacterial translocation, *Bacteroides ssp.* produced large quantities of gamma-aminobutyric acid (GABA), and genome analysis revealed a GABA receptor-mediated excessive inhibitory mechanism of neural activity in the AC mice. The AD mice fed with dietary supplementation of L-arginine and limonoids (ALA mice) exhibited increased diversity of the bacterial flora, suppressed bacterial translocation, and neurodegeneration in the brain. The brains of ALA mice were characterized by decreased 1/128 and 1/15 expressions of both GABA A receptor and carbonic anhydrase 8, and increased 6-5 fold expression of factors Neurod6, Tbr1, and Fezf2, which are crucial in the development and function of the central nervous system, compared with AC. These findings suggest that L-arginine and limonoids are useful in maintaining the homeostasis of the gut microbiota, brain, and gut in AD mice.

Poster 4.52

Anxiolytic effects of CBD are modulated by innate fear-response background in Carioca rat lines

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Anxiety disorders in New Zealand affect 12.4% of the total population and 17.4% of Māori. CBD have been prominently studied and implemented in alternative pharmacological therapies given the significant inefficacy of classical treatments. In this study, we assessed the influence of individual innate behavioural predisposition on the effects of CBD on innate and conditioned fear responses under different levels of stress. Cariocas high-conditioned freezing (CHF) rats were compared to randomly bred animals (CTR; N = 4 - 8) in two paradigms: contextual fear conditioning test (CFC) and Light-Dark box (LD). Previous footshocks (acute stressor) and/or CBD (5 mg/kg, i.p) were applied to selected groups. On the CFC test, increased freezing was observed in CHF rats (vs CTR) and after shock (vs non-shock groups). CBD mitigated or abolished shock-induced increasing in freezing. On the LD test, latency to enter the light compartment was only different between lines (CHF > CTR). Time spent in light compartment was lower in CHF+Shock groups in comparison to CTR+Shock and increased in CTR+Shock+CBD rats in comparison to saline treated ones. Results show that CBD has stronger anxiolytic effects under conditions of higher stress and it`s modulated by the inherent backgrounds of fear responsiveness of Carioca lines.

Poster 4.53

The effect of benzothiazepine S107, a preventative Ca^{2+} leak drug, on ryanodine type II receptor (RyR2) calcium leak

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Alzheimer's disease (AD), characterized by memory and cognitive deficits, is a progressive neurodegenerative disease. A rising theory addressing AD development and progression is the calcium (Ca^{2+}) hypothesis, suggesting that Ca^{2+} dyshomeostasis results in neuronal dysfunction observed in AD patients. Previous studies have shown that Ca^{2+} leak through ryanodine type II receptors (RyR2) leads to AD-like symptoms. FKBP12.6, a regulatory protein that forms a complex with RyR2, modulates Ca^{2+} release by manipulating RyR2 function and ultrastructural arrangement. Current treatment for AD is limited, having minimal effects in alleviating symptoms. S107, a RyR2-stabilizing compound, has been shown to reduce Ca^{2+} leak by preventing FKBP12.6 depletion and therefore might be a novel treatment for AD. However, other studies have suggested S107 acts independently of FKBP12.6. To address this discrepancy, human embryonic kidney (HEK293) cells expressing RyR2 with or without FKBP12.6 were treated with 10 µM S107 or vehicle control. Ca^{2+} leak was determined using the Ca^{2+} indicator, Fura-2. Results showed that FKBP12.6 significantly reduced Ca^{2+} leak, with the addition of S107 reducing this further. However, in the absence of FKBP12.6, S107 had no effect on Ca^{2+} leak. Therefore, this suggests S107 requires FKBP12.6 to reduce leak, potentially restoring Ca^{2+} homeostasis in AD patients.

Poster 4.54

Characterisation of a novel transcription regulation system: Optimising gene therapy in the central nervous system

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Gene therapy has the potential to change the way we treat neurological disease. A significant barrier to widespread clinical application of this technology in the central nervous system is transgene regulation. Our lab has developed a novel regulatory cassette that offers homeostatic control over therapeutic transgene transcription via proteolytic cleavage of a nuclear export signal from auxin response factor 5 (ARF5) in response to pathological stimuli. This project has worked to characterise the function of the regulatory cassette in response to drug-stressors. Drug-stressor-mediated calpain protease activation was induced within transformed *in vitro* systems, and changes in transgene expression with insult severity were assessed through immunocytochemistry and high content screening techniques. It was observed that ARF5 localisation was modified in response to drug-stressors, and the production of the eGFP reporter scaled with the amount of nuclear ARF5. Notably, there was a significant difference in the ability of proteins generated by full-length and truncated ARF5 genes to drive eGFP production. These findings have implications for the utility of these ARF5 genes in future cassettes. Following optimisation, this system may be able to effectively regulate transgene expression in neurological disorders associated with proteolytic induction.

Poster 4.55

Scopolamine's effect on heart rate variability and electroencephalography measures in healthy participants and participants with depression

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Antidepressants appear to decrease EEG alpha power and modulate heart rate variability (HRV). Given scopolamine decreases alpha in healthy individuals and modulates HRV, this trial assessed the antidepressant, EEG, and HRV effects in individuals with depression. Forty individuals with depression were administered 15-minute infusions of scopolamine or glycopyrronium. Glycopyrronium was chosen as the active placebo due to its similar antimuscarinic properties to scopolamine, but its inability to cross the blood-brain barrier. Mood outcomes via the Montgomery–Åsberg Depression Rating Scale (MADRS) were assessed pre-infusion to 6-weeks post-infusion. Furthermore, 12 healthy individuals were administered scopolamine. All 52 individuals underwent EEG and ECG recordings from pre-infusion to 4-hours post-infusion. Scopolamine improved MADRS scores in a similar magnitude to glycopyrronium yielding a non-significant antidepressant effect size (d=0.17) at day 3. Scopolamine modulated HRV with the high frequency metric exhibiting a main effect ($F(2,356)=8.8$, p=0.012). No differences in alpha were reported, however, theta exhibited significant interaction effects between time and group in central ($F(32,403)=76.5$, p=1.6e-5) and occipital $F(32,307)=106$, p=6.9e-10) electrodes. The mood results raise questions about the placebo response. Furthermore, the different effects of scopolamine on healthy individuals and individuals with depression suggest both a central and peripheral antimuscarinic contribution to depression.

5.1

Investigating the effects of novel kappa opioid receptor agonists on the differentiation of oligodendrocyte precursor cells *in vitro*

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Demyelination is a pathological event occurring in many diseases including multiple sclerosis (MS). In MS, lack of myelin repair is largely due to the failure of oligodendrocyte precursor cells (OPCs) to differentiate into myelin-forming oligodendrocytes (OLs). Identification of clinically safe pharmacological agents that can promote differentiation of endogenous OPCs is a promising therapeutic approach to promote recovery following demyelination. To identify compounds that promote differentiation of OPCs, we optimized an *in vitro* medium throughput screening assay using mixed glial cultures from wild-type and transgenic mice expressing eGFP on OPCs (PDGFRα-eGFP). We showed that a range of structurally diverse KOR agonist (U50, 488 analogues, Salvinorin A analogues) stimulated OPC differentiation into mature oligodendrocytes *in vitro*. We confirmed these effects were KOR mediated as the KOR antagonist nor-binaltorphimine prevented the KOR-induced OPC differentiation. The present study demonstrates that KOR agonists promote OPC differentiation and may be a therapeutic candidate for promoting recovery and repair in demyelinating disorders such as MS.

5.2

Uncovering new trafficking routes in axons

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Intracellular trafficking involves the movement of cellular cargoes such as proteins and organelles, by motor proteins that move along cytoskeletal microtubules. In neurons, such trafficking is especially critical, because the extreme length of axons (up to 1 metre in humans) requires that cargoes originating in the cell body travel long distances to reach their destinations. Despite the critical importance of trafficking to proper neuronal functioning, the basic mechanisms regulating the distribution of cargoes in axons are poorly understood. We previously showed that axonal trafficking relies on two microtubule associated proteins (MAPs) that localise to the initial part of the axon: MAP2 and TRIM46. Given the ubiquitous presence of MAPs in axons, these proteins are likely candidates for providing signals for a "MAP code" to coordinate specific trafficking routes. By using high-resolution live-microscopy, genetic and biochemical approaches we have uncovered a new trafficking pathway regulated by MAP1A. We found that MAP1A precisely locates between MAP2 and TRIM46 where it is required for the transport of newly synthesised TRIM46 from the cell body to the axon. Furthermore, neurons depleted of MAP1A display impaired morphology and axon growth. We propose a novel mechanism for axonal trafficking and reveal a critical role for MAP1A.

5.3

Pericyte cell death and α-synuclein – a double hit

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Parkinson's disease (PD) is characterised by the progressive loss of midbrain dopaminergic neurons and the presence of aggregated α-synuclein (α-syn). Recently it was discovered that non-neuronal cells such as pericytes contain α-syn in the human PD brain. Pericytes, found surrounding the capillaries in the brain are important for maintaining the blood-brain barrier, controlling blood flow and mediating inflammation. However, their role in PD pathogenesis is poorly understood. In this study, primary human brain pericytes (n = 4) were pre-treated with the ubiquitin proteasome inhibitor – MG132 and subsequently incubated with two different α-synuclein aggregates – ribbons and fibrils. We found that the two α-syn aggregates alone are devoid of inflammatory and cytotoxic actions on human brain derived pericytes. Interestingly, when pericytes were exposed to MG132 and α-syn aggregates, there was profound cytotoxicity through the production of reactive oxygen species and superoxide release from mitochondria resulting in apoptosis. These results suggest that an additional insult is required to cause pericyte cell death. Therefore, the observed accumulation of α-syn in pericytes in human PD brains likely plays a role in PD pathogenesis, perhaps by causing cerebrovascular instability, under conditions of cellular stress.

5.4

Voluntary exercise restores motor performance in a mouse model of spinocerebellar ataxia type 1 (SCA1)

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Spinocerebellar ataxia type 1 (SCA1) is an autosomal-dominantly inherited, progressive movement disorder, with no effective treatment. One therapy gaining attention is exercise. Yet, the impact exercise has on motor behaviour and cerebellar circuitry remain elusive. Here, four-week-old SCA1 154Q/2Q (SCA1) and wild-type (WT) mice were separated into exercising (E) and non-exercising (NE) groups, and individually housed with/without a running wheel for 4 weeks, then tested on an accelerating rotarod. Since Purkinje neuron (PN) firing is disrupted in SCA1 mice, and inhibitory basket cells (BCs) synapse onto PNs (the cerebellar sole output neuron) to control PN firing regularity, we assessed BC-PN connectivity using fluorescent immunohistochemistry. SCA1 NE mice show clear failure of coordinated motor performance on the accelerating rotarod when compared to WT NE mice (two-way ANOVA with Tukey's multiple comparisons, $p<0.0001$, n=13-14/group). Following voluntary exercise latency to fall scores of SCA1 E mice matched WT NE mice (two-way ANOVA, $p\geq0.05$, n=13-14/group). Similarly, BC-PN connectivity was enhanced in SCA1 NE mice and reduced following voluntary exercise, as BC-PN connectivity in SCA1 E mice was comparable to WT NE mice (unpaired t-tests, n=4-5/group). These exciting findings indicate that voluntary exercise may restore motor coordination in SCA1 mice by normalising BC-PN connectivity to restore PN firing fidelity.

5.5

Immediate early gene expression and intrinsic excitability are not linked in adult-born hippocampal neurons

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The discovery of adult-born dentate granule cells (aDGCs) in the hippocampus of most mammals has raised questions regarding how these cells mature over time. In particular, do these cells retain any special functionality throughout their life-course? Here we examined the excitability of aDGCs in the mouse using a tamoxifen-inducible genetic label to birth-date aDGCs, and characterised their excitability at different times post-neurogenesis using whole-cell patch-clamp methods. Previous work in our lab using rats indicated that the age of the animal at aDGC birth is important in determining the molecular excitability of these cells based on the expression of the immediate early gene, Egr1. We showed that Egr1 expression was high at 4 weeks and remained high in cells born when the animal was 2 mo (early adulthood), but that the high activity did not persist when cells were born in middle-aged animals (7-9 mo). However, our electrophysiology results indicated that only the cells aged 4-6 weeks, regardless of animal age at the time of cell birth, were intrinsically more excitable than at other cell ages. This indicates that, in aDGCs, intrinsic excitability and molecular excitability result from different cellular mechanisms. This work was supported by the Neurological Foundation New Zealand.

6.1

Visualizing in deceased COVID-19 patients how SARS-CoV-2 attacks the respiratory and olfactory mucosae but spares the olfactory bulb

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Anosmia, the loss of smell, is a common and often the sole symptom of COVID-19. The onset of the sequence of pathobiological events leading to olfactory dysfunction remains obscure. We have developed a postmortem bedside surgical procedure to harvest endoscopically samples of respiratory and olfactory mucosae and whole olfactory bulbs. Our cohort of 85 cases included COVID-19 patients who died a few days after infection with SARS-CoV-2, enabling us to catch the virus while it was still replicating. We found that sustentacular cells are the major target cell type in the olfactory mucosa. We failed to find evidence for infection of olfactory sensory neurons, and the parenchyma of the olfactory bulb is spared as well. Thus, SARS-CoV-2 does not appear to be a neurotropic virus. We postulate that transient insufficient support from sustentacular cells triggers transient olfactory dysfunction in COVID-19. Olfactory sensory neurons would become affected without getting infected. Understanding the mechanisms whereby human sustentacular cells normally support OSNs in countless ways may yield clues for therapeutic interventions aimed at preventing, alleviating, or curing olfactory dysfunction in COVID-19. The spotlight ought to be shone on the unsung heroes of the sense of smell - the humble sustentacular cells.

Poster 7.1

Communicative and hippocampal gene expression changes in the serotonin transporter knockout rat following poly I:C -induced maternal immune activation

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The aetiology of neurodevelopmental disorders (NDDs) such as autism spectrum disorder and schizophrenia is poorly understood, however potentially driven by complex interactions of genetic and environmental risk factors. One strong risk factor is serotonergic signalling, with NDDs typically exhibiting altered serotonin homeostasis and serotonin-regulated neuronal morphology/connectivity. Maternal immune activation (MIA) due to maternal infection during pregnancy is an environmental risk factor, shown in human epidemiological studies and in animal models to increase NDD/NDD-like outcomes in offspring. This pilot study aimed to investigate potential interaction between genetically reduced serotonergic signalling and MIA, induced by administering the viral mimic poly I:C to pregnant heterozygous serotonin transporter knockout dams. Behavioural and molecular outcomes in offspring grouped by treatment (poly I:C or saline), genotype (wildtype or heterozygous), and sex were investigated. Communicative behaviour was assessed through pup ultrasonic vocalisations (USVs) following maternal separation, while molecular analysis targeted mRNA expression of the spine-remodelling, schizophrenia-associated Rac1/Kal7/Disc1 signalosome by qRT-PCR and ddPCR techniques. Strong genotype effects were observed in overall pup communication, with treatment/genotype interaction in USV call complexity. Molecular analyses showed significant treatment effects in signalosome expression. This study overall provides preliminary evidence of serotonergic and MIA risk factor interaction and warrants further investigation.

Poster 7.2

Developing models of dynamic interoceptive learning

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Interoception, the perception of the internal state of the body, has been shown to be closely linked to emotions and mental health. Of particular interest is interoceptive learning; the higher-order processes involved in learning from body signals to make predictions about the future. Here we extended an interoceptive Breathing Learning Task (BLT) to incorporate continuous measures of prediction certainty, and tested its application using a Rescorla Wagner (RW) associative learning model. Sixteen healthy participants completed the continuous version of the BLT, where they were asked to predict the likelihood of breathing resistances. The previous version of the task had utilised binary predictions (yes/no), and thus did not capture prediction certainty. The RW model was used to fit a learning rate to each participant's continuous and binarised predictions, and was additionally extended to test whether learning rates differed according stimuli valence. The empirical data demonstrated excellent replicability to that collected previously using binary predictions, and the continuous model fits closely captured participant behaviour at the group level. Furthermore, fatigue severity was found to be related to both prediction certainty and learning rate. These results will inform multiple longitudinal studies assessing the effect of both pharmacotherapy and exercise on anxiety and interoception.

Poster 7.3

Molecular and cellular characterisation of the Parkinson's disease olfactory bulb: An origin of disease pathology

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Parkinson's disease (PD) is a neurodegenerative disorder that results in the progressive degeneration of striatal dopaminergic neurons in the substantia nigra. Although more than 20 genes are associated with PD, most cases have an unknown underlying cause. Interestingly, up to 95% of PD cases have olfactory dysfunction prior to motor symptom onset, and alpha-synuclein pathology has been identified in the early stages of PD in the olfactory bulb (OB). Despite this, the human OB remains largely uncharacterised, particularly in the context of disease processes. Therefore, the aim of my project is to evaluate the human OB as a source of disease origin in PD by integrating genomic (whole genome sequencing, WGS), transcriptomic (total RNA sequencing and spatial RNA sequencing), and proteomic (RNAscope®) evidence from 26 PD brains from the New Zealand Neurological Foundation Human Brain Bank. WGS revealed one causal variant in LRRK2 (p.Gly2019Ser) and one susceptibility variant in GBA (p.Leu444Pro) in two separate cases. RNA sequencing will be performed on the OB of cases and controls to characterize cell types. Results will be overlaid with RNAscope® on the same cohort to determine the pathogenic cascade from gene to protein and identify novel disease mechanisms in the PD OB.

Poster 7.4

Secreted amyloid precursor protein alpha has widespread effects on the transcriptome and proteome of human neurons related to memory mechanisms

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Secreted amyloid precursor protein alpha (sAPPα) processed from a parent human brain protein, APP, can modulate learning and memory. It has potential for development as a therapy preventing, delaying, or even reversing Alzheimer's disease. Here, we analysed how sAPPα affects the transcriptome and proteome of human neurons. Human inducible pluripotent stem cell (iPSC)-derived glutamatergic neurons in culture were exposed to 1 nM sAPPα and changes in the transcriptome and proteome were identified with RNA sequencing and Sequential Window Acquisition of All THeoretical Fragment Ion Spectra-Mass Spectrometry (SWATH-MS), respectively. A large subset (~30%) of differentially regulated transcripts and proteins were functionally involved with the molecular biology of learning and memory, consistent with reported links of sAPPα to memory enhancement, as well as neurogenic, neurotrophic, and neuroprotective phenotypes in previous studies. Differentially regulated proteins included those encoded by previously identified Alzheimer's risk genes, proteins involved in APP processing, synaptogenesis, synaptic vesicle cycling and neurite outgrowth. We have identified a complex set of genes affected by sAPPα, which may aid further investigation into the mechanism of how this neuroprotective protein affects memory formation and how it might be used as an Alzheimer's disease therapy.

Poster 7.5

Multiplex immunohistochemistry and spatial proteomic analysis of the human olfactory bulb in Alzheimer's and Parkinson's disease

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Multiplexed immunehistochemical (MP-IHC) biomarker labelling is an efficient and powerful technique to study the heterogeneity and complexity of brain structure in aging and disease. However, current approaches require slow iterative cycles of low-content IHC labelling or time-consuming and expensive direct conjugation of DNA tags to primary antibodies. We present a high-content MP-IHC approach that improves the throughput of current methods but maintains accessibility in set-up time and cost by using commercially available reagents, standard immunofluorescence labelling protocols and conventional widefield microscopy equipment with relatively low-cost modifications. We demonstrate this approach by screening 89 antibodies on formalin-fixed paraffin-embedded sections of human olfactory bulb (OB) from normal, Alzheimer's, and Parkinson's disease patients. The OB is involved early in the symptomatology and pathophysiology of these neurodegenerative diseases. To analyse the high-content anatomical information from such large tissue sections, we developed a "spatial proteomics" approach to assess tissue features using 28 antibodies targeting different parts of OB cytoarchitecture in an unsupervised manner. Using this pipeline we have produced a comprehensive neurochemical characterisation of human OB anatomy and a summary of differentially expressed markers in disease which include tau, GFAP and tyrosine hydroxylase. Overall, this approach offers a powerful and versatile platform for neuroanatomical discovery.

Poster 7.6

Non-spatial memory and the anterior thalamic nuclei

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The anterior thalamic nuclei (ATN) form a central node in a hippocampal-diencephalic-cingulate memory system, but there is little evidence for non-spatial memory deficits after ATN lesions. We trained rats to learn an arbitrary association between non-spatial object-odour pairings (A+X or B+Y were rewarded; but not A+Y or B+X), with or without a 10-second delay between exposure to the two non-spatial stimuli. Acquisition was completely abolished by ATN lesions, irrespective of the presence of the temporal delay (Lesion, $F=151.24$, $df=1, 27$, $p<0.001$). ATN-lesion rats showed reduced Zif268 expression in prefrontal and retrosplenial cortex after a re-test 5 days after the end of training (50 days). Sham rats were tested 5 days after reaching criterion and showed elevated Zif268 expression in hippocampal CA1 for the trace compared to no-trace condition. These results provide further evidence that the hippocampus is engaged when a trace condition is used in non-spatial tasks. The effects of ATN lesions, however, are not the same as those of hippocampal lesions. This is the first evidence that ATN lesions impair non-spatial paired-associate tasks. The ATN may be critical for learning arbitrary associations in general.

Poster 7.7

Multimodal MRI predictive biomarkers for cognition Across the lifespan

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Alterations in cognitive abilities are found in several mental/neurological disorders, from depression, ADHD to Alzheimer's. Yet, we do not have robust brain-based biomarkers for cognitive abilities that can help our studies of these illnesses. We have recently proposed the use of multimodal-MRI along with machine learning to create robust biomarkers. We tested our method on 873 young adults, 22-35 years old, from the Human Connectome Project (HCP) young-adult (https://doi.org/10.1101/2021.10.31.466638), whose multimodal-MRI data included non-task-MRI modalities (e.g., cortical thickness and area, subcortical volume, resting-state functional connectivity) and task-fMRI contrasts. Our multimodal biomarker was able to predict cognitive abilities with good performance (r=.57). Here we tested if the same approach was applicable to participants across the left span. We found a similar predictive performance in 754 aging participants from the HCP-Aging, 36-100 years old (r=.55) and in 503 middle-aged participants from the Dunedin study, 45 years old (r=53). Moreover, because the three datasets share similar non-task MRI modalities, we also tested the generalisability of the predictive biomarkers trained from non-task MRI of one dataset to predict the cognitive abilities of participants in another dataset. We found reasonable generalisability at r~.24. Accordingly, we developed predictive and generalisable biomarkers for cognitive abilities.

Poster 7.8

A focused ultrasound-mediated drug delivery system in a hemiparkinsonian rat model

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Current pharmacological strategies for Parkinson's disease aim to alleviate disabling motor symptoms by dopamine supplementation using a prodrug (levodopa) or receptor agonist (e.g. ropinirole). However, oral delivery of these drugs results in non-physiologic dopaminergic stimulation at striatal nuclei, and off-target effects. To circumvent these issues, we present proof of concept of a novel, ultrasound (US)-mediated system capable of releasing ropinirole from packaged liposomes (ropinisomes) in targeted areas. We systemically administered ropinisomes and subsequently directed transcranial US to the striatum, to locally release ropinirole and induce contralateral turning in hemiparkinsonian rats. Additionally, we exposed rats to single and repeated sonications and assessed the potential for US-induced blood-brain barrier (BBB) disruption and adverse tissue damage, specifically architectural, haemorrhagic and gliotic changes. US-mediated release of ropinirole was observed in most trials, without BBB compromise, or significant tissue damage. No turning was observed in the absence of ropinisomes and US, but some turning was observed following initial ropinisome administration, prior to US application, indicative of spontaneous release. Thus, we demonstrate *in vivo* the feasibility and safety of US to mediate ropinirole release from ropinisomes. Further translation requires improvement in ropinisome stability, and more sensitive *in vivo* assessment of drug uncaging to complement behavioural findings.

Poster 7.9

Development of a visual decision-making task to investigate the mechanisms of visual hallucinations in Parkinson's disease

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The hierarchical Bayesian predictive processing framework suggests that hallucinations are driven by impaired integration of bottom-up sensory input and top-down prior knowledge. We designed a visual decision-making task to test this model. Participants are required to judge the overall horizontal direction of a random-dot motion stimulus. Prior knowledge is supplied by a cue that is either helpful, unhelpful or neutral in indicating the dot-motion direction. We have tuned variables to optimise the precision and difficulty level of the task. Key parameters are dot coherence (percentage of dots moving in the same direction vs. randomly), overall dot speed, cue type, and cue duration. With detailed within-subject testing (n=1) and psychophysical investigations comprising 1260 trials over four testing sessions, we established that coherence values between 0-30% and a dot speed of 0.15 degrees/s/screen refresh provide acceptable task difficulty. This task will now be piloted in a group of healthy controls. We then aim to use this task to improve our understanding of the underlying mechanisms of visual hallucinations in Parkinson's disease.

Poster 7.10

Tau pathology in the Huntington's disease human brain

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Huntington's disease (HD) is a heritable neurodegenerative condition caused by a mutation in the huntingtin (htt) gene, resulting in production of mutant htt protein. Alongside mutant htt, other pathogenic proteins have been documented in HD which may contribute to the observed HD toxicity and variable symptomatology. One of these pathogenic proteins is tau, with its many isoforms and modifications, that has not been well characterised in the HD human brain particularly in the context of clinicopathology. This study aims to extensively characterize tau pathology in HD brain tissue using immunohistochemical analyses of tau and its various isoforms in HD human brain tissue microarrays. Preliminary results demonstrate approximately 15% of HD cases examined contain tau immunoreactivity, however, the specific isoforms are still being investigated. The next steps involves quantification of tau expression and its isoforms in HD versus matched control cases, and further analysis to determine if differential tau expression correlates with HD clinicopathological features such as CAG repeat, Vonsattel neuropathological grade, and age of disease onset. Further studies will also investigate relationships between tau and mutant htt protein. Characterising tau immunoreactivity in HD will provide the necessary insight to elucidate the contribution of tau to HD clinicopathology.

Poster 7.11

Sociodemographic and clinical characteristics of 1350 patients with young onset dementia: a comparison with older patients

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This study aimed to determine the sociodemographic and clinical characteristics of a large cohort of patients with young onset dementia (YOD; aged <65), and whether they differ from older (age 65+) adults with dementia. This was a retrospective cross-sectional study. Participants were New Zealanders who were assessed with International Residential Assessment Instrument (interRAI) assessments (including community-dwelling adults and those in long-term care) from 2016-2019 and had a diagnosis of dementia. Outcomes were sociodemographic and clinical characteristics captured in the interRAI assessment. People with YOD were more likely to be male, non-European, and live in a dwelling other than a private home or be homeless. They were more likely to exhibit problematic behaviours and neuropsychiatric symptoms but were less frail and less dependent for activities of daily living. Financial strain and loneliness were more common in people with YOD. Carers of people with YOD were more likely to feel distress, anger, or depression, and families of people with YOD were more likely to feel overwhelmed. People with YOD have different needs than older adults with dementia. These differences must be considered by clinicians and organizations that provide care and support to people living with dementia.

Poster 7.12

Identifying the cellular mechanisms of Alzheimer's disease (AD) in vivo.

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Alzheimer's disease (AD) is the most common neurodegenerative disease worldwide, with patients exhibiting gradual cognitive decline. Direct evidence of real-time circuit and subcellular changes with AD progression is lacking, as this requires measuring cellular activity in live animals (*in vivo*) during behavioural tasks. However, the development of head-mounted miniaturised microscopes (miniscopes) allows the chronic recording of neuronal activity in freely moving rodents. We hypothesise that amyloid plaque pathology specifically impairs the function of hippocampal neurons, leading to aberrations in spatial memory and object recognition. To that end, AD ($APP_{swe}/PS1_{dE9}$) and control mice received CA1 viral injections of a calcium activity reporter (GCaMP7), were superiorly implanted with a GRIN lens for visualisation, and had a miniscope baseplate attached to the skull. They were subjected to open field, y-maze, and novel object recognition behavioural tests. The simultaneously recorded neuronal dynamics were correlated with behavioural findings and compared across groups. The two groups exhibited various significant behavioural and neuronal differences, exemplifying the potential of this technology. Additionally, our results indicated the weight of the miniscope model has a significant impact on rodent behaviour. We will record neuronal activity in aged AD mice during hippocampus-dependent behaviours, and correlate activity with proximity to amyloid plaques.

Poster 7.13

Childhood social isolation as a predictor of retinal neuronal thickness in middle age: A lifecourse birth cohort study

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Childhood social isolation may become biologically embedded, with effects on physical health, including poor brain health, remaining apparent across the life course into old age. The retina has the potential to be a cheap and accessible biomarker of brain health. We investigated whether child social isolation was associated with retinal nerve fibre layer (RNFL) in midlife. Participants were members of the Dunedin Multidisciplinary Health and Development Research Study, a representative birth cohort born in 1972-1973 (*n*=1037). Social isolation was measured at ages 5-11. RNFL was measured at age 45. Childhood social isolation was associated with adult RNFL thickness (average thickness *B*=-0.739, *p*=.02; nasal quadrant *B*=-1.118, *p*=.005; and inferior quadrant *B*=-1.524, *p*=.007). These associations were not mediated by adult loneliness or social support, nor fully explained by other risk factors in childhood or adulthood. Thus, childhood social isolation appears to be an independent predictor of RNFL at age 45. This exploratory study is the first of its kind to investigate the association between childhood social isolation and retinal thickness in adulthood. Better understanding the relationship between lifecourse psychosocial risks and retinal dysfunction may help elucidate the nature of the long-term effects of stress in childhood on later physical health.

Poster 7.14

A bad influence: Do glia with defective lysosomes harm healthy neurons?

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Efficiently functioning lysosomes, the recycling system of cells, are essential for maintaining brain health. Ubiquitous disruption of lysosomal function, as in CLN6 Batten disease, causes childhood neurodegeneration, and late onset neurodegenerative disorders show lysosomal defects. Batten disease, as well as neurodegenerative diseases of old age feature glial activation. However, the specific contribution of lysosomal dysfunction in glia in these disorders is, as yet, unknown. We hypothesised that lysosome disruption in astrocytes or microglia impairs not only glial function, but also incites deterioration of neurons. We separately cultured primary astrocytes and microglia from mice with a CLN6 mutation that disrupts lysosomal function. We observed a 29% increase in the number of astrocytes from the CLN6 deficient mice compared to wildtype C57/B6 mice; microglia numbers did not differ significantly. CLN6 deficient or control glia were co-cultured with healthy human, induced pluripotent stem cell-derived cortical neurons. Survival of neurons grown on CLN6 deficient glia was unchanged compared to wildtype glia. Lysosomal and mitochondrial phenotypes of pure glia cultures, and their effect on the morphology and lysosomal function of co-cultured, healthy human neurons are being assessed. This research, interrogating the cellular drivers of neurodegeneration, will help advise future treatment options for neurodegenerative diseases.

Poster 7.15

Parkinson's disease: The role of perivascular spaces in cognitive decline

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MRI-visible perivascular spaces (PVS) are a radiological marker of cerebral small vessel disease (SVD) and are commonly observed in neurodegenerative and neuroinflammatory disorders. Within Parkinson's disease (PD) the clinical significance of PVS burden remains uncertain, particularly with respect to cognitive decline. To understand this relationship, we applied an automated detection algorithm to 3T MRI T1 and FLAIR scans from 117 individuals with PD (72 = normal cognition (PD-N), 39 = mild cognitive impairment (PD-MCI), 6 = dementia (PDD)) and 43 age and education matched controls, yielding PVS counts within cerebral white matter. Contrary to reports of increased PVS burden in PD relative to controls, we found that those with PD exhibited significantly fewer PVS in the white matter supplied by the anterior cerebral artery ($\beta<-2$, $p<0.05$), with no changes observed in other vascular territories or according to cognitive group. These findings suggest that the SVD profile observed in the supratentorial white matter of those with PD is unlikely to independently contribute to cognitive decline. Rather, cognitive decline in PD may be more associated with PVS in the subcortical grey matter.

Poster 7.16

Poorer executive function performance is associated with lower white matter fibre in the superior longitudinal fasciculus in Alzheimer's disease risk groups

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Decline in executive functions (EF) and white matter degeneration may be critical in the development of Alzheimer's disease (AD). Using diffusion-weighted MRI and fixel-based analysis (FBA), we investigated the relationship between white matter fibre properties, fibre density (FD), fibre cross-section (FC), and fibre density cross-section (FDC), in the superior longitudinal fasciculus (SLF) and EF in AD risk groups. Participants from the Dementia Prevention Research Clinic (DPRC), *n* = 229, comprised five groups: a control group of older adults (C), individuals with subjective cognitive decline (SCD), single-domain amnestic MCI (aMCI), multiple-domain MCI (mMCI), and AD. Cross-sectional analyses were conducted with longitudinal changes investigated in a subset (*n* = 124). Linear trend decreases and between-group differences were found in FD and FDC, and EF, largely in inhibition, cross-sectionally. Longitudinal decreases were found in FD and FC, and in processing speed. Only the MCI groups declined in EF and processing speed over time. While the C and SCD groups performed similarly well in EF, the C group had greater FD and FDC in SLF3 than the SCD group, and in several SLF tracts compared to other groups. Finally, a behaviour partial least-squares analysis showed poorer EF was associated with lower FD and FDC.

Poster 7.17

The effects of nalfurafine a kappa opioid receptor agonist on glial cell activation in preclinical models of multiple sclerosis

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Demyelination is a pathological feature of multiple sclerosis, and no current therapeutics induce remyelination or promote repair and recovery. New therapeutics targeting remyelination are urgently needed. Astrocytes and microglia play important roles in maintaining myelin health, clearing debris and promoting anti-inflammatory cytokine release. The kappa opioid receptor (KOR) has been identified as a potential target for the development of remyelinating pharmacotherapies. This study investigated nalfurafine, a clinically available KOR agonist, in cuprizone toxin-induced preclinical models of demyelination. There was an increase in glial cell infiltration ($p<0.05$) following demyelination, and nalfurafine treatment failed to alleviate microglia and astrocyte activation, as assessed through both cell number and morphology. The expression of KOR on both astrocytes and microglia was analysed following demyelination. Fewer than 5% of astrocytes expressed KOR in healthy mice, and this expression was significantly decreased following demyelination. There was no change following treatment with nalfuarfine ($p<0.05$). Preliminary data suggested that approximately 5% of microglia express KOR in healthy mice, and KOR expression appeared to increase following demyelination and treatment with nalfurafine. Overall, the effects of nalfurafine on glial cells is still being investigated and future directions will assess functional changes in these cell types.

Poster 7.18

A spiking neural network model of motor cortex activity

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The motor cortex is directly involved in movement, but how activity in this brain region relates to muscle activation is still unclear. A model of the motor cortex containing over 35,000 leaky-integrate and fire neurons with more than 150 million excitatory and inhibitory synapses was built to represent a segment of the cortex equivalent to a surface area of $1mm^2$ and its spiking activity. Using a canonical cortical circuit model with reciprocal and recurrent connections between eight neuron populations in a layered structure, this model replicates experimentally measured spontaneous firing activity and the high frequency bursts of corticospinal activity, known as I-waves, in response to Transcranial Magnetic Stimulation (TMS). The neuronal circuitry in this model supports the idea that high density, recurrent inter and intralaminar corticocortical projections can result in the low frequency, asynchronous firing observed during spontaneous activity and generate I-waves. Building more biologically plausible neural networks than have been proposed previously, our model lays the foundation for modelling the motor pathway from cortex to muscle. This work furthers the understanding of the integrated circuits within the motor cortex and enables exploration into the dynamics of cortical control for voluntary movement.

Poster 7.19

Hippocampal place cells form a multi-scale representation of megaspace

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Spatially firing "place cells" within the hippocampus form internal maps of the environment necessary for navigation and memory. Exclusively studied in rodents in small environments (<4 m^2), the manner in which these place cells encode more ethologically realistic large environmental scales is unknown. Here, we recorded rats navigating in a 'megaspace' (18.6 m^2), an environment over four times larger than used previously. We found that the majority of dorsal CA1 place cells exhibited multiple place subfields of different sizes, akin to those observed along the septo-temporal axis. Furthermore, the sum area covered by the subfields of each cell was similar, irrespective of the number of subfields a cell had, and increased with the scale of the environment. The multiple different-sized subfields exhibited by place cells in the megaspace suggest that the ensemble population of subfields form a multi-scale representation of space within the dorsal hippocampus. Our findings point to a new dorsal hippocampus ensemble coding scheme that simultaneously supports navigational processes at both fine- and coarse-grained resolutions. This helps to explain how humans make use of complex place cells maps over many overlapping spatial scales, from single rooms, to buildings, to streets, to cities, and beyond.

Poster 7.20

The exploration of depression and anxiety like behaviour using novel techniques in SERT Knockout rats

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The establishment of animal models of depression and anxiety would significantly improve the development of pharmacological interventions for these disorders. The development of these interventions has been stagnant likely due to the use of "gold standard" behavioural methods that contains important flaws (i.e., interpretation of immobility time in the FST, and the one trial tolerance (OTT) effect in the elevated plus maze). Here we use novel methods in an attempt to overcome these flaws using rats with a genetic reduction in the serotonin transporter ($SERT^{-/-}$ rats), i.e. a well-established risk factor for depression and anxiety in both animals and humans. Using social conditioned place preference (Social CPP) and quantitative analysis of play behaviour, we found a significant social anhedonia in $SERT^{-/-}$ rats, an essential diagnostic criterion for major depressive disorder. Furthermore, using a modified version of the successive alleys test, we found a significant increase in anxiety—like behaviour that persists for at least 6 days. Together, these data provide new avenues of testing the efficacy of novel antidepressant and anxiolytic pharmacological interventions.

Poster 7.21

Glutamatergic characterisation of the human globus pallidus in Huntington's and Parkinson's disease

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The globus pallidus (GP) is a core component of the basal ganglia (BG), a group of subcortical nuclei in the brain involved in motor, associative and limbic functions. The connections of the BG rely on a balance of excitatory and inhibitory activity for normal brain function. Therefore, this study investigates glutamatergic changes in the GP of post-mortem human brain in normal, Huntington's and Parkinson's disease. 6 control, 6PD and 9HD cases were used to run western blot experiments for glutamatergic markers (GluA1, GluA2, GluN1, PSD95, VGluT1, VGluT2, EAAT2). The pilot immunohistochemical study utilised 3 control, 3 PD, 3 HD cases for DAB staining. Having western blot and immunohistochemical data gives insight into the overall changes in protein levels and anatomical/localisation information between the GP segments and between disease states. Key findings from the study include the pallidal loss of AMPA receptor subunit GluA2 in samples from HD patients ($p=0.0054$), which in contrast is increased in samples of PD patients ($p=0.0242$). There was also a pallidal loss of EAAT2 in both HD and PD cases ($p=0.0165$ and 0.0094, respectively). Finally, there was shrinkage of pallidal cells in PD cases labelled with GluA1, GluA2, and GluN1.

Poster 7.22

Increased microglial CD68 expression in human Amyotrophic Lateral Sclerosis is associated with pTDP-43 pathology load

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Microglia, the innate immune cells of the brain, are activated by damage or disease. In mouse models of Amyotrophic Lateral Sclerosis (ALS), microglia shift from neurotrophic to neurotoxic states with disease progression. It remains unclear how human microglia change relative to the TDP-43 aggregation that occurs in 97% of ALS cases. Here we examine spatial relationships between microglial activation and ALS pathology in the human ALS brain. Post-mortem human brain tissue from the Neurological Foundation Human Brain Bank was utilised from 10 normal and 10 ALS cases. The relationship between microglial activation changes and ALS pathology was determined by investigating microglial changes in brain regions with low- and high-TDP-43 burden at end-stage disease: hippocampus and motor cortex, respectively. Sections were immunohistochemically-labelled with a 2-round multiplex panel, encompassing microglial-specific and functional markers (HLA-DR, L-ferritin, CD68, CD74, and Iba1), anatomical markers (NeuN, SMI32, and MAP2), vascular markers (GFAP and lectin), and pathological TDP-43. We developed novel image analysis pipelines to quantify single cell levels of microglial functional markers and spatially map microglial changes to anatomical regions and ALS pathology. Overall, I will demonstrate whether changes in microglial activation are responsive to, and may further drive, pathological load and neurodegeneration in ALS.

Poster 7.23

Uncovering neural activity in the spinal cord recorded by a novel bioelectronic implant

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Spinal cord injury is a devastating medical event, introducing many neurological problems. There is a lack of understanding of changes in electrical activity in an injured spinal cord. We have developed a polyimide bioelectronic implant to record spinal electrical activity, where we aim to identify electrical biomarkers related to injury. Electrical activity was recorded from the dorsal surface of the spinal cord in freely moving rats using a subdural implant containing 22 recording electrodes. This activity was bandpass filtered (300-6000Hz) to reveal high-frequency voltage spikes with waveforms similar to compound action potentials (CAPs). We hypothesised that these spikes were CAPs in the fibre tracts and validated this by investigating the propagation speed of these waveforms between electrodes. Spikes were extracted when the recorded voltage crossed a threshold. These spikes were assessed for similarity between channels and timing delays were determined. We demonstrate a detectable delay in spike propagation, with velocities in the expected range of CAPs in spinal fibre tracts. Propagation was detectable in both directions, suggesting afferent and efferent activity. These results provide confidence that our implant is recording signals indicative of neural activity, paving the way for investigation into how properties of these events may change with injury.

Poster 7.24

Neuroinflammatory pathways in the midcingulate cortex in Huntington's disease.

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Huntington's disease (HD) is a genetic neurodegenerative disorder that can result in motor, mood and cognitive symptoms. HD pathophysiology has been linked to neuroinflammation – the presence of inflammatory mediators and reactive glial cells in the brain parenchyma. Many signalling pathways likely interact to propagate neuroinflammation in the brain. Neuroinflammation is thought to cause cell loss, and cell loss in the anterior cingulate cortex is linked to HD mood symptoms. The presence of neuroinflammation in the HD midcingulate cortex (MCC) has not yet been investigated. We studied neuroinflammatory pathways in 14 HD and 9 control post-mortem human MCC samples using mRNA sequencing. HD cases were split into the symptom profiles of motor, mood and mixed. This data was analysed using Gene Ontology (GO) enrichment analysis. We found 24 upregulated inflammation-related genes including toll-like receptors, classical complement, AQP4, CHI3L1, P2X7R, S100A9 and SPP1 across HD cases. However, 13 inflammation-related markers including chemokines were downregulated. GO enrichment analysis reflected this, with multiple inflammation-related GO terms being upregulated and downregulated in HD. In mood HD cases, 7 inflammation-related genes were upregulated and none were downregulated. These results present a complex picture of potential inflammation priming in the HD MCC, rather than overt neuroinflammation.

Poster 7.25

DARPP-32 positive cell proportions in the striosome and matrix compartments of the post-mortem human dorsal striatum

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The human striatum is a vital nucleus of the basal ganglia circuitry that aids in motor, cognitive and limbic processing. The medium spiny neurons (MSNs) are the main projection neurons of the striatum. Furthermore, within the dorsal striatum exist two intermingled yet neurochemically distinct compartments, termed the striosomes and the matrix. To identify MSNs in the rodent striatum, both calbindin (a calcium binding protein), and DARPP-32 (a dopamine dependent protein phosphatase) have been used in previous research. Immunohistochemical studies in rodents has exhibited the homogenous expression of DARPP-32 in both the striosomes and matrix. However, using post-mortem human brain tissue from normal cases, multiplex paraffin immunohistochemistry and automated cell counting techniques, we demonstrate that DARPP-32 is highly concentrated in the striosomes, specifically the neuropil and the cell bodies. Additionally, some DARPP-32 positive cell bodies were observed to be scattered within the matrix compartment. We also demonstrate that DARPP-32 colocalises to some degree with the calbindin-positive cell bodies in the striosomes and matrix, but does not colocalise with striatal interneuronal cell populations (ChAT, NPY, parvalbumin, calretinin). From these results, we determine that DARPP-32 identifies a novel sub-type of striatal neurons in the human brain, some of which may be MSNs.

Poster 7.26

Cholinergic basal forebrain integrity and cognition in Parkinson's disease

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Most Parkinson's disease (PD) patients experience cognitive impairment, albeit at variable rates and with variable expression. The integrity of the cholinergic basal forebrain (cBF), which innervates the cortical mantle, may be a key factor. Here, we examined the association between cognition and subregions of the cBF using structural and diffusion-weighted MRI acquired from 60 PD with normal cognition (PD-N), 37 PD with mild cognitive impairment (PD-MCI), 12 PD with dementia (PDD), and 42 controls. After accounting for age and sex, significant differences were observed between the control and combined PD groups in diffusion tensor metrics in the anterior-intermediate Ch4 region (Ch4a-i; MD $p=0.05$, FA $p<0.01$) and horizontal limb of the diagonal band (Ch3; MD $p<0.01$, FA $p<0.01$), but not in the posterior (Ch4p) or lateral-anterior (Ch4al) Ch4 regions, or the medial septum/vertical limb of the diagonal band (Ch1-2). There was no difference between PD groups. Among PD participants, neuropsychological test performance was significantly associated with volume in Ch4al ($\beta=-0.17$, $p=0.03$), and diffusion metrics in Ch4p (FA $\beta=0.19$, $p=0.02$; MD $\beta=-0.15$, $p=0.05$) and Ch1-2 (MD $\beta=-0.26$, $p<0.01$; FA $p>0.09$), but not in other subregions ($p>0.1$). Our results suggest that cBF alterations are present irrespective of cognitive impairment in PD. Future work will explore cBF projections.

Poster 7.27

Identifying networks of genes interacting with α-synuclein in pericytes

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Parkinson's disease (PD) pathology is characterised by the abnormal aggregation of α-synuclein in neuronal and non-neuronal cells. Vascular cells, such as pericytes, are among those affected, however, changes in pericyte gene expression in PD have not been studied to the same degree as other cell types. Pericytes regulate the vasculature and have been shown to be disrupted by α-synuclein pathology. We aimed to gain a broader understanding of the interaction between α-synuclein and the genetic architecture of pericytes by analysing the interactions between genes differentially expressed according to α-synuclein pathology load. We identified differentially expressed genes in pericytes derived from PD versus control human brains and highlighted 522 transcripts correlated to α-synuclein pathology load. We identified protein interactions of each transcript using the DB String database, then clustered genes into groups using Girvan and Newman's Edge-Betweenness algorithm. Of 111 communities, 67 interacted with each other in a broad network. We hypothesise that this network of genes indicates pathways that influence, or are influenced by, α-synuclein in pericytes. Identifying pathways rather than single effector genes highlights transcriptomic changes within the cell at a broader scale, hopefully to identify drug targets that modulate more significant components of the transcriptome of pericytes.

Poster 7.28

Pūnaha Io – The New Zealand NeuroGenetic Registry and Biobank

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Pūnaha Io - the New Zealand Neuro-Genetic Registry and Biobank is intended to be an easily accessible repository of clinical data linked to biological samples donated from patients with rare neurogenetic disorders. It will provide infrastructure aimed at translational research and is designed to facilitate and expedite the conduct of all stages of research in rare neuro-genetic disorders, from basic science and pre-clinical work through to clinical trial recruitment and post-market monitoring. Pūnaha Io has partnered with Te Ira Kāwai, gained ethics approval and importantly, stakeholder support. As well as scientists and clinician-researchers key stakeholders include the study population, which comprises participants with neuromuscular diseases in childhood and adult life such as muscular dystrophies (n = 329), spinal muscular atrophies (n = 62), hereditary neuropathies (n = 175), congenital myopathies, myasthenias, myotonic syndromes (n = 228), metabolic myopathies, inflammatory myopathies; and also predominantly central nervous genetic diseases such as Huntington's disease (n = 220), inherited ataxias (n = 124), inherited movement disorders, and hereditary spastic paraparesis (n = 39). The number of patients consented to participate and for whom clinical datasets have been established are indicated in parentheses. Unaffected familial and unrelated population controls are also able to be included. Disease-specific datasets containing Real World Data (RWD) have been adopted that are Findable, Accessible, Interoperable and Reusable (FAIR) and meaningful for translational research. Sample collection, storage as well as governance of the collection is according to Te Ira Kāwai's established procedures. Sample collection has commenced in 2022.

Poster 7.29

Assessing the relationship between intrinsic motivations, personality traits and mental health

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Mental health issues such as anxiety and depression are on the rise, with nearly 40% of New Zealanders experiencing difficulties at some point in their life. Psychology theories proport that there are basic needs (such as physical and social needs) that must be met for human wellbeing. Recently, the Institute for Personality-oriented Management has developed a tool to measure basic needs (or 'intrinsic motivations') from a deep-learning analysis of written text, and this analysis can also tell us whether our current behaviours are meeting these needs. Using this methodology, we proposed to test whether behavioural over- or under-representation of our intrinsic motivations may be related to both personality and mental health traits such as anxiety and depression, using an online study sample (n=421). Preliminary results have demonstrated the anticipated strong correlations between personality traits (extraversion and neuroticism) with all mental health measures. Furthermore, novel findings regarding intrinsic motivations show that the difference between the importance placed on self-assertion vs. its behavioural expression is correlated with level of anxiety. Understanding the links between (unfulfilled or overfulfilled) basic needs, personality and mental health will help us to better evaluate and treat conditions such as anxiety and depression in New Zealand.

Poster 7.30

Neuropathology of the x-linked dystonia parkinsonism striatum

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X-linked Dystonia Parkinsonism (XDP) is an X-linked recessive hereditary neurodegenerative disorder endemic to the island of Panay in the Philippines. XDP has an adult-onset typically characterised by its dystonia-parkinsonism disease progression. Clinical symptoms typically present in the third or fourth decade of life and are defined by progressive dystonia, with Parkinsonism-like symptoms manifesting and becoming the predominant phenotype, typically after 10-15 years. However, detailed neuropathological studies of the XDP human brain are currently limited. In a unique NZ-USA-Philippines collaboration, we are currently investigating a broad suite of neurochemical markers in XDP post-mortem human brains compared with neurologically normal control cases to elucidate and classify neurodegenerative-associated pathology, with a focus on delineating the degree of basal ganglia pathology. Our preliminary examination of 9 XDP cases suggests a loss of calbindin-positive medium spiny neurons within the caudate nucleus (50.2% decrease) and putamen (55.3% decrease) of the XDP striatum. We also note a variable degree of astrocytosis and microgliosis within the XDP striatum, denoted by increased GFAP, IBA1 and HLA-DR immunoreactivity. Further studies will examine subsets of medium spiny neurons, interneurons and non-neuronal cells to extend upon these findings to define the extent XDP basal ganglia pathology.

Poster 7.31

Linking the dynamics of cognitive control to individual differences in working memory capacity: Evidence from reaching behaviour

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This study used a technique known as reach tracking to investigate how individual differences in working memory capacity (WMC) relate to the functioning of two processes proposed to underlie cognitive control: a threshold adjustment process that inhibits motor output in response to signals of conflict and a controlled selection process that recruits top-down control to guide stimulus-response translation. Undergraduates (N = 135) performed two WMC tasks (Updating Counters and Symmetry Span) and a reach-tracking version of the Eriksen flanker task. Consistent with previous research using button-press flanker tasks, WMC significantly correlated with response time (RT) performance, with higher WMC scores corresponding to smaller congruency effects. A significant association between WMC and participants' reach trajectories was also observed, with higher WMC scores corresponding to more direct reach movements on incongruent trials involving stimulus-response overlap with the preceding trial. This effect was interpreted to reflect a process-specific link between WMC and the functioning of the controlled selection process. We discuss the observed links between WMC and cognitive control in relation to the functioning of prefrontal and striatal dopamine. The preregistration, data, and analysis files for this project are available at the following links: https://osf.io/qae49; https://osf.io/6hz3a/.

Poster 7.32

Glutamate transporter expression in the hippocampus, subiculum, entorhinal cortex and superior temporal gyrus in Alzheimer's disease

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Alzheimer's disease (AD) is the most common form of dementia. Its burden is increasing, warranting research into novel therapeutic targets. Two classes of glutamatergic transporter, vesicular glutamate transporters (VGluTs) and excitatory amino acid transporters (EAATs), play critical roles in regulating neurotransmission. Expressional alterations to VGluTs/EAATs previously reported in AD tissue likely disrupt synapse function and contribute to the pathophysiology of AD. However, human studies examining the expression of these transporters are limited, especially in the hippocampus, the most severely affected brain region. Therefore, we aimed to investigate the regional and layer-specific expression of VGluT1/2 and EAAT1/2 in the medial temporal lobe. Fluorescent immunohistochemistry and confocal imaging were used to quantify and compare the density of VGluT1/2 and EAAT1/2 in the hippocampus, subiculum, entorhinal cortex and superior temporal gyrus (STG) between control and AD cases. In AD, VGluT1 density was significantly reduced in the str. moleculare of the dentate gyrus ($p= 0.0051$). VGluT2 density was decreased in the subiculum ($p= 0.015$) and STG ($p= 0.0023$). Astrocytic EAAT1 staining was significantly higher in AD across most regions examined, while EAAT2 expression on astrocytic main branches appeared reduced. These results validate further investigation of VGluT1/2 and EAAT1/2 as therapeutic targets in AD.

Poster 7.33

The development of electrically stimulated release of neurotrophic growth factors

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Spinal cord injury is a devastating condition with a NZ incidence rate of 44 cases per million people. Injuries to the spinal cord cause axonal connection disruptions resulting in neurological dysfunction and long-term disability. Current clinical management strategies aim to prevent further injury and are not truly regenerative. Neurotrophic growth factors are a family of polypeptides that have been shown to positively influence neuronal regrowth, however its delivery to the affected area is challenging, needing deliberate control over exposure to cells. We hypothesise an electrically responsive delivery system can tune the release of growth factors. We have developed a delivery system comprising of a hydrogel (gelatin methacryloyl, (GelMA)) infiltrated with a conducting polymer, (poly(3,4-ethylenedioxythiophene)), to form an electrically responsive polymer for drug delivery. Incorporation of proteins as models of growth factors into the electroconductive delivery system was investigated and controlled release was tested under various stimulation conditions. Electrical stimulation increased the release rate by up to 17-fold compared to passive diffusion over a 21 day period. Altering electrical stimulation parameters modulate the release of proteins. Future studies will utilise the delivery system to demonstrate controlled axonal regeneration after an *in vitro* cell culture model of injury.

Poster 7.34

Characterisation of the distribution of calcium binding buffer proteins in the human spinal cord

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A spinal cord injury (SCI) affects the conduction of sensory and motor signals resulting in tetraplegia or paraplegia. Excess intracellular Ca^{2+} influx leads to the activation of Ca^{2+}-dependent cell death pathways and is a key pathological feature of SCI through facilitating inappropriate neurotransmission, excitotoxicity neuroinflammation, and apoptosis. Parvalbumin, calbindin, and calretinin are Ca^{2+} binding buffer proteins (CaBPs) that reduce levels of Ca^{2+} and so represent a putative neuroprotective role; however, their expression has not been described in the human spinal cord. This is essential to understanding the roles they play in modulating the neuroinflammatory process following trauma to the spinal cord. Multi-label, fluorescent immunohistochemistry on FFPE human spinal cord tissue revealed distinct patterns of labelling for calretinin, parvalbumin, and calbindin within C5, T5, and L1 segments. Further, spatial mapping allowed us to produce heat maps of expression based on fluorescence intensity. This is the first description of CaBPs in the human spinal cord. The differential pattern of distribution across spinal levels C5, T5, and L1 has implications for Ca^{2+} buffering capacity at different levels following injury. A multiplexed approach represents an opportunity to examine the distribution of CaBPs and identify potential areas of vulnerability in SCI.

Poster 7.35

Artificial Intelligence as a novel form of motion tracking in Parkinson's disease

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The gold-standard for Parkinson's disease assessment is the Unified Parkinson's Disease Rating Scale (UPDRS), a quantified but subjective clinical rating scale. Despite high inter-rater reliability, variability is apparent between experienced and inexperienced raters. We seek to minimise subjectivity through artificial intelligence (AI) motion capture. We will capture video of 75 motor assessments, applying deep learning algorithms to train our AI network, DeepLabCut, to track participants' movements. In this pilot study, we recorded a 20.6 second (1217 frame) video of finger tapping (n=1). Initially, 20 frames were manually labelled for training. Subsequently, automatically labelled outlier frames were identified by DeepLabCut and manually corrected iteratively to refine the network, for a total of 5.75% of the frames. The network was applied to capture finger tap frequency across an 8.7 second interval. DeepLabCut successfully tracked 100% of the taps, yielding a frequency of 4.6 Hz, compared to a manually measured frequency of 4.5 Hz. Given training on a larger cohort, DeepLabCut could generate further metrics of movement, such as absolute quantification of movement decrement and freezing. This indicates the promise of applying objective automated techniques, potentially as an alternative to subjective and variable human ratings in the context of clinical trials.

Poster 7.36

Psychophysical evidence for a relationship between cortical distance and illusion magnitude in the Ebbinghaus and Delboeuf illusions

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Recent converging evidence has suggested that Ebbinghaus and Delboeuf illusions are driven by interactions between contours, which in turn may be mediated by cortical distance within V1. Here we tested the effect of cortical distance in both illusions using two methods: First, we manipulated the retinal distance between inducers and annuli in a two-interval forced choice design. Our results showed that targets appeared larger with closer surrounds. Secondly, we predicted that due to lower cortical magnification in the peripheral visual field – and thus smaller cortical distances between illusion components – targets in the Ebbinghaus Illusion presented peripherally should appear larger compared to when they are presented centrally. We tested the illusion strength when positioning the stimuli at various eccentricities and our results supported this hypothesis. We calculated estimated cortical distances between illusion elements in each experiment and used these estimates to compare the relationship between cortical distance and illusion strength across our experiments, finding that estimated cortical distance outperformed retinal distance as a predictor of illusion strength. In summary, our study supports a contour-interaction hypothesis for these illusions and adds to the existing literature by showing a predictable relationship between two visual illusions and an estimated feature of cortical topography.

Poster 7.37

Determining the relationship between molecular changes in the amygdala and the emergence of associative learning in the rat

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Understanding the neural basis of learning is a fundamental question facing neuroscientists. Although much is known about the relationship between LTP and consolidated information, we know very little about what happened when the association between an event or behaviour and a consequence is realised. This has been defined as a moment of insight and the specific molecular changes which accompany such moments are not well understood. To shed light on this mechanism we used a classical conditioning protocol paired with an algorithm that allows us to specify when a rat has learned the association between a stimulus (sound) and its outcome (delivery of a food pellet). We quantified the phosphorylation of ERK, a signalling molecule related to learning, in the central amygdala, a region of the brain involved in behaviour driven by the value of a stimulus during normal associative learning and during aberrant behaviour towards addictive stimuli. We found that rats that had experienced the moment of insight expressed significantly more p-ERK than those that did not or those that were overtrained following acquisition. Thus, learning in our paradigm is accompanied by cellular changes that transiently peak when the “moment of insight” occurs and then subside following it.

Poster 7.38

Serum levels of S100B are significantly correlated with injury severity

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Severe traumatic injury is a leading cause of death in young adults worldwide. Because of this, research has focused on identifying suitable biomarkers to facilitate appropriate treatments. S100B is a favourable biomarker for traumatic brain injury, however, recent studies have shown its expression in many extracranial tissues. This raised the question as to whether serum levels of S100B correlate with overall injury severity. If so, its use as an adjunct in trauma management could be explored. We aimed to investigate whether serum levels of S100B correlate with overall injury severity using the injury severity scoring system (ISS). Trauma patients were recruited from the Emergency Department. Serum samples (8ml) were drawn at time of study enrolment and stored at -80°C until analysed. Regional Abbreviated Injury Scale scores were used to compute an overall ISS for each patient. Pearson’s correlation was used to examine the relationship between S100B (mg/L) and ISS. In our cohort (n=44), serum levels of S100B (mg/L) were significantly correlated with injury severity scores (p=0.0001, r=0.54). Our findings indicate that S100B may have utility as a diagnostic tool. Future studies should investigate its usefulness as a predictive biomarker for outcomes including hospital length of stay, intervention requirement, and mortality.

Poster 7.39

Circadian dysregulation of the choroid plexus with age and amyloid pathology

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The choroid plexus (CP) is responsible for the majority of cerebrospinal fluid (CSF) production in the brain. While impairment of CP function and CSF production is evidenced in animal models and human neurological disease studies, the underlying mechanisms for this dysfunction are unclear. Recently, circadian rhythmicity in the CP have suggested diurnal and potentially sleep playing a role in CSF dynamics and CP function. Notably both sleep and circadian dysrhythmia are common in neurodegenerative diseases where CP dysfunction is observed. We therefore measured the circadian and sleep-dependent transcriptional profile of the CP in mice at 3 months, 12 months, and in the presence of amyloidopathy. We observed that in young healthy mice, circadian rhythms- not sleep, govern changes in gene expression in the CP. Circadian-dependent gene changes are enriched for inflammatory and immune pathways in young mice, but in old mice shift to prioritizing membrane transport and ion channel genes. In contrast, in mice with amyloid accumulation circadian regulation is all but lost in the CP. Our data suggest a circadian dysregulation in the CP with age in the absence of pathology, and age-related circadian shifts in inflammatory regulation, and CSF homeostasis at the CP may drive disease processes.

Poster 7.40

Investigating the relationship between microRNA expression, brain structure and biochemistry in anxiety disorders and their potential treatment with ketamine

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Anxiety is a major clinical health problem due to its high prevalence, low recovery rates and a poor understanding of their underlying pathology. This research aims to improve our understanding of such pathology by linking correlates of altered gene expression with neurostructural and neurochemical alterations across various levels of symptom severity. Preliminary neurostructural data in a large subclinical population (n=188), analysed with FSL-VBM, showed a significant interaction between anxiety scores and gender ($p<0.05$) in the precentral gyrus. Additionally, exploratory significance ($p<0.1$) in the middle frontal gyrus and the occipital pole with combined trait anxiety (STAI-T) and depressive scores (CES-D). This dataset and ongoing results will help to clarify the current incongruent findings seen across the literature, which are confounded by issues regarding gender, sample size, patient comorbidities and current/past treatments across participants with anxiety. These results further suggest benefit to robustly investigating differences in neurobiology in the clinical population. We are currently collecting data from a cohort of people ($n\approx20$) with moderate-to-severe symptoms who are resistant to both pharmacological- and psychotherapy-based treatments. We will investigate how gene expression (TaqMan Arrays) and/or selected regional neurotransmitter (GABA/Glu) levels in the brain (FSL-MRS) might explain the relationship between brain structure and anxiety.

Poster 7.41

Alterations in normalised EEG power across the cognitive spectrum in Parkinson's disease

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Cognitive impairment is common in people with Parkinson's disease (PD). Here, we assessed the association between cognitive status and neural oscillations in PD based on EEG power. The current study assessed 28 healthy controls (HC), 54 PD with relatively normal cognition (PD-N), 22 PD with mild cognitive impairment based on MDS Level-II criteria (PD-MCI), and 8 PD with dementia (PDD). Resting-state EEG was collected from 64-channels. Following pre-processing, normalised power was extracted for each frequency band and permutation tests with TFCE were used to examine group differences. We found widespread higher theta power for PD-N, PD-MCI and PDD when compared with HC (all *ps*<.05), with a similar pattern for PD-MCI compared to PD-N (all *ps*<.05). Beta power was lower in the central regions for PD-MCI and PDD when compared to HC and PD-N (all *ps*<.05). Although not significant, topographical maps suggest a trend of decreasing posterior and frontal alpha power, and widespread increases in delta power as cognition declines. The results suggest cognitive decline is associated with alterations in EEG activity. The future research will focus on using a data-driven approach to identify functional nodes from EEG and examine the mediatory effect of structure on the function of the brain.

Poster 7.42

Retromer is crucial for autophagy and restrains Alzheimer disease-related pathology in human neurons

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The macroautophagy/autophagy-lysosome axis enables the clearance and degradation of cytoplasmic components including protein aggregates, such as tau, and damaged organelles. Work from our laboratory has demonstrated extreme lysosomal system dysfunction in mouse models of Alzheimer disease as well as in brains of people who lived with this disease. The endosomal-sorting complex retromer is important for lysosomal system function, and spatial overlap between depletion of retromer and tau aggregation in the brain has been previously reported. However, whether retromer dysfunction plays a direct role in mediating tau aggregation remains unclear. Using both chemical and genetic approaches in cell models of amyloid tau aggregation we demonstrate that the autophagy-lysosome axis is the primary mode for the clearance of aggregated species of tau. We show that depletion of the central retromer component VPS35 causes a block in the resolution of autophagy. We establish that this defect underlies marked accumulation of cytoplasmic tau aggregates upon VPS35 depletion, and that VPS35 overexpression has the opposite effect. This work illustrates how retromer complex integrity regulates the autophagy-lysosome axis to suppress tau aggregation and spread.

Poster 7.43

Reliability of remote gait and balance assessment of people with Parkinson's disease.

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There are validated gait and balance tests for people with Parkinson's disease face-to-face. We tested the reliability of these assessments of people with Parkinson's disease remotely compared to face-to-face. Fifteen people with Parkinson's disease (aged 57-82, 11 males) performed 14 gait and balance tests twice: (i) face-to-face, and (ii) remotely, via videoconference between 7 and 14 days after. A trained physiotherapist rated participant performance. The tests included items from the Berg Balance Scale, Functional Gait Assessment, and Timed-Up-And-Go. The videoconference was recorded. Comparison of face-to-face and videoconference performance gave assessment reliability. The physiotherapist and another rater rated the recording to obtain intra-rater and inter-rater reliability, respectively. Reliability was measured using intraclass correlation (continuous measures) and Fleiss' Kappa test (ordinal measures). Most tests showed moderate to very good assessment reliability (ICC = 0.5-1), intra-rater reliability (ICC = 0.5-1) and good to very good inter-rater reliability (ICC = 0.63-1). Reliability appeared to improve in quantitatively, rather than qualitatively, measured tests. A ceiling effect was noted in some tests maximally scored face-to-face and remotely. This supports the feasibility of remote assessment in clinical practice for people with Parkinson's disease. Research with a larger cohort and adjusted assessments to avoid ceiling effects is necessary.

Poster 7.44

The development of a hydrogel-based ultrasound-triggered delivery system for neurotrophic growth factors

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Growth factors have recently been explored as therapeutic agents for tissue engineering. Neurotrophic growth factors (NF), specifically, have been shown to support and direct the regrowth of nerve cells and have potential for the treatment of a range of disease states and injuries, including spinal cord injuries. However, key challenges in using NFs include their short half-life *in vivo* and their potential for off-target effects. These challenges could be overcome by encapsulation and spatial and temporal targeting of NF delivery. Therefore, a stimuli-responsive hydrogel where release of an active payload is triggered by ultrasound might improve the therapeutic efficacy of NFs. A small, positively-charged model drug (ibuprofen) was loaded into alginate and poloxamer hydrogel drug delivery systems, and different ultrasonic parameters were explored. The release of ibuprofen was compared at low-frequency (24 kHz), high-frequency (1 MHz), and no ultrasound stimulation. The results show that ultrasound stimulation increased ibuprofen release and low-frequency stimulation was the most efficient at triggering release from both hydrogels. Alginate hydrogel was more responsive to ultrasound stimulation than poloxamer hydrogel. In the future, these hydrogel-based ultrasound-triggered delivery systems will be loaded with NFs, and NFs will be released controllably to support the regrowth of nerve cells.

Poster 7.45

Patterned simulation of the chrimson opsin in glutamatergic motor thalamus neurons improves forelimb akinesia in a chronic rat model of Parkinson's disease

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Parkinson's disease (PD) is a motor disorder characterised by altered neural activity throughout the basal ganglia thalamocortical motor circuit. Electrical deep brain stimulation is efficacious in alleviating motor symptoms, but has side-effects, most likely reflecting the non-specific nature of electrical stimulation and/or the brain regions targeted. We determined whether specific optogenetic activation of glutamatergic motor thalamus (Mthal) neurons alleviated forelimb akinesia in a chronic rat model of PD. Parkinsonian rats (unilateral 6-hydroxydopamine injection) were injected with an adeno-associated viral vector (AAV5-CaMKII-Chrimson-GFP) to transduce glutamatergic Mthal neurons with the red-shifted Chrimson opsin. Optogenetic stimulation with orange light at 15 Hz tonic and a physiological pattern, previously recorded from a Mthal neuron in control rat, significantly increased forelimb use in the reaching test ($p<0.01$). Orange light theta-burst stimulation, 15 Hz and control reaching patterns significantly reduced akinesia ($p<0.0001$) assessed by the step test. In contrast, forelimb use in the cylinder test was unaffected by orange light stimulation with any pattern. Blue light (control) stimulation failed to alter behaviours. Activation of Chrimson using complex patterns in the Mthal may be an alternative treatment to recover movement in PD. These vector and opsin changes are important steps towards translating optogenetic stimulation to humans.

Poster 7.46

Aberrant feeding patterns and gene expression in the valproic acid-induced rat model of autism

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A core - yet understudied - symptom of autism in children is a very narrow dietary preference and aberrant food intake. We have observed this trait in our valproic acid-induced (VPA) rat model of autism; our rats display self-inflicted underfeeding of 'bland food', even after food deprivation. They tend to have slightly lower body weight and slower weight gain compared to healthy controls. We also found aberrant c-fos immunoreactivity in the brain areas responsible to govern consummatory behaviour upon energy deprivation in VPA-rats. Furthermore, expression of feeding-related genes remained largely unchanged in response to food deprivation in VPA animals in contrast to several transcripts affected by fasting in the controls. This anomalous hunger processing also encompasses the hedonic aspect of feeding – reward-driven intake is elevated in VPA rats and we observed that these animals consume more sugar than their controls. The feeding behaviour and brain activity patterns respond differentially to relatively lower dosage of oxytocin (OT) as compared to their healthy controls. OT, which is clinically tested to alleviate other symptoms of autism such as social deficits, may be effective to curb overconsumption of sweet tasting palatable foods in the context of autism as well.

Poster 7.47

Assessing the relationship between sub-clinical anxiety and resting state functional connectivity

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Anxiety is a psychological and physiological state characterised by cognitive, physiological, and behavioural components. Although anxiety is a natural adaptive reaction, anxiety disorders differ from healthy anxiety by being excessive or persistent. Whilst anxiety disorders are primarily diagnosed by behavioural properties, neuroimaging can help us to understand the underpinnings of these behaviours. Resting-state functional magnetic resonance imaging (fMRI) measures spontaneous fluctuations in the blood oxygen level-dependent (BOLD) signal. By using the relative temporal changes in the BOLD signal, 'functional connectivity' (rsFC) of spatially distinct brain regions can be investigated. Here, we analysed the relationship between resting-state fMRI scans of 40 healthy individuals and their trait anxiety (STAI-T) and anxiety sensitivity (anxiety related to anxiety symptoms; ASI) scores, to investigate differences in rsFC within a healthy population. Widespread increases in rsFC with greater levels of anxiety were found between amygdala subnuclei (basolateral and centromedial) and regions in the frontal, temporal, occipital and parietal cortex, precuneus, cingulate gyrus, insula, putamen and thalamus. Importantly, significant differences in this connectivity profile were observed between men and women. These results contribute to a better understanding of the neural circuitry involved in anxiety, aiming to improve diagnosis `and treatment of this condition in the future.

Poster 7.48

Valproate usage correlates with changes in brain volumes in ultra-treatment-resistant schizophrenia

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In ultra-treatment-resistant schizophrenia (UTRS), sodium valproate is sometimes prescribed to help relieve residual symptoms. However, the effects of combining valproate and clozapine in those with UTRS are not well understood. There is considerable evidence that mood stabilisers such as sodium valproate can change the brain volumes of people with bipolar disorder, which has a neurological profile similar to schizophrenia. This research investigated the potential impact of combining valproate with clozapine on the brain volumes of people with schizophrenia using magnetic resonance imaging. Four groups of participants were assessed: healthy controls, individuals with schizophrenia responding to first-line medication, individuals with schizophrenia receiving a clozapine monotherapy and those with UTRS who were receiving sodium valproate combined with clozapine. Brain tissue volumes were determined using the FMRIB Software Library to measure differences between groups and identify regions where significant differences existed. Whole brain ($p < 0.05$) and white matter volumes ($p < 0.05$) were overall significantly lower in the group taking valproate compared to controls. This suggests that valproate usage could reduce brain volumes in those with UTRS. These findings may inform clinicians of the effects of their prescription and the understanding of the long-term consequences of a treating UTRS with sodium valproate.

Poster 7.49

Investigating the interaction between HDAC4 and Ankyrin2 in *Drosophila melanogaster* neuronal function: It's not just about physical attraction

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Histone deacetylase 4 (HDAC4) is implicated in several neurodevelopmental and neurodegenerative diseases that involve deficits in memory and cognition. Increased expression of HDAC4 in the *Drosophila* brain impairs neuronal development and memory, thus *Drosophila* is an ideal model to investigate the molecular pathways through which HDAC4 acts. A recent genetic screen in *Drosophila*, for genes that interact in the same molecular pathway as HDAC4, identified the cytoskeletal adaptor Ankyrin2 (Ank2). Knockdown of Ank2 in the brain resulted in deficits in axon morphogenesis (Fisher's, $p < 0.01$) with reduced elongation and guidance defects as well as significantly reduced dendritic branch lengths (Student's t-test, $p < 0.05$), all of which are similar phenotypes to those resulting from increased expression of HDAC4. HDAC4 contains a putative ankyrin-binding motif, suggesting that it may interact physically with Ank2, however no interaction was detected via co-immunoprecipitation. Further investigation revealed that expression of HDAC4 with a mutated ankyrin-binding motif retained the ability to interact genetically with Ank2 to synergistically impair photoreceptor development (ANOVA, $p < 0.01$), furthermore, this genetic interaction was dependent on the presence of HDAC4 in the nucleus. Together these data show that Ank2 and nuclear HDAC4 indirectly interact to regulate neuronal morphogenesis and function.

Poster 7.50

Prediction of tinnitus therapy success using Artificial Intelligence (AI) decision tool

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Tinnitus (ear and head noise) is a highly prevalent condition affecting between 5-20% of the world's population. Tinnitus is strongly associated with mental health and wellbeing. No treatment is currently able to eliminate the perception of tinnitus but reducing its impact through the management of associated depression and anxiety. However, this treatment is complicated by the large variability in tinnitus, and response to treatments, amongst sufferers. This research proposes a new methodology for prediction of patients' response to tinnitus therapies using Artificial Intelligence (AI) techniques and computational modelling algorithms derived from multi-modal sets of data (behavioural and spatiotemporal brain data). Results show that the newly developed AI models differentiate the patients' outcomes into either treatment responder or non-responder with accuracy ranging from 98%–100% and predict the severity of tinnitus indexed by tinnitus scores with error ranging from 2-5. The brain data was related to clinically significant changes in the behavioural data. The results will be further used to improve the AI model toward developing a new personalised predictive model for an early diagnosis/prognosis of an individual response to tinnitus therapy.

Poster 7.51

E2730, a GABA transporter-1 inhibitor, suppresses epileptic seizures in a rat model of chronic drug resistant mesial temporal lobe epilepsy

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One-third of mesial temporal lobe epilepsy (mTLE) patients remain resistant to anti-seizure medications, commonly experiencing adverse effects such as dizziness and motor incoordination. Here, we evaluated the pharmacokinetics and epilepsy outcomes of E2730, a novel uncompetitive GABA-transporter-1 inhibitor, in a rat model of mTLE. Wistar rats received 10, 20 or 100mg/kg/day of E2730 (n=4/group) for one week via osmotic-pumps to determine plasma drug levels and evaluation of any adverse effects. Rats (n=22) underwent kainic acid-induced status epilepticus, and 9 weeks later, randomly assigned to either one of the E2730 doses or vehicle. Video-EEG monitoring was performed for a week. The pumps were then replaced by a different dose and repeated evaluations until animals received all treatments. Plasma E2730 levels were present in a dose-dependent manner. The drug was well-tolerated, with very mild and short-lasting sedation. E2730 in chronically epileptic rats led to significant dose-dependent reduction in seizures (p=0.0006), with 63% rats became seizure-free, compared to 0% in vehicle group (p=0.0001). E2730 led to a dose-dependent suppression of epileptic seizures, without any remarkable neurological adverse effects, in a rat model of chronic drug resistant mTLE, showing strong promise for the mechanism to be translated into clinical trials.

Poster 7.52

Early phase amyloid PET as a surrogate marker of brain metabolism in neurodegenerative disorders

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In vivo neuroimaging techniques visualizing metabolic and cerebrovascular changes are vital in diagnosing many neurodegenerative disorders. The current gold standard, ^{18}F -Fluorodeoxyglucose (^{18}F-FDG) PET imaging, demonstrates regional metabolic deficits associated with particular causes of neurodegeneration, such as Alzheimer's disease and frontotemporal dementias. However, emerging imaging modalities may provide alternatives to ^{18}F-FDG PET with unique advantages. PET radiological tracers binding to pathological proteins, such as amyloid-β (Aβ) and neurofibrillary tau, are increasingly used as molecular biomarkers for diagnosis. While these scans are usually read after ~90 min ("late-phase"), growing evidence suggests that the images acquired immediately after tracer injection provide cerebrovascular information analogous to ^{18}F-FDG PET. Another alternative – Arterial Spin Labelling (ASL)-MRI – non-invasively and quantitatively measures cerebral perfusion, which is closely linked to metabolism. We hypothesized that "early-phase" uptake of an Aβ PET tracer Florbetaben (FBB) would strongly correlate with ^{18}F-FDG and ASL-MRI in individuals investigated for cognitive impairment (n=20). Results from our pilot participant indicate visually striking similarities between early-phase FBB and ^{18}F-FDG, with high correlations between 95 cortical and subcortical structural regions ($r = 0.89$, $p<0.0001$). Validating this early-phase modality will permit simultaneous assessment of pathological protein status and regional brain metabolism, markedly increasing clinical utility.

Poster 7.53

KCC2 expression in the human Alzheimer's disease medial temporal lobe

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Alzheimer's disease (AD) is a neurodegenerative disorder that currently has no cure. Hallmarks of the disease include declining cognitive function and neuronal death in the hippocampus and cerebral cortex. The co-transporters K+–Cl − co-transporter 2 (KCC2) and Na-K-Cl (NKCC1) regulate intracellular chloride levels. Mouse models of AD and other neurological disorders have demonstrated altered neuronal KCC2 and NKCC1 expression that makes GABA, the primary inhibitory neurotransmitter, switch to excitatory resulting in cognitive impairment. The excitatory/inhibitory equilibrium is a delicate feature of the brain that needs to be maintained to avoid pathological consequences. We hypothesize that altered expression of KCC2 in the AD human medial temporal lobe might be a contributing factor to the excitatory/inhibitory balance disruption and cognitive deficit observed. We quantified KCC2 density in the hippocampus, subiculum, entorhinal cortex, and superior temporal gyrus (STG) of healthy and AD post-mortem human brains by using free-floating fluorescent immunohistochemistry and confocal laser-scanning microscopy. We detected significant downregulation of KCC2 levels in the STG when comparing control healthy cases to AD cases, suggesting a disturbed excitatory/inhibitory balance in this brain region. Other brain regions examined showed no altered KCC2 expression. These findings could provide a possible novel avenue of treatment for AD.

Poster 7.54

Inducing traumatic brain injury in human pericytes using dielectric elastomer actuators

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Traumatic brain injury (TBI) is an external force that damages brain tissue. Worldwide 69 million people experience it annually with NZ having the highest incidence in the developed world. To investigate the underlying mechanism of TBI, we developed an injury model using dielectric elastomer actuators (DEA). DEAs are devices with fast response times and produce high strain, ideal for mimicking TBI. When connected to a power supply, the electrodes' attraction to each other causes a deformation of the elastomer layer, resulting in a mechanical strain. Pericytes are mural cells found ubiquitously throughout the brain that are important for maintaining homeostasis and supporting blood-brain barrier integrity. Evidence suggest pericytes are involved in brain scarring, a consequence of TBI that becomes a barrier to full recovery. We modelled TBI by plating the pericytes isolated directly from the human brain onto the DEAs and caused injury through rapid bursts of strain that exceeded 20%. Several key markers associated with pericyte injury and scarring were found to be upregulated, and we are currently investigating the significance of these changes in modelling TBI. The results demonstrate the validity of using DEAs as an injury model to damage primary human cells to recapitulate TBI *in vitro*.

Poster 7.55

40Hz sensory entrainment impedes kindling epileptogenesis

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Sensory stimulation is a novel, non-invasive method to induce gamma oscillations. One hour of 40Hz audio-visual stimulation entrains gamma rhythms and increases microglial phagocytic clearance of amyloid-beta (Aβ) peptide in 5XFAD mice, a mouse model of Alzheimer's disease associated with rapid Aβ accumulation which also display susceptibility to epilepsy. Here, we aim to test whether 40Hz entrainment can improve the inherent sensitivity to epilepsy of 5xFAD mice. 5xFAD mice and wild-type littermates receive 1hr/day 40Hz audio-visual stimulation or sham 1hr/day dark box, beginning two weeks before and continuing through an electrical amygdala kindling protocol. Kindling consists of electrical stimulation at pre-determined seizure threshold current, once per day, until five convulsive (class V) seizures. 40Hz entrainment reduced sensitivity to epilepsy by increasing the number of stimulations required to reach five class V seizures ($p = 0.0164$). 5xFAD mice required significantly less stimulations to reach the first convulsive seizure ($p = 0.0004$), and five class V seizures ($p = 0.0001$). To conclude, we report a novel finding whereby 40Hz entrainment slows the rate of kindling epileptogenesis. The 5xFAD mice consistently showed enhanced kindling. Since 40Hz entrainment slows kindling in both genotypes, the therapeutic underpinnings of 40Hz entrainment to epilepsy requires further investigation.

8.1

Autism spectrum disorder: Understanding the impacts of SNPs on biological pathways in the human fetal and adult cortex

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by significant and complex genetic etiology. Genome-wide association studies (GWAS) have identified hundreds of genetic variants associated with ASD. However, the majority of these variants are non-coding, and the mechanisms by which these variants can influence the development of ASD remain poorly defined. In this study, we integrated four distinct levels of biological information (GWAS, gene expression, spatial genome organization and protein-protein interactions) to identify potential regulatory impacts of ASD-associated variants on biological pathways within human fetal and adult cortical tissues. We found 80 and 58 regulatory variants in the fetal and adult cortex, respectively. Functional annotation of these variants revealed significant enrichment within regions repressed by Polycomb proteins in the fetal cortex compared to the adult cortex. Further protein-protein interaction and pathway analyses identified the impacts of these variants on immune pathways, fatty acid metabolism, ribosome biogenesis, aminoacyl-tRNA biosynthesis and spliceosome in the fetal cortex. By contrast, in the adult cortex, variants primarily impact immune pathways. Collectively, our findings highlight potential regulatory mechanisms and pathways through which ASD-associated variants can contribute to the development and maintenance of ASD. Our integrative approach can contribute to an individualized mechanistic understanding of ASD.

8.2

Deep-learning-based automated infant movement tracking scheme for early diagnosis of neurodevelopmental disorders

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Abnormal neonatal General Movements (GMs) during 6-20 weeks of age are strong predictors of whether an infant is at-risk of developing cerebral palsy (CP). Current protocols for manual GM scoring is time-consuming and human resource intensive, requires specialist training, and does not scale to wider application. In this work, we developed a robust markerless pose-estimation scheme, based on advanced deep-learning technology, to automatically track neonatal GMs in standard iPad video recordings. Video recordings from 6 infants (2-5 months) were used to assess generalization of learning. 12 anatomical locations (3 per limb) were manually labelled in 2000 frames from 5 infants to shape the training set (total of 24,000 points). A Resnet152 deep-neural-network was trained using the annotated data. The network's performance was then tested on the entire video from the 6th infant (train/test ratio: 19:1). Validation results demonstrated generalization feasibility with exceptional accuracy of 98.84% in tracking body-parts in the novel data, calculated from the sensitivity and selectivity measures of >99.86% and 97.93%, respectively, associated with <10 false-negatives and 153 false-positives. Our preliminary results indicate the possibility of establishing a fully automated platform for accurate analysis of neonatal GMs, for early diagnosis of neurodevelopmental disorders (including CP) in early infancy.

8.3

Knockdown of specific hyaluronan synthases inhibits neurite development in hippocampal neurons *in vitro*

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The brain's extracellular matrix (ECM) provides key structural and functional support to neurons. Hyaluronan is a major component of the developing brain's ECM, and is synthesised by the family of hyaluronan synthases (HAS1–3). Our lab previously demonstrated that developing neurons express functional HAS2 and HAS3 enzymes *in vitro*. However, the role of HAS enzymes and hyaluronan in neurodevelopment remains unclear. This study examined the effects of HAS2 or HAS3 knockdown on the morphological development of immature hippocampal neurons *in vitro*. Knockdown was achieved using short hairpin loop RNA (shRNA)-based interference of protein translation. Primary hippocampal neuron cultures were established from E18 rat embryos. Neurons were transfected at days *in vitro* 0 (DIV0; 2 hr) using Lipofectamine 3000 with shHAS2, shHAS3, and scrambled controls. To quantify changes in HAS protein and hyaluronan expression, cells were fixed at DIV7 for immunocytochemistry with HAS2–3 antibodies and hyaluronic acid binding protein. For morphological analyses, transfected cells were live-imaged at DIV7 and traced with Neurolucida software. Results suggest that HAS2 and HAS3 knockdown reduced HAS protein and hyaluronan expression, and reduced neurite outgrowth and complexity. Overall, these findings suggest that hyaluronan synthesis by developing hippocampal neurons is important for control of neurite extension.

8.4

The hyaluronan cornerstone: An extracellular matrix molecule that regulates early neurite outgrowth in hippocampal neurons

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The targeted outgrowth of axons and dendrites is a key event in hippocampal development. An early dysregulation of this neurite growth can initialise hippocampal circuit defects, as seen in a range of neurodevelopmental disorders. However, the underlying mechanisms remain unclear. This study aims to understand the contribution of the extracellular matrix in regulating neurite outgrowth, with a focus on the early expression of the polysaccharide hyaluronan. Hippocampal neuron cultures (from E18 rats), were used for high-resolution immunocytochemistry and live–imaging analyses. Cytoskeletal dynamics were resolved with total internal reflection fluorescence (TIRF)–microscopy. Hyaluronan was detected from the early stages of development on soma, neurites and 'growth-cone' tips of hippocampal neurons. Its close spatial proximity with hyaluronan synthase (HAS 2–3) enzymes and the CD44 hyaluronan receptor suggests a local synthesis and signalling unit. Pharmacological inhibition of HASes (4-methylumbelliferone, 300µM) accelerated the early outgrowth of the putative axon (24–48 hr). This effect was associated with slowed F-actin trafficking to the growth cone, but interestingly, a facilitation of neurite consolidation and elongation. Hyaluronan–signalling is known to regulate cytoskeletal dynamics in fast-growing cells (e.g. cancers). Our novel neuronal data suggest that the cornerstorne deposition of hyaluronan regulates early hippocampal neurite outgrowth.

9.1

A pathogenic PINK1 gene variant is a common cause of early-onset Parkinson's disease in people of Western Polynesian ethnicities

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Two unrelated patients with early-onset Parkinson's disease (EOPD), one Samoan, one Tongan, were found to be homozygous for a rare pathogenic *PINK1* variant, NM_032409.3(*PINK1*):c.1040T>C p.(Leu347Pro). This observation led us to ask: is *PINK1*:c.1040T>C variant a common cause of EOPD in Western Polynesian and Eastern Polynesian patients? The *PINK1* gene of 23 unrelated EOPD patients was sequenced; patients included two Eastern Polynesian (Māori) and 21 Western Polynesian (Samoan, Tongan and Tokelauan) people. Of the latter group, 17 were homozygous for *PINK1*:c.1040T>C, while one was compound heterozygous; the two Māori patients were wildtype for *PINK1*. *PINK1*:c.1040T>C carrier-rates in control populations are as follows: NZ Western Polynesian (n=137), 1 in 20; NZ Eastern Polynesian (Māori, n=126), 1 in 126; Samoan (part of Western Polynesia, n=1285), 1 in 16; Hawaiian (part of Eastern Polynesia, n= 4150) 1 in 143 (imputed with R^2 of 0.76). In conclusion we report that *PINK1*:c.1040T>C homozygosity is a common cause of EOPD in patients of Western Polynesian ethnicities. Western Polynesian patients with EOPD should be tested for *PINK1* variants; if gene positive, family members can be referred to Genetic Services. Further research into the ancestral Pacific origin of this variant, patient impact and targeted therapies is ongoing.

9.2

Development of miniaturised microscope imaging in freely behaving rats to examine cortical plasticity following spinal cord injury

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Neuronal imaging in freely moving animals has become a key tool for a better understanding of how the central nervous system processes information. We are currently developing the use of head-mounted microscopes (UCLA Miniscope) to monitor cortical changes following spinal cord injury in rats. The miniscope allows the study of neural activity and network function during dynamic behaviour in unrestrained rodents. This is achieved through calcium imaging, using genetically encoded calcium indicators (GCAMP), which acts as a neuronal activity indicator. To optimize GCAMP expression in the rat cortex we varied adeno-associated viral (AAV) vector volume, dilution, injection rate and depth. We found that cortical injection of AAV lead to inconsistent GCAMP expression, damage to the cortex, and increased inflammation. To overcome this a novel injection method, transverse sinus injection, has been adopted. This successfully allows for homogenous expression of GCAMP, with no cortical damage. Data will be presented demonstrating transverse sinus injection allows chronic *in vivo* imaging of neurons in restrained and unrestrained rats. We are now applying this technology to investigate the dialog between the motor cortex and spinal cord following spinal cord injury.

9.3

Modelling thalamocortical circuitry shows that visually induced LTP changes laminar connectivity in human visual cortex

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Long-term potentiation (LTP) is a key mechanism of neuroplasticity that has been studied extensively in non-human animals. Translation to human application largely relies on the validation of non-invasive measures of LTP. The current study presents a generative thalamocortical computational model of visual cortex that can be applied to electroencephalography (EEG) recordings of a visual based LTP task in humans to investigate interlaminar connectivity changes. The study implemented a canonical neural-mass model of visual cortex and thalamic input connectivity. The model was combined with a visual LTP paradigm and fit to EEG data using dynamic causal modelling. Twenty recordings provided the in vivo validation data. The thalamocortical model demonstrated remarkable accuracy recapitulating post-tetanus changes seen in invasive research, including increased excitatory connectivity from thalamus to layer IV ($F_{(2,54)}$=6.079, p=0.015FDR) and from layer IV to II/III ($F_{(2,54)}$=22.36, p=4.203e-6FDR), established major sites of LTP in visual cortex. The results also demonstrated specificity to the input stimulus. These findings provide justification for the implementation of the presented thalamocortical model for non-invasive human sensory induced LTP research. Future applications include translating and replicating invasive non-human animal findings concerning deficits to LTP that may underlie neurological and psychiatric disease.

9.4

Progress towards developing a novel model of parkinsonism based on the dopamine transporter knockout (DAT-KO) rat

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Dopamine (DA) neurotransmission is tightly regulated by the dopamine transporter (DAT). DAT expression/activity is reduced in several neurological disorders including Parkinson's disease (PD), and after exposure to drugs of abuse. Our aim was to characterise changes in DA neurotransmission in the DAT- KO rat we created using CRISPR/cas9 technology, and to exploit this mutant to produce a novel animal model of PD. The experiments were conducted *in vivo* and in brain slices. DAT-KO rats which we have generated are profoundly hyperactive, have an elevated basal extracellular DA levels and display a very slow DA clearance after electrically-evoked release both in the dorsal striatum and Substantia Nigra *pars compacta* (SNc). DA precursor L-DOPA produced a larger increase in tonic DA levels than in control (WT) rats, which was further potentiated by blocking monoamine oxidase. Despite increased extracellular DA levels, robust pacemaker firing (~2Hz) exhibited by SNc neurons was retained in brain slices from DAT-KO rats. Inhibiting tyrosine hydroxylase with alpha-methyl-*p*-tyrosine (AMPT) reduced basal and stimulated extracellular DA levels, and lead to bradykinesia. Thus, DAT-KO rats treated with AMPT provide a novel, reversible model of parkinsonism which can be utilised to test new therapeutic strategies for PD.

10.1

Predicting children's general intelligence through multimodal brain-based models

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Childhood intelligence is strikingly predictive of key future life outcomes, but we remain ignorant about its brain involvement. We address this gap by developing a novel predictive-modelling approach, leveraging the unique power of the large-scale, longitudinal, multimodal MRI data from the Adolescent Brain Cognitive Development (ABCD) study (n ~11k). Our models combine six MRI modalities (task-fMRI from three tasks, resting-state fMRI, structural MRI, DTI) using machine-learning algorithms: Elastic Net, Random Forest and Opportunistic Stacking. We examine the value of our brain-based models in three steps. First, we show that brain-based models are predictive. They achieve an unprecedented longitudinal association (r=.41) with childhood intelligence across two years in unseen data. Second, we demonstrate the interpretability of the models. Using permutation-based inference, we found fronto-parietal networks during a working-memory task to drive childhood-intelligence prediction. Finally, we illustrate the explanatory value of these models. The models significantly explain the variance of childhood intelligence due to (1) key socio-demographic and psychological and (2) genetic factors. In summary, our work shows that novel models of human multimodal neuroimaging data are powerful in helping us predict and understand childhood intelligence.

10.2

Volitional suppression of parkinsonian resting tremor: A role for the limbic system in modulating tremor-related activity in the striatopallidal motor circuit

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We have previously reported that patients with Parkinson's disease (PD) can suppress their resting tremor at will, for brief periods, using conscious mental processes and muscular relaxation. This volitional suppression of tremor modulated key neurophysiological tremor characteristics without altering tonic muscle activity, however, the underlying neural mechanisms remain unclear. We used fMRI to examine changes in brain activity associated with conscious tremor suppression together with accelerometry to measure tremor oscillations in the most-affected hand of 35 tremulous PD patients (on-medication). Participants completed sixteen 1-minute trials, consisting of alternating consecutive 30-second periods of resting tremor and 30-seconds of attempted tremor suppression. In 25 patients showing prominent tremor during the resting period, attempted tremor suppression reduced tremor amplitude (peak power) and increased the frequency of tremor oscillation. This suppression (contrasted with tremor at rest) was associated with increased activity in the putamen, anterior cingulate and orbitofrontal cortices, supplementary motor area, and cuneus. These data indicate engagement of corticostriatal circuitry during volitional suppression of tremor. Involvement of frontocortical regions implicated in motivational processes, cognitive control, and action monitoring may indicate an important role for these limbic areas in top-down modulation of striatopallidal output, that my interfere with tremor circuitry, thereby diminishing tremor impact.

10.3

Zebrafish on "P": Behavioural effects of methamphetamine

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This study is our first attempt to document the behavioural effects of methamphetamine in zebrafish (*Danio rerio*), a species that has gained incredible momentum in the study of neurological disorders. The fish (n=7-10) were first immersed into a 200 ml beaker containing 100 ml methamphetamine (0.01-3.0 mg/l) or water for 10 min. After the exposure they were transferred to a 1 l tank. Various aspects of swimming behaviour were measured in 5-min intervals during a 50-min test. Exposure to low concentrations of methamphetamine (0.01, 0.03 mg/l) failed to produce significant changes in any of the measures. Exposure to the 0.3 mg/l concentration produced decreased swimming in the bottom of the tank and increased swimming in the middle of the tank, suggesting an anxiolytic effect. Exposure to this concentration and to the lower concentration of 0.1 mg/l also increased the number of transitions along the outside edges of the tank. Higher doses decreased most measures and swimming was almost exclusively in the bottom of the tank, suggesting an anxiogenic effect. These data provide initial indications of behaviourally effective doses of methamphetamine in zebrafish that will guide future studies.

10.4

Thalamic paraventricular nucleus: Bridging homeostatic and reward pathways in the control of feeding

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Food intake is modulated by metabolic state and food reward. The thalamic paraventricular nucleus (PVT) may be a key node integrating these controls. PVT receives afferents from hypothalamic arcuate nucleus (ARC), which responds to peripheral hormones signalling metabolic state, and projects to the nucleus accumbens (nAcc), important in reward-seeking behaviour. To investigate the role of PVT in linking these pathways, we injected male rats with a viral vector (AAVrg-Syn-ChR2(H134R)-GFP) to retrogradely label either ARC-to-PVT or PVT-to-nAcc projection neurons. Fasted ARC-PVT-labelled rats received a s.c. leptin injection and were perfused 90 min later. Immunohistochemical labelling for GFP and pSTAT3 (downstream activation marker for leptin) revealed PVT-projecting neurons in all ARC sub-regions, while GFP-pSTAT3 co-localization was only found in medial and lateral ARC. PVT-nAcc-labelled rats underwent a 30-min conditioning session in which a light cue either predicted food reward (signaled-reward) or had no temporal association with food (control group). Tissue was collected 30 min later and stained for GFP and cFos (indirect marker of neuronal activation). Results showed significantly more cFos-labelling in PVT overall, and in neurons projecting to nAcc, in signaled-reward rats compared to controls. These results confirm that PVT may integrate metabolic and reward-signal learning to influence food consumption.