2021

AWCBR

Australasian Winter Conference on Brain Research

AWCBR 2021

Neurological Foundation

A pathway to hope

Sunday 29 August 2021

3.30 pm-6.00 pm		REGISTRATION, CROWNE PLAZA HOTEL
3.00 pm-5.00 pm		BRNZ WĀNANGA, MĀORI DELEGATES, *please register with BRNZ* at chelseacunningham23@gmail.com
6.00 pm		OPENING RECEPTION, CASH BAR AND LIGHT FOOD, Atrium
7.00 pm		OPENING REMARKS

7.15 pm 1. PLENARY LECTURE:

CHAIR: RUTH EMPSON

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

Environmental determinants of obesity

---

2. Disorders of the Nervous System

CHAIR: BRIGID RYAN

8.00 pm	2.1	**Blake Highet, *University of Auckland, Auckland, New Zealand*** Altered expression of PSA-NCAM regulatory genes in Alzheimer's disease detected using spatial transcriptomics
8.15 pm	2.2	**Emma Scotter, *University of Auckland, Auckland, New Zealand*** Building the New Zealand motor neuron disease genetics study
8.30 pm	2.3	**Jiaxian Zhang, *University of Otago, Dunedin, New Zealand*** Maternal immune activation affects behavioural function, neurochemistry and microglia in juvenile rat offspring
8.45 pm	2.4	**Maize Cao, *University of Auckland, Auckland, New Zealand*** Identifying TDP-43 loss-of-function markers in amyotrophic lateral sclerosis with human derived brain pericytes
9.00 pm	2.5	**Caitlin Oyagawa, *University of Auckland, Auckland, New Zealand*** Investigating the mechanisms of cardiac glycosides as modulators of barrier inflammation

8.15 am Coffee/tea

8.30 am

3. PLENARY LECTURE:

CHAIR: STEPHANIE HUGHES

Li-Huei Tsai, *Massachusetts Institute of Technology, Cambridge, United States of America*

Uncovering the role of Alzheimer's disease risk genes using stem cells and human brains

4. Development

CHAIR: SIMON O'CARROLL

9.15 am	4.1	**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	4.2	**Molly Abraham, *University of Auckland, Auckland, New Zealand*** Knockdown of specific hyaluronan synthases inhibits neurite development in hippocampal neurons *in vitro*
9.45 am	4.3	**Evgeniia Golovina, *University of Auckland, Auckland, New Zealand*** Autism spectrum disorder: understanding the impacts of SNPs on biological pathways in the human foetal and adult cortex
10.00 am	4.4	**Maryam Tayebi, *University of Auckland, Auckland, New Zealand*** The subcortical structures of contact-sport players' brains show significant differences when compared to the age-matched control group

10.15 am Morning tea available

5. Novel Methods and Technology

CHAIR: VICTOR DIERIKS

10.45 am	5.1	**Indranil Basak,** ***University of Otago, Dunedin, New Zealand*** Loss of Batten disease associated CLN5 leads to neuronal lysosomal defects, and impaired neurogenesis in induced pluripotent stem cell-derived human neurons
11.00 am	5.2	**Samuel McCullough,** ***University of Auckland, Auckland, New Zealand*** Development of an iPSC-derived model of brain pericytes to investigate their role in blood-brain barrier function and neuroinflammation
11.15 am	5.3	**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
11.30 am	5.4	**Sophie Farrow,** ***University of Auckland, Auckland, New Zealand*** Establishing gene regulatory networks from Parkinson's disease risk loci

6. Poster Session

Light lunch available

11.45 am-1.45 pm

Presenters with odd numbers should put up their posters by 8.00 am and be in attendance from 11.45 am-12.45 pm. Please remove your poster by 1.45 pm to allow the next person to use your board.

Presenters with even numbers should put up their posters at 8.00 am and be in attendance from 12.45-1.45 pm. Please remove your poster by 1.45 pm to allow the next person to use your board.

6.1 **Mackenzie Ferguson,** ***University of Auckland, Auckland, New Zealand***
mHTT aggregates and neuroinflammation in the Huntington's disease midcingulate cortex

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

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

6.4 **Ashly Jose,** ***University of Auckland, Auckland, New Zealand***
Design and development of multiscale microscopic imaging systems for neuroscience applications

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

6.6 **Brad Raos,** ***University of Auckland, Auckland, New Zealand***
Stretchable multi-electrode arrays for measuring electrical activity in an *in vitro* model of neural injury

6.7 **Bria Pengelly,** ***Victoria University of Wellington, Wellington, New Zealand***
Exploring the augmented cuprizone model of demyelination

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

6.9 **Bruce Harland, *University of Arizona, Tucson, United States of America***
Hippocampal place cells form a multi-scale representation of megaspace

6.10 **Connor Clemett, *University of Auckland, Auckland, New Zealand***
Transcriptomic analysis of the contusive spinal lesion reveals the digestion of the inhibitory matrix scar to impact the immunological profile and potential of remyelination therapies

6.11 **Catherine Webb-Robinson, *University of Auckland, Auckland, New Zealand***
The influence of insulin resistance on PSA-NCAM load in the entorhinal cortex

6.12 **David Moreau, *University of Auckland, Auckland, New Zealand***
A principled approach to consider theory in the evaluation of empirical findings

6.13 **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

6.14 **Donisha Liyanagamage, *University of Waikato, Hamilton, New Zealand***
High glucose induces upregulation of mitochondrial stress protein HSP60 in human cortical neuron cells and potential modulation of neuroinflammation by *Macropiper excelsum*

6.15 **Shane Ohline, *University of Otago, Dunedin, New Zealand***
Immediate early gene expression and intrinsic excitability are not linked in adult-born hippocampal neurons

6.16 **Eryn Kwon, *University of Auckland, Auckland, New Zealand***
Analysis and visualisation of physiological changes before and after a mild traumatic brain injury using amplified, 4D flow, and diffusion MRI

6.17 **Oluwatobi Eboda, *University of Otago, Dunedin, New Zealand***
ATP13A2: Characterization of a novel human IPS cell model of Batten and Parkinson’s disease

6.18 **Katie Peppercorn, *University of Otago, Dunedin, New Zealand***
Secreted amyloid precursor protein alpha affects the transcriptome of IPSC derived human cortical neurons

6.19 **Finbar Argus,** ***University of Auckland, Auckland, New Zealand***
A model predictive control method for simulating the sympathetic/parasympathetic control of the circulatory system

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

6.21 **Yewon Jung,** ***University of Auckland, Auckland, New Zealand***
Dietary Zinc supplementation rescues autism-associated behaviours and synaptic deficits in the Tbr1 haploinsufficiency mouse model of autism spectrum disorders

6.22 **Julia Plank,** ***University of Auckland, Auckland, New Zealand***
The validity of magnetic resonance spectroscopy combined with echo-planar spectroscopic imaging for the measurement of human neuroinflammation

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

6.24 **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

6.25 **Jena Macapagal Foliaki,** ***University of Auckland, Auckland, New Zealand***
The upregulation of SMAD2/3 signalling in GBM stromal cells in response to inflammatory stimuli

6.26 **Jessica Crockett,** ***University of Auckland, Auckland, New Zealand***
The role of glia in the Parkinson's disease striatum

6.27 **Jennifer Hamilton,** ***University of Canterbury, Christchurch, New Zealand***
Non-spatial memory and the anterior thalamic nuclei

6.28 **Joseph Chen,** ***University of Auckland, Auckland, New Zealand***
Scopolamine: A potential new pharmacotherapy for depression?

6.29 **Kyla-Louise Horne,** ***New Zealand Brain Research Institute (NZBRI); University of Otago, Christchurch, New Zealand***
Parkinson's disease non-motor symptoms did not worsen during COVID-19 lockdown

6.30 **Miriam Rodrigues,** ***Auckland City Hospital, Auckland, New Zealand***
Pūnaha Io: The New Zealand NeuroGenetic Research Bank

6.31 **Ruben Vergara,** ***University of Otago, Dunedin, New Zealand***
Ryanodine Receptor: The next target for Alzheimer's disease

6.32 **Katherine Witt,** ***Victoria University of Wellington, Wellington, New Zealand***
The role of the dopamine D1 receptor in the negative symptoms of schizophrenia

6.33 **Eileen Luders,** ***University of Auckland, Auckland, New Zealand***
Postpartum changes of the amygdala

6.34 **Jerram Sheehan,** ***University of Auckland, Auckland, New Zealand***
Understanding the expression of oligodendrocyte-specific ADAMTS4 following an SCI and its role as a potential modulator of oligodendrocyte maturation

6.35 **Miran Mrkela,** ***University of Auckland, Auckland, New Zealand***
Whodunnit: Inferring ALS Genotype from archival tissue

6.36 **Kate Godfrey,** ***University of Auckland, Auckland, New Zealand***
Decreased salience network fMRI functional connectivity following a course of repetitive transcranial magnetic stimulation for treatment-resistant depression

6.37 **Natasha Lust,** ***University of Auckland, Auckland, New Zealand***
The role of CD44 in neurodevelopment: Interactions with hyaluronan during neurite outgrowth within the rat hippocampus

6.38 **Nikita Lyons,** ***University of Otago, Dunedin, New Zealand***
A bad influence: Do glia with defective lysosomes harm healthy neurons?

6.39 **Luke Phillips,** ***University of Otago, Dunedin, New Zealand***
RyR2 trafficking and its role in Alzheimer's disease

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

6.41 **Richard Roxburgh,** ***University of Auckland, Auckland, New Zealand***
The University of Auckland, Centre for Brain Research, Neurogenetics Research Clinic: An opportunity for translational research collaboration

6.42 **Sahir Hussain,** ***Victoria University of Wellington, Wellington, New Zealand***
Paternal alcohol consumption causes reduced sensitivity to the motor coordination deficits of ethanol in offspring

6.43 **Sheein Hong,** ***Victoria University of Wellington, Wellington, New Zealand***
Evaluation of evoked versus non-evoked behavioural responses in a preclinical model of demyelination mimicking multiple sclerosis

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

6.45 **Shruthi Sateesh,** ***University of Otago, Dunedin, New Zealand***
Mechanisms of astrocyte-mediated regulation of synaptic plasticity in the hippocampus

6.46 **Skylar Pollack,** ***University of Auckland, Auckland, New Zealand***
Measuring hippocampal activity in conjunction with behaviour utilising head-mounted miniaturised microscopes

6.47 **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

6.48 **Susan Li,** ***University of Auckland, Auckland, New Zealand***
Investigating platelet-derived growth factor signalling in primary human brain cells for elucidation of physiological function and GBM disease mechanism

6.49 **Phoebe Anscombe,** ***University of Auckland, Auckland, New Zealand***
Preparation of human brain tissue for studies of neurodegenerative diseases

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

6.51 **Thulani Palpagama,** ***University of Auckland, Auckland, New Zealand***
Microglial and astrocytic changes in the human cingulate cortex in Huntington's disease

6.52 **Kristina Wiebels,** ***University of Auckland, Auckland, New Zealand***
Dense sampling to enable precision mapping in systems neuroscience

6.53 **Victoria Hawkins,** ***University of Auckland, Auckland, New Zealand***
Development of a large animal model of Fragile X syndrome for therapeutic testing

6.54 **Rashi Karunasinghe,** ***University of Auckland, Auckland, New Zealand; Marine Biological Laboratory, Woods Hole, United States of America***
The hyaluronan cornerstone: An extracellular matrix molecule that regulates early neurite outgrowth in hippocampal neurons

6.55 **Wei Jun Tan,** ***Massey University, Palmerston North, New Zealand***
Investigating the subcellular roles of *HDAC4* in *Drosophila* neuronal development

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

7. Symposium: Brain Tumours: From Neurosurgery to Research

CHAIR: THOMAS PARK

2.45 pm	7.1	**Edward Mee,** ***University of Auckland, Auckland, New Zealand*** Excising the lesion: A history of surgery for brain tumours in New Zealand
3.00 pm	7.2	**Thomas Park,** ***University of Auckland, Auckland, New Zealand*** Finding the NEURO in neuro-oncology
3.15 pm	7.3	**Tania Slatter,** ***University of Otago, Dunedin, New Zealand; Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand*** Ultrasmall superparamagnetic iron oxide MRI to distinguish brain tumours with a high-content of tumour associated macrophages
3.30 pm	7.4	**Scott Graham,** ***Centre for Brain Research; University of Auckland, Auckland, New Zealand*** Glioblastoma's incredible ability to suppress and evade anti-tumour immunity: How does glioblastoma do it?
3.45 pm	7.5	**Melanie McConnell,** ***Malaghan Institute of Medical Research; Centre for Biodiscovery; Victoria University of Wellington, Wellington, New Zealand*** Mechanisms of therapy resistance in glioblastoma

8. Poster Session

Afternoon tea available

4.00 pm-6.00 pm

Presenters with odd numbers should put up their posters by 1.45 pm and be in attendance from 4.00 pm-5.00 pm.

Presenters with even numbers should put up their posters at 1.45 pm and be in attendance from 5.00 pm-6.00 pm.

All posters to be removed ay 6.00 pm.

8.1 **Anusha Dravid,** ***University of Auckland, Auckland, New Zealand***
Towards an *in vitro* model to investigate the effects of neurotrophic gradients on neuronal cells

8.2 **Oliver Wood,** ***University of Auckland, Auckland, New Zealand***
EAAT2 expression in the Alzheimer's disease hippocampus, subiculum, entorhinal cortex and superior temporal gyrus

8.3 **Panzao Yang,** ***University of Auckland, Auckland, New Zealand***
Connexin hemichannel mimetic peptide attenuates cortical interneuron loss and perineuronal net disruption following cerebral ischemia in near-term foetal sheep

8.4 **Alina Tetereva,** ***University of Otago, Dunedin, New Zealand***
Task-based fMRI activation predicts intelligence better than resting-state functional connectivity and structural MRI

8.5 **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

8.6 **Kevin Lee,** ***University of Auckland, Auckland, New Zealand***
Dietary zinc supplementation partially rescues autism-associated behavioural deficits but not synaptic dysfunction in Shank2 knock-out mice

8.7 **Brittany Scouller,** ***Victoria University of Wellington, New Zealand***
Evaluating the effects of novel mixed opioid agonists on respiratory depression

8.8 **Henry Chafee,** ***Victoria University of Wellington, Wellington, New Zealand***
The therapeutic efficacy of psilocybin in a rodent model of depressive- and anxiety-like symptomology

8.9 **Kelly Paton,** ***Victoria University of Wellington, Wellington, New Zealand***
The Salvinorin A analogue, EOM Salvinorin B, promotes remyelination in preclinical models of multiple sclerosis

8.10 **Kirstin McDonald,** ***University of Otago, Dunedin, New Zealand***
Stepping outside the cell: Establishing the secretome as a marker of CLN6 Batten Disease

8.11 **Sahan Jayatissa,** ***University of Auckland, Auckland, New Zealand***
A high throughput *in vitro* platform for traumatic brain injury: A stretchy solution

8.12 **Conor Nelson,** ***University of Auckland, Auckland, New Zealand***
Characterisation of a novel transcription regulation system: Optimising gene therapy in the central nervous system

8.13 **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

8.14 **Florence Layburn,** ***University of Auckland, Auckland, New Zealand***
Immunohistochemical mapping of huntingtin protein distribution using human brain tissue microarrays

8.15 **Florian Kurth,** ***University of Auckland, Auckland, New Zealand***
Long-term meditators show reduced age-related grey matter loss in areas of the subgenual cingulate cortex

8.16 **Dympna Mulroy,** ***Auckland City Hospital, Auckland, New Zealand***
The New Zealand motor neurone disease registry: Four years on

8.17 **Elizabeth Cooper,** ***University of Auckland, Auckland, New Zealand***
Overexpression of nutrient transporters for targeted drug-delivery of anti-cancer agents: Conjugation with heptamethine cyanine dyes

8.18 **Gurleen Singh,** ***University of Auckland, Auckland, New Zealand***
Emergence of functional connectivity networks on a brain-inspired spiking neural network model

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

8.20 **Ieuan Sargent, *University of Auckland, Auckland, New Zealand***
Blood-brain barrier pathology in the Huntington's disease human brain

8.21 **Helen Murray, *University of Auckland, Auckland, New Zealand; National Institutes of Health, Bethesda, United States of America***
Multiplex immunohistochemistry and spatial proteomic analysis of the human olfactory bulb in Alzheimer's and Parkinson's disease

8.22 **Isabella Lavas, *University of Auckland, Auckland, New Zealand***
Optogenetic modulation of beta amyloid-induced brain network changes in the mouse hippocampus

8.23 **James Wiseman, *University of Auckland, Auckland, New Zealand***
Identification and characterisation of distinct α-synuclein strains in different human α-synucleinopathies

8.24 **Janet Boyu Xu, *University of Otago, Dunedin, New Zealand***
Development of a unique set of human neuron knockdown models of Batten disease using human CRISPRi in derived neurons

8.25 **Zoe Woolf, *University of Auckland, Auckland, New Zealand***
Mapping the myeloid landscape of glioblastoma tumours

8.26 **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

8.27 **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

8.28 **Kaaryn Cater, *Whitireia Weltec, Wellington, New Zealand***
Environmental Sensitivity and its impact on learning for higher education students

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

8.30 **Suresh Muthukumaraswamy, *University of Auckland, Auckland New Zealand***
Identification of treatment-specific biomarkers in mood disorder research: The problem of placebo variance

8.31 **Joan Chan, *University of Otago, Dunedin, New Zealand***
The effect of S107 on RyR2 clustering in AD-like neuronal cells

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

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

8.34 **Lysea Haggie, *University of Auckland, Auckland, New Zealand***
A spiking neural network model of motor cortex circuits and responses to TMS simulation

8.35 **Jasmine Lock, *University of Otago, Dunedin, New Zealand***
Combined effects of cannabidiol oil and gene therapy in a mouse model of Batten disease

8.36 **Lucia Schweitzer, *University of Otago, Dunedin, New Zealand***
Human brain cells derived from iPSCs – applications, tools and opportunities

8.37 **Victor Birger Dieriks, *University of Auckland, Auckland, New Zealand***
Stopping Parkinson's disease: Are 'strains' the solution?

8.38 **Rabia Bibi, *Victoria University of Wellington, Wellington, New Zealand***
Evaluating the use of primary mouse glial cultures to model oligodendrocyte maturation as a screening tool to identify drugs that promote remyelination

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

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

8.41 **Pablo Ortega-Auriol,** ***University of Auckland, Auckland, New Zealand***
Muscle synergy expression is influenced by motor impairment after stroke and task context

8.42 **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

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

8.44 **Molly Swanson,** ***University of Auckland, Auckland, New Zealand***
Spatial relationship between microglial activation and pathological TDP-43 deposition in Amyotrophic Lateral Sclerosis

8.45 **Abby Sabrini,** ***University of Auckland, Auckland, New Zealand***
Reward and loss anticipation during ambiguous risk

8.46 **Soo Kim,** ***University of Auckland, Auckland, New Zealand***
Optogenetic modulation of GABAergic systems improves Aβ-induced memory deficits

8.47 **Samuel Harrison,** ***New Zealand Brain Research Institute; University of Otago, Christchurch, New Zealand***
Predictors of apathy in Parkinson's disease

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

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

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

8.51 **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

8.52 **Tessa Peck,** ***Victoria University of Wellington, Wellington, New Zealand***
Selective inhibition of inflammatory but not homeostatic immune cell trafficking into the CNS in a model of multiple sclerosis

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

8.54 **Zohreh Doborjeh,** ***University of Auckland, Auckland, New Zealand***
Personalised brain-inspired AI technology, based on integrated neurological, clinical, and psychological data for prediction of an individual response to tinnitus therapy

Conference Dinner

7.30 pm

Skyline Restaurant

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

The Skyline is a licensed restaurant but wine and beer will be provided.
The function room will be open from 7.00 pm,
with dinner commencing at 7.30 pm.

Musical entertainment will be provided.

8.45 am Coffee/tea

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

CHAIR: JOHN DALRYMPLE-ALFORD

9.00 am	9.1	**Taylor Stevenson,** ***University of Auckland, Auckland, New Zealand*** Pericyte cell death and α-synuclein – a double hit
9.15 am	9.2	**Andrea Kwakowsky,** ***University of Auckland, Auckland, New Zealand*** Network dysfunction in the Alzheimer's disease hippocampus
9.30 am	9.3	**Adelie Tan,** ***University of Auckland, Auckland, New Zealand*** A growing problem in Huntington's disease
9.45 am	9.4	**Emma Deeney,** ***University of Otago, Dunedin, New Zealand*** Voluntary exercise restores motor performance in a mouse model of spinocerebellar ataxia type 1 (SCA1)
10.00 am	9.5	**Macarena Pavez,** ***University of Otago, Dunedin, New Zealand*** Uncovering new trafficking routes in axons
10.15 am	9.6	**Deanna Barwick,** ***University of Otago, Dunedin, New Zealand*** Septin 2 stabilises the axonal initial segment of induced pluripotent stem cell derived neurons

10.30 am Morning tea available

10. Sensory and Motor

CHAIR: SUSAN SCHENK

11.00 am	10.1	**Christina Buchanan,** ***Auckland City Hospital, Auckland, New Zealand*** Potential PINK1 founder effect in Polynesia causing early onset Parkinson's disease
11.15 am	10.2	**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
11.30 am	10.3	**Rachael Sumner,** ***University of Auckland, Auckland, New Zealand*** Modelling thalamocortical circuitry shows that visually induced LTP changes laminar connectivity in human visual cortex
11.45 am	10.4	**Serey Naidoo,** ***University of Auckland, Auckland, New Zealand*** Cell-type specific responses to neuroinflammation in human leptomeninges

11. Cognition and Behaviour

CHAIR: KYLA-LOUISE HORNE

12.00 pm	11.1	**Narun Pat,** ***University of Otago, Dunedin, New Zealand*** Predicting children's general intelligence through multimodal brain-based models
12.15 pm	11.2	**Rebekah Blakemore,** ***New Zealand Brain Research Institute, Christchurch, New Zealand; 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
12.30 pm	11.3	**Susan Schenk,** ***Victoria University of Wellington, Wellington, New Zealand*** Zebrafish on "P": Behavioural effects of methamphetamine
12.45 pm	11.4	**Sonja Seeger-Armbruster,** ***University of Otago, Dunedin, New Zealand*** Thalamic paraventricular nucleus: Bridging homeostatic and reward pathways in the control of feeding
1.00 pm		Closing Remarks and Student Prize Presentation
		Light lunch, Atrium

Acknowledgements
We are very grateful to the Neurological Foundation of New Zealand for its generous financial assistance towards student and ECR travel and registration, and for delegate carer support.

Email Addresses

Hamid Abbasi
h.abbasi@auckland.ac.nz
Cliff Abraham
cliff.abraham@otago.ac.nz
Molly Abraham
m.abraham@auckland.ac.nz
Nidhi Aggarwal
nidhi.aggarwal@auckland.ac.nz
Tim Anderson
tim.anderson@cdhb.health.nz
Phoebe Anscombe
p.anscombe@auckland.ac.nz
Christine Arasaratnam
c.arasaratnam@auckland.ac.nz
Finbar Argus
farg967@aucklanduni.ac.nz

Duncan Bakke
dbak576@aucklanduni.ac.nz
Deanna Barwick
deanna.barwick@otago.ac.nz
Indranil Basak
indranil.basak@otago.ac.nz
Rabia Bibi
rabia.bibi@vuw.ac.nz
Brittney Black
brittney.black@auckland.ac.nz
Rebekah Blakemore
rebekah.blakemore@otago.ac.nz
Christina Buchanan
c.buchanan@adhb.govt.nz

Celine Camon
camce602@student.otago.ac.nz
Maize Cao
m.cao@auckland.ac.nz
Kaaryn Cater
kaaryn.cater@whitireia.ac.nz
Amy Chapman
a.chapman@auckland.ac.nz
Bhavya Chawdhary
b.chawdhary@auckland.ac.nz
Henry Chafee
chafeehe@vuw.ac.nz
Joan Chan
chajo611@student.otago.ac.nz
Ernest Cheah
e.cheah@auckland.ac.nz
Joseph Chen
joseph.chen@auckland.ac.nz
Juliette Cheyne
j.cheyne@auckland.ac.nz

Janelle Chong
janelle.chong@auckland.ac.nz
Connor Clemett
c.clemett@auckland.ac.nz
William Cook
william.cook@auckland.ac.nz
Elizabeth Cooper
e.cooper@auckland.ac.nz
Jessica Crockett
jessica.crockett@auckland.ac.nz
Maurice Curtis
m.curtis@auckland.ac.nz

Emma Deeney
emma.deeney@postgrad.otago.ac.nz
Victor Birger Dieriks
v.dieriks@auckland.ac.nz
Zohreh Doborjeh
Zohreh.doborjeh@auckland.ac.nz
Anusha Dravid
a.dravid@auckland.ac.nz

Guy Eaden
Guy@psychsolutions.co.nz
Oluwatobi Eboda
ebool499@student.otago.ac.nz
Christopher Erb
christopher.erb@auckland.ac.nz
Marika Eszes
m.eszes@auckland.ac.nz

Sophie Farrow
s.farrow@auckland.ac.nz
Richard Faull
rlm.faull@auckland.ac.nz
Mackenzie Ferguson
mfer778@aucklanduni.ac.nz
Helen Fitzsimons
h.l.fitzsimons@massey.ac.nz
Jena Macapagal Foliaki
Jena.macapagal@auckland.ac.nz
Peter Freestone
peter.s.freestone@gmail.com

Kate Godfrey
k.godfrey@auckland.ac.nz
Evgeniia Golovina
e.golovina@aucland.ac.nz
E Scott Graham
s.graham@auckland.ac.nz
Laura Gumy
laura.gumy@otago.ac.nz

Email Addresses

Lysea Haggie
lmun373@aucklanduni.ac.nz
Jennifer Hamilton
jjh75@uclive.ac.nz
Bruce Harland
bruce.harland@auckland.ac.nz
Samuel Harrison
sam.harrison@nzbri.org
Victoria Hawkins
victoria.hawkins@auckland.ac.nz
Hannah Hawley
h.hawley@massey.ac.nz
Blake Highet
b.highet@auckland.ac.nz
Sheein Hong
sheein.hong@vuw.ac.nz
Kyla-Louise Horne
kyla.horne@nzbri.org
Kristina Hubbard
k.hubbard@auckland.ac.nz
Stephanie Hughes
stephanie.hughes@otago.ac.nz
Sahir Hussain
Sahir.Hussain@vuw.ac.nz

Sahan Jayatissa
cjay511@aucklanduni.ac.nz
Ashly Jose
ajos486@aucklanduni.ac.nz
Yewon Jung
y.jung@auckland.ac.nz

Delshad Kalantary
delshad.kalantary@auckland.ac.nz
Rashi Karunasinghe
karunasinghe@auckland.ac.nz
Meyrick Kidwell
Meyrick.kidwell@vuw.ac.nz
Soo H Kim
soo.kim@auckland.ac.nz
Bronwyn Kivell
bronwyn.kivell@vuw.ac.nz
Florian Kurth
f.kurth@auckland.ac.nz
Andrea Kwakowsky
a.kwakowsky@auckland.ac.nz
Eryn Kwon
e.kwon@matai.org.nz

Brett Langley
blangley@waikato.ac.nz

Zahra Laouby
zlao031@aucklanduni.ac.nz
Isabella Lavas
isabella.lavas@auckland.ac.nz
Florence Layburn
florence.layburn@auckland.ac.nz
Rebecca Lee
rebecca.lee@nzbri.org
Kevin Lee
kevin.lee@auckland.ac.nz
Susan YS Li
susan.li@auckland.ac.nz
Henry Liu
henry.liu@auckland.ac.nz
Donisha Liyanagamage
dk129@students.waikato.ac.nz
Jordan Lloyd
jt.lloyd@auckland.ac.nz
Jasmine Lock
locja386@student.otago.ac.nz
Victoria Low
v.low@auckland.ac.nz
Eileen Luders
e.lueders@auckland.ac.nz
Natasha Lust
natasha.lust@aucklanduni.ac.nz
Nikita Lyons
Nikita.Lyons@otago.ac.nz

Melanie McConnell
melanie.mcconnell@vuw.ac.nz
Samuel McCullough
s.mccullough@auckland.ac.nz
Kirstin McDonald
kirstin.mcdonald@otago.ac.nz
Natasha Mckean
nmck309@aucklanduni.ac.nz
Marion Mckinnon
mcc17@students.waikato.ac.nz
Laura Marriott
l.marriott@auckland.ac.nz
Sophie Mathiesen
matso768@student.otago.ac.nz
Edward Mee
edward.mee@xtra.co.nz
Svenja Meissner
svenja.meissner@auckland.ac.nz

Lorna Mitchell
l.mitchell@biocurate.com

Ruth Monk
r.monk@auckland.ac.nz

Email Addresses

David Moreau
d.moreau@auckland.ac.nz
Margaret Morris
m.morris@unsw.edu.au
Miran Mrkela
miran.mrkela@auckland.ac.nz
Dympna Mulroy
dympnam@adhb.govt.nz
Helen Murray
h.murray@auckland.ac.nz
Suresh Muthukumaraswamy
sd.muthu@auckland.ac.nz

Serey Naidoo
s.naidoo@auckland.ac.nz
Conor Nelson
conor.nelson@auckland.ac.nz
Denise Neumann
d.neumann@auckland.ac.nz
Julia Newland
julia.newland@auckland.ac.nz

Simon O'Carroll
s.ocarroll@auckland.ac.nz
Shane Ohline
shane.ohline@otago.ac.nz
Ashleigh O'Mara Baker
ashleigh.baker@auckland.ac.nz
Pablo Ortega-Auriol
p.ortegaauriol@auckland.ac.nz
Mahyar Osanlouy
m.osanlouy@auckland.ac.nz
Caitlin Oyagawa
c.oyagawa@auckland.ac.nz

Thulani Palpagama
t.palpagama@auckland.ac.nz
Thomas Park
thomas.park@auckland.ac.nz
Remai Parker
remai.parker@auckland.ac.nz
Narun Pat
narun.pat@otago.ac.nz
Kelly Paton
kelly.paton@vuw.ac.nz
Macarena Pavez
macarena.pavez@otago.ac.nz
Tessa Peck
tessa.peck@vuw.ac.nz
Giovanni Pedone
pedgi962@student.otago.ac.nz
Bria Pengelly
bria.pengelly@vuw.ac.nz

Katie Peppercorn
katie.peppercorn@otago.ac.nz
Luke Phillips
philu654@student.otago.ac.nz
Julia Plank
j.plank@auckland.ac.nz
Skylar Pollack
skylar.pollack@aucklanduni.ac.nz

Brad Raos
b.raos@auckland.ac.nz
John Reynolds
john.reynolds@otago.ac.nz
Laverne Robilliard
l.robilliard@auckland.ac.nz
Nicola Rodger
rodni139@student.otago.ac.nz
Miriam J Rodrigues
mrodrigues@adhb.govt.nz
Richard Roxburgh
richard.roxburgh@auckland.ac.nz
Brigid Ryan
b.ryan@auckland.ac.nz

Abby Sabrini
s.sabrini@auckland.ac.nz
Soroush Safaei
soroush.safaei@auckland.ac.nz
Ieuan Sargent
ieuan.sargent@auckland.ac.nz
Shruthi Sateesh
shruthi.sateesh@postgrad.otago.ac.nz
Susan Schenk
susan.schenk@vuw.ac.nz
D Samuel Schwarzkopf
s.schwarzkopf@auckland.ac.nz
Lucia Schweitzer
lucia.schweitzer@otago.ac.nz
Emma Scotter
emma.scotter@auckland.ac.nz
Brittany Scouller
brittany.scouller@vuw.ac.nz
Sonja Seeger-Armbruster
sonja.seeger-armbruster@otago.ac.nz
Shabah Shadli
shabah.shadli@otago.ac.nz
Jerram Sheehan
jshe969@aucklanduni.ac.nz
Jiantao Shen
jshe690@aucklanduni.ac.nz

Gurleen Singh
gsin255@aucklanduni.ac.nz

Email Addresses

Malvindar Singh-Bains
m.singh-bains@auckland.ac.nz
Tania Slatter
tania.slatter@otago.ac.nz
Rebecca Slykerman
r.slykerman@auckland.ac.nz
Katie Smith
ksmi944@aucklanduni.ac.nz
Taylor Stevenson
t.stevenson@auckland.ac.nz
Rachael Sumner
r.sumner@auckland.ac.nz
Darren Svirskis
d.svirskis@auckland.ac.nz
Molly Swanson
m.swanson@auckland.ac.nz

Adelie Tan
adelie.tan@auckland.ac.nz
Sheryl Tan
sheryl.tan@auckland.ac.nz
Wei Jun Tan
w.j.tan@massey.ac.nz
Maryam Tayebi
mtay316@aucklanduni.ac.nz
Alina Tetereva
alina.tetereva@postgrad.otago.ac.nz
Kyrah Thumbadoo
k.thumbadoo@auckland.ac.nz
Li-Huei Tsai
lhtsai@mit.edu

Poutasi Urale
tasi.watson@auckland.ac.nz

Ruben Vergara
verru146@student.otago.ac.nz

Karen Waldie
k.waldie@auckland.ac.nz
Henry John Waldvogel
h.waldvogel@auckland.ac.nz
Catherine Webb-Robinson
c.webb@auckland.ac.nz
Kristina Wiebels
k.wiebels@auckland.ac.nz
Sarah Wilson
swilson3@massey.ac.nz
James Wiseman
j.wiseman@auckland.ac.nz
Katherine Witt
kate.witt@vuw.ac.nz
Oliver Wood
oliver.wood@auckland.ac.nz
Zoe Woolf
z.woolf@auckland.ac.nz
Yihan Wu
yihan.wu@auckland.ac.nz

Janet Boyu Xu
janet.xu@otago.ac.nz

Panzao Yang
p.yang@auckland.ac.nz
Debbie Young
ds.young@auckland.ac.nz

Jiaxian Zhang
zhaje795@student.otago.c.nz

Goddard Prize and Poster Prize Winners

1990	**Steven Morrison,** University of Otago, New Zealand
1991	**Oliver Davidson,** University of Otago, New Zealand
1992	**Nadia Solowij,** University of New South Wales, Australia
1993	**Kjesten Wiig,** University of Otago, New Zealand
1994	**Niki Butterworth,** University of Auckland, New Zealand
1995	**Gerald Ahern,** John Curtin School of Medical Research, Australia
1996	**Judy Swanson,** University of Otago, New Zealand
1997	**Donna Briggs,** University of Otago, New Zealand
1998	**Johanna Montgomery,** University of Otago, New Zealand
	Suzanne Habjan, University of Sydney, Australia
1999	**Wendy Brooks,** University of Otago, New Zealand
2000	**John Lin,** University of Auckland, New Zealand
2001	**Tina Hinton,** University of Sydney, Australia
	Michael Christie, University of Canterbury, New Zealand (Poster)
2002	**Gemma Irvine,** University of Otago, New Zealand
2003	**Evangelene Daniela,** Victoria University of Wellington, New Zealand
2004	**Bronwen Kelly,** University of Canterbury, New Zealand
2005	**Adam Errington,** University of Otago, New Zealand
	Wendy Imlach, AgResearch, New Zealand (Poster)
2006	**David Cumin,** University of Auckland, New Zealand
	Andrew Tattersfield, University of Auckland, New Zealand (Poster)
2007	**Carthur Wan,** University of Auckland, New Zealand
	Suzanne Ackerley, University of Auckland, New Zealand (Poster)
2008	**Thomas Park,** University of Auckland, New Zealand
	Joan Liu, University of Auckland, New Zealand (Poster)
2009	**Bill Connellly,** University of Otago, New Zealand
	Bridget Simonson, Victoria University of Wellington, New Zealand (Poster)
2010	**Tracy Melzer,** Van der Veer Institute, New Zealand
	Yeri Kim, University of Otago, New Zealand (Poster)
2011	**Kajsa Igelstrom,** University of Otago, New Zealand
	Malinda Tantirigama, University of Otago, New Zealand (Poster)
2012	**Malinda Tantirigama,** University of Otago, New Zealand
	Malvindar Singh-Bains, University of Auckland, New Zealand (Poster)
2013	**Amy Smith,** University of Auckland, New Zealand
	Peter Bosch, Victoria University of Wellington, New Zealand
	Laura Boddington, University of Otago, New Zealand (Poster)
2014	**Emmet Power,** University of Otago, New Zealand
	Lakshini Mendis, University of Auckland, New Zealand (Poster)
2015	**Christine de Lance,** University of Canterbury, New Zealand
	Christine Arasaratnam, University of Auckland, New Zealand (Poster)
2016	**Jennifer Robertson,** Australian National University, Australia
	Allanah Kenny, University of Canterbury, New Zealand (Poster)
2017	**Hannah Best,** University of Otago, New Zealand
	Ashwini Hariharan, University of Otago, New Zealand (Poster)

Prize Winners

2018	**Jarred Griffin,** University of Auckland, New Zealand
	Alice McDouall, University of Auckland, New Zealand (Poster)
2019	**Mohammed Ibrahim,** University of Otago, New Zealand
	Kendra Boyes, Victoria University of Wellington, New Zealand (Poster)
	Nikita Lyons, University of Auckland, New Zealand (Infoblitz)
2020 by Zoom	**Karan Govindpani,** University of Auckland, New Zealand

Proceedings of the 38th International Australasian Winter Conference on Brain Research, 2021

Editor: Dr Kristin Hillman

(ISSN 1176-3183)

Abstracts in Presentation Order

Proceedings of the International Australasian Winter Conference on Brain Research, 2021, 38, will be published on the AWCBR website.

1

Environmental determinants of obesity

Margaret Morris

University of New South Wales, Sydney, Australia

m.morris@unsw.edu.au

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 consumption of such diets, even short-term, 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 in addition to 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.

2.1

Altered expression of PSA-NCAM regulatory genes in Alzheimer's disease detected using spatial transcriptomics

Blake Highet, Richard L M Faull, Helen C Murray, Maurice A Curtis

University of Auckland, Auckland, New Zealand

b.highet@auckland.ac.nz

Alzheimer's disease (AD) is the most common form of dementia, for which there is currently no effective treatment. A feature of the disease is that neurons involved in memory function lose the ability to change their physical structure. This is suggested to be due to loss of a protein called polysialylated neural cell adhesion molecule (PSA-NCAM). To identify the mechanism that causes loss of PSA-NCAM in AD, we utilized a multiplexed fluorescent in situ hybridization and immunohistochemistry (mxFISH+IHC) technique to investigate 10 genes involved in PSA-NCAM regulation in *post-mortem* human brain tissue while maintaining spatial context. Using an unsupervised single-cell clustering approach, we observed a decrease in *CALB2* and *PST* high cell populations in the AD entorhinal cortex (EC). Spatial mapping of these cell populations highlighted ubiquitous loss of both populations in the AD EC across all layers. Therefore, this project identified potential novel targets proposed to maintain memory function and delay AD progression. Furthermore, this mxFISH+IHC and single-cell analysis pipeline is an efficient approach to study gene and protein expression in situ.

2.2

Building the New Zealand motor neuron disease genetics study

Emma L Scotter[1], Miran Mrkela[1], Jules B L Devaux[1], Chitra Vinnakota[1], Christina M Buchanan[2], Emily P McCann[3], Lyndal Henden[3], Kelly L Williams[3], Elsa M Parker[4], Anjali K Henders[5], Naomi R Wray[5], Miriam J Rodrigues[2], Richard H Roxburgh[2]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand, [3]Macquarie University, Sydney, Australia, [4]Canterbury Health Laboratories, Christchurch, New Zealand, [5]University of Queensland, Brisbane, Australia

emma.scotter@auckland.ac.nz

At least 15% of motor neuron disease (MND) internationally is attributable to known genetic factors. The same MND-causing genetic variants can be found in familial and apparently sporadic cases, who are clinically indistinguishable and whose offspring are at the same risk. Yet access to clinical genetics in NZ is based on this fuzzy distinction between 'familial' and 'sporadic' inheritance. Additionally, the genetics of MND in NZ has not been characterised. We sought to investigate MND genetics in NZ and return results to interested participants, regardless of inheritance. We established this study with research and clinical 'arms' through national and international collaboration. We ethically collect and store participant data, coordinate participant progress through our study pipeline, interpret genetic assays, and return results. Our study has enrolled 87 participants with MND, 22 unaffected family members, and 12 controls. To date, we have mapped 7 large multigenerational MND pedigrees, and are examining relatedness and founder origin. We have identified causative genes in 8 individuals, risk genes in 6, and variants of unknown significance for further testing in 9. Our study will inform: the distribution of MND resources nationally, any decision to extend clinical genetics access, and the feasibility of NZ MND clinical trials.

2.3

Maternal immune activation affects behavioural function, neurochemistry and microglia in juvenile rat offspring

Jiaxian Zhang, Yu Jing, Hu Zhang, Ping Liu

University of Otago, Dunedin, New Zealand

zhaje795@student.otago.ac.nz

Maternal immune activation (MIA) is a neurodevelopmental model of schizophrenia, based on the epidemiological evidence of increased risk of schizophrenia in individuals with prenatal exposure to infections. Recent research has implicated altered metabolism of L-arginine in the pathogenesis of schizophrenia. We have shown that MIA induced by polyinosinic–polycydilic acid on gestational day 15 alters brain arginine metabolic profile in the neonatal and adult rat offspring. The present study systematically investigated how MIA affected behavioural functions and hippocampal arginine metabolism and microglia immunoreactivity in juvenile male and female offspring at postnatal day 35. MIA offspring of both sexes displayed impaired pre-pulse inhibition (a measure of sensorimotor gating) and anxiety-like behaviour. High-performance liquid chromatography and liquid chromatography/mass spectrometry showed significantly reduced agmatine (decarboxylated arginine) levels, but increased glutamine/glutamate ratios, in the CA2/3 and dentate gyrus sub-regions of the hippocampus in MIA offspring regardless of sex. The combination of immunohistochemistry and stereology revealed significantly reduced number of hippocampal microglia accompanied with marked morphological changes in MIA offspring at both sexes. Collectively, these results demonstrate dramatic effects of a single MIA insult on juvenile offspring, which may underlie functional and structural changes seen in adult ages.

2.4

Identifying TDP-43 loss-of-function markers in amyotrophic lateral sclerosis with human derived brain pericytes

Maize C Cao, Jane Wu, Mike Dragunow, Emma L Scotter

University of Auckland, Auckland, New Zealand

m.cao@auckland.ac.nz

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, and 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 *RANBP1*, *PFKP* and *KIAA1324*. Additionally, TDP-43 knockdown led to the inclusion of 'cryptic exons' in the transcripts of several genes. These included *EXD3*, *NYNRIN* and ALS-associated gene *UNC13A*. These changes were all confirmed by quantitative RT-PCR. To extend these findings, we aim to evaluate whether these TDP-43 loss-of-function mRNA markers and their cognate proteins can be detected in ALS brain tissue. 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.

2.5

Investigating the mechanisms of cardiac glycosides as modulators of barrier inflammation

Caitlin Oyagawa, Rebecca Johnson, Kevin Lee, Miranda Aalderink, Sheryl Feng, Michael Dragunow

University of Auckland, Auckland, New Zealand

c.oyagawa@auckland.ac.nz

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 were performed to investigate effects on the $Na^{+/}K^{+}$-ATPase in pericytes. Results indicated that the anti-inflammatory phenotype was not phosphoinositide 3-kinase (PI3K) signalling-mediated, but likely downstream of Src kinase activity, and is reliant on the endocytosis of tumour necrosis factor 1 receptor (TNFR1). Patch-clamping revealed that the anti-inflammatory effects occur at concentrations that also inhibition $Na^{+}K^{+}$ 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.

3

Uncovering the role of Alzheimer's disease risk genes using stem cells and human brains

Li-Huei Tsai

Massachusetts Institute of Technology, Cambridge, United States of America

lhtsai@mit.edu

Alzheimer's disease (AD) is a debilitating brain disorder with staggering human and financial costs. While genomic studies increasingly identify genetic risk alleles that correlate with AD, there is still no clear picture of the underlying molecular and cellular mechanisms involved. My lab uses a multi-pronged approach to delineating how cellular, molecular and brain circuit dysfunctions contribute to AD. We recently reported the first single-nucleus transcriptomic analysis of the prefrontal cortex to accurately map the cell types and molecular pathways impacted by AD. Apolipoprotein E4 (ApoE4) is the strongest known genetic risk variant for sporadic Alzheimer's disease (AD), but a comprehensive understanding of the cell-type-specific effects of APOE4 in the human brain in the presence and absence of AD pathology has yet to be achieved. Our recent analysis of single nucleus transcriptomics from a sex-balanced cohort of individuals comprised of APOE3 and E4 carriers indicated that cell-type-specific ApoE effects can arise in non-ApoE-expressing cell types. We also identified multiple processes that are perturbed in AD pathology exclusively in the context of ApoE4. In parallel, we conducted lipidomic analyses in ApoE4-expressing yeast and iPSC-induced astrocytes derived from human ApoE4 carriers. These results revealed that ApoE4 causes widespread changes in lipid homeostasis that result in increased unsaturation of fatty acids and an accumulation of neutral lipids in lipid droplets. Finally, we investigated the role of ApoE4 in cerebral amyloid angiopathy (CAA), a condition seen in a large proportion of AD patients, using an iPSC-derived human blood brain barrier model (iBBB). Through combinatorial experiments, we pinpointed ApoE4 pericytes that play key roles in amyloid accumulation along the iBBB, and identified druggable pathways that are dysregulated in ApoE4 pericytes. Taken together, our collected body of work illustrates how ApoE4 causes widespread molecular and cellular alterations in multiple cell types to facilitate the development of AD phenotypes.

4.1

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

Hamid Abbasi[1], Sarah Mollet[1], Sian Williams1, Malcolm Battin[2], Thor Besier[1], Angus McMorland[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

h.abbasi@auckland.ac.nz

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 are time-consuming and human resource intensive, require specialist training, and do 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. Twelve 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 frames). 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.

4.2

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

Molly I Abraham, Rashika Karunasinghe, Tania Fowke, Jaya Prasad, Justin M Dean

University of Auckland, Auckland, New Zealand

m.abraham@auckland.ac.nz

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.

4.3

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

Evgeniia Golovina[1], Tayaza Fadason[1], Thiery J Lints[1], Caroline Walker[1], Mark H Vickers[1], Justin M O'Sullivan[2]

[1]University of Auckland, Auckland, New Zealand, [2]University of Southampton, Southampton, United Kingdom

e.golovina@aucland.ac.nz

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by significant and complex genetic aetiology. 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 foetal and adult cortical tissues. We found 80 and 58 regulatory variants in the foetal and adult cortex, respectively. Functional annotation of these variants revealed significant enrichment within regions repressed by Polycomb proteins in the foetal 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 foetal 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.

4.4

The subcortical structures of contact-sport players' brains show significant differences when compared to the age-matched control group

Maryam Tayebi[1], Samantha Holdsworth[2], Madeline Parker[1], Harrison Ng[1], Justin Fernandez[1], Alan Wang[1], Poul Nielsen[1], Vickie Shim[1]

[1]University of Auckland, Auckland, New Zealand, [2]Matai Medical Research Institute, Gisborne, New Zealand

mtay316@aucklanduni.ac.nz

Contact-sport players are exposed to multiple head impacts during the game. Incidence of sport related mild traumatic brain injury (mTBI) is up to one-third of all cases suffered from TBI. Yet, there have been very few studies that investigate the effect of repeated head impacts on the brain's subcortical structures. The aim of this study is to analyse the morphological changes in these brain structures after years of playing contact-sport. We used the magnetic resonance images of collegiate (19-21 y) Canadian-football players (n=20) and age-matched healthy control subjects (n=20). 3D T1_weighted structural images of the whole brain were acquired using a 3.0 T MRI machine. The subcortical structures were automatically segmented first. They were then turned into surface meshes to perform principal component analysis (PCA) on all 40 subjects, which quantitatively characterises the shape differences between these two groups. The results showed that there is a clear morphological difference in some of the subcortical structures between contact-sports players and the age-matched healthy control group. This difference was also statistically significant on the volume of thalamus, putamen, pallidum, and corpus callosum. This difference will be further analysed and compared with other advanced MRI techniques such as diffusion tensor imaging.

5.1

Loss of Batten disease associated CLN5 leads to neuronal lysosomal defects, and impaired neurogenesis in induced pluripotent stem cell-derived human neurons

Indranil Basak[1], Rachel Hansen[1], Harry Dolan[1], Michael E Ward[2], Stephanie M Hughes[1]

[1]University of Otago, Dunedin, New Zealand, [2]National Institute of Health, Bethesda, United States of America

indranil.basak@otago.ac.nz

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 knocked down (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 investigating transcriptome changes using RNA sequencing. Knockdown of CLN5 in human neurons resulted in reduced lysosomal acidity, defective anterograde lysosome trafficking, and increased percentage of non-motile lysosomes. Although mitochondrial health in CLN5i i^3Ns was not compromised, the CLN5i i^3Ns showed elongated mitochondria, and autophagy was impaired. Transcriptomic analysis revealed neurogenesis as an over-represented pathway, whereas ion transport was downregulated in the CLN5i i^3Ns compared to healthy i^3Ns. The impaired lysosomal function and trafficking due to the loss of CLN5 could lead to improper waste clearance, leading to neuronal dysfunction. Furthermore, impaired neurogenesis and ion transport due to the loss of CLN5 could be secondary effects that lead to neurodegeneration in CLN5 Batten disease.

5.2

Development of an iPSC-derived model of brain pericytes to investigate their role in blood-brain barrier function and neuroinflammation

Samuel McCullough, Eliene Albers, Scott Graham, Bronwen Connor, Simon J O'Carroll

University of Auckland, Auckland, New Zealand

s.mccullough@auckland.ac.nz

Brain pericytes are cells found within the basement membrane of the vasculature, where they support endothelial cells in the formation of the blood-brain barrier and play a unique role in the mediation of neuroinflammation. It is important to study human-derived brain pericytes to determine their role in human disease. Human brain pericytes can be obtained from surgically transected brain tissue, however, access to tissue is limited. Another option is to generate brain pericytes from induced pluripotent stem cells (iPSCs). This study confirms our ability to generate iPSC-derived brain pericytes and the response of human brain pericytes to inflammatory signals. Human iPSCs were primed towards a neural crest stem cell (NCSC) lineage, before undergoing a p75-directed isolation. Isolated p75+ NCSCs were differentiated into pericyte-like cells. We investigated the expression of pericyte markers PDGFRβ, NG2, αSMA, and CD13 using immunocytochemistry and qRT-PCR. Gene expression of pericyte markers was seen by day 21, with protein expression by day 32, which was maintained throughout differentiation. These cells also express NFκB and STAT1 and respond to IL-1β, TNFα, LPS, and IFNγ. The results of this study demonstrate the production of an iPSC-derived human brain pericyte model which can be used for further studies in neuroinflammation.

5.3

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

Darren Svirskis[1], Brad Raos[1], Maria Asplund[2], Simon O'Carroll[1], Bruce Harland[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Freiburg, Freiburg, Germany

d.svirskis@auckland.ac.nz

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 recovering, while facilitating the delivery of electroceutical and chemical treatments.

5.4

Establishing gene regulatory networks from Parkinson's disease risk loci

Sophie L Farrow[1], William Schierding[1], Sreemol Gokuladhas[1], Evgeniia Golovina[1], Tayaza Fadason[1], Antony A Cooper[2,3], Justin M O'Sullivan[1,2,4]

[1]University of Auckland, Auckland, New Zealand, [2]Garvan Institute of Medical Research, [3]University of New South Wales, Sydney, Australia, [4]University of Southampton, Southampton, United Kingdom

s.farrow@auckland.ac.nz

Parkinson's disease (PD) is a complex neurodegenerative illness. The latest meta-analysis of genome wide association studies (GWAS) identified 90 independent variants across 78 genomic regions associated with PD. However, the majority of these variants are non-coding, and thus elucidating underlying functional mechanisms and identifying interactions remains a challenge. To gain a global understanding of these variants, we analysed the variants within a regulatory network, as opposed to in isolation. To establish the functional gene regulatory networks associated with these 90 variants, we utilised an approach combining spatial (chromosomal conformation capture) and functional eQTL data. We identified 518 genes subject to regulation by 76 of the 90 variants across 49 tissues (36 peripheral and 13 CNS). Notably, one third of these genes, including a known *PARK* gene – *SYNJ1* – were regulated via *trans*- acting mechanisms (>1Mb). Through utilising Louvain clustering we extracted nine significant and highly intra-connected clusters within the entire gene regulatory network. The nine clusters are enriched for specific biological pathways, some of which have only recently been considered in association with PD, such as DNA replication and repair. Together, our results contribute to an overall understanding of the mechanisms and impact of specific combinations of PD GWAS variants.

Poster 6.1

mHTT aggregates and neuroinflammation in the Huntington's disease midcingulate cortex

Mackenzie W Ferguson[1], Aimee R Mills[1], Thulani H Palpagama[1], Clinton Turner[2], Henry J Waldvogel[1], Richard L M Faull[1], Andrea Kwakowsky[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

mfer778@aucklanduni.ac.nz

Huntington's disease (HD) is a neurodegenerative disorder that can result in motor, mood and cognitive symptoms. HD mood symptomotology correlates with neuronal death in the cingulate cortex. Neuroinflammation, involving reactive glial cells and inflammatory mediators in the brain parenchyma, may influence HD pathophysiology. Accumulation of mutant huntington (mHTT) aggregates has also been linked to neuroinflammation and neuronal loss. Importantly, the degree to which these neuroinflammatory changes are detrimental to neurons and contribute to HD pathology progression is not well understood. Using fluorescent immunohistochemistry, we stained HD and control post-mortem human midcingulate cortex tissue with HLA DP/DQ/DR, an inflammatory marker, and Iba-1, labelling microglia. We qualitatively and quantitatively assessed activation and morphology changes, indicating neuroinflammation, and mHTT levels – linking neuroinflammation and mHTT burden. We found increased activated microglial morphologies across all HD cases (53.82%), and increased ramified microglia in control cases (67.41%). HD cases showed decreased number of ramified and ameboid microglia. Activated microglia were localised close to neurons containing mHTT aggregates in HD cases, which positively correlated with mHTT burden. Total microglia number did not increase in HD cases, suggesting ramified microglia change to activated states. This data indicates an association between mHTT burden and neuroinflammation in HD.

Poster 6.2

The development of electrically stimulated release of neurotrophic growth factors

Ernest Cheah, Zimei Wu, Simon J O'Carroll, Darren Svirskis

University of Auckland, Auckland, New Zealand

e.cheah@auckland.ac.nz

Spinal cord injury is a devastating condition that often affects young and healthy individuals worldwide. Injuries to the spinal cord cause axonal connection disruptions and the reestablishment of these networks is required for functional recovery. Neurotrophic growth factors are a family of polypeptides that have been shown to positively influence neuronal regrowth. We hypothesise an electrically responsive delivery system can tune the release of growth factors upon electrical stimulation. We have developed a delivery system comprising of a hydrogel (gelatin methacryloyl, (GelMA)) infiltrated with a conducting polymer, (poly(3,4-ethylenedioxythiophene)), to form a swellable and electrically responsive polymer for drug delivery. Incorporation of different proteins as models of growth factors into the electroconductive delivery system was investigated and controlled release was tested under various stimulation conditions. Protein loading into the delivery system required tailoring of conditions. Electrical stimulation at 0.1 Hz increased the release rate by two-fold compared to passive diffusion over several hours. Further optimisation of electrical stimulation parameters can modulate the release of proteins. Furthermore, this delivery system can be patterned onto a multi-electrode array for *in vitro* cell culture to assess biocompatibility and to study the effects of growth factors on neuronal cell populations.

Poster 6.3

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

Brigid Ryan[1], Adrian Martinez Ruiz[1,2], Claudia Rivera-Rodriguez[1], Maurice Curtis[1], Gary Cheung[1]

[1]*University of Auckland, Auckland, New Zealand,* [2]*National Institute of Geriatrics of Mexico, Mexico City, Mexico*

b.ryan@auckland.ac.nz

Objective: Determine the sociodemographic and clinical characteristics of a large cohort of patients with young-onset dementia (aged <65), and whether they differ from older (age 65+) adults with dementia. Methods: 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. Results: People with young-onset dementia 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 young onset dementia. Carers of people with young-onset dementia were more likely to feel distress, anger, or depression, and families of people with young-onset dementia were more likely to feel overwhelmed. Conclusions: Young-onset dementia patients 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 6.4

Design and development of multiscale microscopic imaging systems for neuroscience applications

Ashly Jose, Stanley Tang, Marco Bonesi,Yukti Vyas, Claude Aguergaray, Neil Broderick, Frederique Vanholsbeeck, Juliette E Cheyne

University of Auckland, Auckland, New Zealand

ajos486@aucklanduni.ac.nz

Multiscale imaging systems enable measurement of micro-scale activity from individual neurons and meso-scale activity from diverse regions of brain for understanding functional properties and correlations of widely separated neurons. Live fluorescence two-photon microscopy allows imaging up to 450µm deep in tissue with subcellular resolution and mesoscopy offers a large field of view for imaging whole cortex in mice. These optical imaging techniques are often expensive, with complex designs. Our research aims to develop cost-effective imaging systems (mesoscope and two-photon microscope) to visualize structural and functional details of brain in rodents. We have optimized a custom-built fibre optic laser to deliver the short intense pulses required for two-photon excitation. This passively mode-locked laser has a wavelength of 1030nm and repetition rate of 4MHz. We have obtained high resolution images of *in vitro* samples and are currently customising the two-photon microscope for *in vivo* imaging. We have developed the mesoscope with a large field of view (10mm x 10mm), while maintaining its spatial resolution (~20µm). Both systems have the possibility to integrate functionalities for future developments. In future studies, these technologies will be applied to gain insights about auditory dysfunction in a mouse model of Autism Spectrum Disorder.

Poster 6.5

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

William Cook[1], Angela Wu[1], Elizabeth Cooper[1], Alexandre Mouravlev[1], Dahna Fong[1], Jason Correia[2], Edward Mee[1], Patrick Schweder[1,2], Thomas In-Hyeup Park[1], Mike Dragunow[1], Deborah Young[1]

[1]University of Auckland, [2]Auckland City Hospital Auckland, New Zealand

william.cook@auckland.ac.nz

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 6.6

Stretchable multi-electrode arrays for measuring electrical activity in an *in vitro* model of neural injury

Brad Raos, Simon O'Carroll, Darren Svirskis

University of Auckland, Auckland, New Zealand

b.raos@auckland.ac.nz

Spinal cord injuries result from mechanical damage to axon tracts in the spinal cord. Recent evidence has suggested that exogenous electrical fields can promote axonal growth. Multi-electrode arrays (MEAs) provide a valuable tool for investigating the potential for axonal regrowth following injury because they enable simultaneous recording and stimulation of electrical activity. MEAs are widely used to measure electrical activity within *in vitro* cell cultures. Traditional MEAs are made from rigid substrates, such as glass, and use metals for the electrodes and wire tracts. Such materials have no ability to support large strains and therefore limit the utility of MEAs when investigating electrical activity in conjunction with mechanical forces. Data will be presented on the development of an all-in-one stretchable MEA that is capable of supporting mechanical strain injury in a neuronal culture. The conductive polymer poly(3,4-ethylenedioxythiophene) (PEDOT) was deposited on polydimethylsiloxane (PDMS) to form electrodes and was found to support strain up to 50%, while maintaining electrical conductivity. The electrical characteristics of stretchable MEAs will be described. Proof of principle data of electrical activity from cultures of human SH-SY5Y neurons before and after a strain induced injury will also be presented.

Poster 6.7

Exploring the augmented cuprizone model of demyelination

Bria Pengelly[1], Andrew Biggerstaff[1], Anne La Flamme[1,2], Bronwyn Kivell[1]

[1]Victoria University of Wellington, [2]Malaghan Institute of Medical Research, Wellington, New Zealand

bria.pengelly@vuw.ac.nz

Demyelination is a pathological feature of many neurodegenerative diseases and there is a dire need for the development of pharmacotherapies that can induce remyelination to promote repair and recovery. There are currently no therapeutic drugs available that induce remyelination. The standard preclinical cuprizone toxin-induced model of demyelination selectively kills oligodendrocytes and is used to investigate the mechanism of action underlying both demyelination and remyelination. However, in this model spontaneous remyelination occurs, which provides a small therapeutic window for investigating potential remyelinating pharmacotherapies. The augmented cuprizone model is a more robust model of demyelination that combines cuprizone with the mTOR inhibitor rapamycin to prevent spontaneous remyelination and provides a greater therapeutic window to investigate remyelination pharmacotherapies. This study assessed remyelination in the augmented cuprizone and rapamycin model of demyelination using immunohistochemistry and transmission electron microscopy to evaluate remyelination. We show that cuprizone and rapamycin treated mice showed significantly more glial cell infiltration ($p<0.05$) into the corpus callosum and less oligodendrocyte and oligodendrocyte progenitor cells than healthy control groups ($p<0.05$). Additionally, animals treated with cuprizone and rapamycin had significantly increased g-ratios ($p<0.05$) indicating less myelinated axons than healthy controls. This study shows the importance of a larger therapeutic window when investigating novel remyelinating pharmacotherapies.

Poster 6.8

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

Brittney L Black, Henry J Waldvogel, Richard L M Faull

University of Auckland, Auckland, New Zealand

brittney.black@auckland.ac.nz

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, to understand the role of the excitatory function more fully, this study investigates glutamatergic changes in the GP of post-mortem human brain in normal, Huntington's and Parkinson's Disease. Six control, 6 PD and 9HD cases were used to run western blot experiments for glutamatergic markers including: EAAT2, GluA1, GluA2, GluN1, PSD95, VGluT1 and VGluT2. 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. Thus far, our study has indicated a decrease in the protein signal of EAAT2 between both the control and HD($p=0.0165$) and PD($p=0.0094$). GluA2 was significantly decreased in the HD compared to control ($p=0.0054$). However, in PD, there is a significant increase in GluA2($p=0.0242$). PSD95 showed no significant changes. Further data analysis is ongoing and ready for AWCBR.

Poster 6.9

Hippocampal place cells form a multi-scale representation of megaspace

Bruce Harland[1,2], Marco Contreras[1], Madeline Souder[1], Jean-Marc Fellous[1]

[1]University of Arizona, Tucson, United States of America, [2]University of Auckland, Auckland, New Zealand

bruce.harland@auckland.ac.nz

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 6.10

Transcriptomic analysis of the contusive spinal lesion reveals the digestion of the inhibitory matrix scar to impact the immunological profile and potential of remyelination therapies

Connor Clemett, Amy McCaughey-Chapman, Bronwen Connor, Simon O'Carroll

University of Auckland, Auckland, New Zealand

c.clemett@auckland.ac.nz

Spinal injury induces dramatic transcriptomic and inflammatory responses within tissue and infiltrating immune cell types. CNS demyelination is a key pathology of contusive injury and a barrier to locomotor recovery. The post-injury deposition of extracellular matrix chondroitin sulphate proteoglycans (CSPGs) enhances inflammatory activation of immune infiltrates and restricts endogenous remyelination, limiting glial recovery. To investigate the effect of CSPG clearance on the sub-acute injury immune and remyelination responses we employed a CSPG-targeting gene therapy and bulk RNA transcriptomics to analyse the response of the thoracic cord to contusive injury and CSPG digestion. We performed microarray immune profiling to characterise the contribution of immune cell types to the injury site. Enrichment for key transcription factors identified *Bach2* and *Ets2* as central to the post-contusion response. Mapping of their functional involvements implicated for the first time in spinal injury *Bach2* in the regulation of B-cell activation and humoral control, and *Ets2* in control of wound healing and the regulation of key cytokine signaling pathways. Further we show that CSPG digestion enhances the expression of genes involved in antigen presentation and may contribute to a tissue environment more favourable to myelin recovery. These advances will underpin further work to enhance post-injury remyelination therapies.

Poster 6.11

The influence of insulin resistance on PSA-NCAM load in the entorhinal cortex

Catherine Webb-Robinson, Helen Murray, Mark Vickers, Sheryl Tan, Ankita Umapathy, Maurice Curtis

University of Auckland, Auckland, New Zealand

c.webb@auckland.ac.nz

Insulin resistance is a major risk factor in Alzheimer's disease. Insulin regulates structural plasticity of cells *in vitro* through 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 (EC) in Alzheimer's disease. Since the EC 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 insulin resistance in rats by feeding a high-fat diet. We confirmed this model using fasting Homeostatic Model Assessment for Insulin Resistance and oral glucose tolerance curves. Transcardially-perfused brain tissue was immunohistochemically labelled for insulin receptor and PSA-NCAM and co-labelling will be analysed in the EC on a cell-by-cell basis using confocal images. Findings will be discussed in full by time of presentation. By unravelling the link between insulin resistance and reduced structural plasticity, this study will indicate whether diabetic treatments have potential benefits for dementia patients.

Poster 6.12

A principled approach to consider theory in the evaluation of empirical findings

David Moreau, Kristina Wiebels

University of Auckland, Auckland, New Zealand

d.moreau@auckland.ac.nz

Over the last decade, the fields of psychology and neuroscience have implemented a number of changes in methods and practices to increase the reliability of their findings—calling for systematic preregistration, open data and material, large-scale replications, and stricter error control. The importance of theory, and particularly its influence on the evaluation of empirical findings, has recently gained traction amidst these reforms. Here, we explore how the two pillars of scientific research—theory and data—mutually inform each other, and thus need to be jointly considered to improve inferences. Specifically, we demonstrate that the prior probability of hypotheses, derived from a theoretical framework, is key to evaluate reliability, and that its direct estimation can complement theory-agnostic strategies such as replication or stricter error control. We propose a principled approach that addresses common challenges in prior probability estimation, and discuss current large-scale initiatives with the potential to inform estimation across a number of research areas.

Poster 6.13

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

Delshad Kalantary, Soo Kim, Deborah Young, Alexandre Mouravlev, Henry Waldvogel, Richard Faull, Andrea Kwakowsky

University of Auckland, Auckland, New Zealand

delshad.kalantary@auckland.ac.nz

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 introduce 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 6.14

High glucose induces upregulation of mitochondrial stress protein HSP60 in human cortical neuron cells and potential modulation of neuroinflammation by *Macropiper excelsum*

Donisha Liyanagamage, Michèle R Prinsep, Ryan D Martinus

University of Waikato, Hamilton, New Zealand

dk129@students.waikato.ac.nz

Mitochondrial dysfunction is a plausible hypothesis to explain neuroinflammation in the diabetic brain. Upregulated mitochondrial protein HSP60 can initiate inflammatory signalling cascades via activating TLR receptors in the peripheral vascular system, however, its role in CNS inflammation is poorly understood. Thus, we investigated HSP60 expression in human cortical neuron cells (HCN-2) under different glucose concentrations and in relation to TNF-α secretion. Undifferentiated and differentiation-induced HCN-2 cells were exposed to normal and high glucose levels and stress control (metformin). High glucose treatments significantly reduced mitochondrial dehydrogenase activity (MTT assay) without significant effect on cell membrane integrity (LDH assay). Western blot showed statistically significant upregulation of HSP60 expression in high glucose treated cells. Considerable extracellular secretion of HSP60 was detected in high glucose treated groups (ELISA). TNF-α levels in conditioned media were comparatively higher in high glucose treated cells than control cells (ELISA), and positively correlated with extracellular HSP60 levels. *Macropiper excelsum* (Kawakawa) extract statistically reduced expression of HSP60 in neuron cells cultured in high glucose (Western blot). Extract fractionation is in progress (monitored by LC-MS). We propose a possible link between glucose-induced upregulation of HSP60 and neuroinflammation in the diabetic brain and a potential anti-inflammatory effect of Kawakawa.

Poster 6.15

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

Shane M Ohline, Stephanie M Hughes, Wickliffe C Abraham

University of Otago, Dunedin, New Zealand

shane.ohline@otago.ac.nz

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 NZ.

Poster 6.16

Analysis and visualisation of physiological changes before and after a mild traumatic brain injury using amplified, 4D flow, and diffusion MRI

Eryn Kwon[1,2], Catherine Emata[1], Maryam Tayebi[1,2], Leo Dang[1], Adam Donaldson[3], Vickie Shim[1], Allen Champagne[4], Alan Wang[1], David Dubowitz[1,5], Sarah-Jane Guild[1], Miriam Scadeng[1,5], Samantha Holdsworth[1,2]

[1]University of Auckland, Auckland, New Zealand, [2]Mātai Medical Research Institute, Gisborne, New Zealand, [3]University of Canterbury, Christchurch, New Zealand, [4]Queen's University, Kingston, Canada, [5]University of California San Diego, San Diego, United States of America

e.kwon@matai.org.nz

The majority of traumatic brain injuries that result in hospitalisation are mild (mTBI). Both diagnosis and prognosis in mTBI relies heavily on clinical evaluation of self-reported symptoms, resulting in over 50% of likely mTBI cases going undiagnosed. Here we used three advanced magnetic resonance (MR) sequences in conjunction to characterize the physiological changes associated with the acute phase of mTBI. Using a large animal model (n = 3), a controlled impact was delivered to the frontal area of the head and MR imaging was performed pre- and post- injury using a 3T MAGNETOM Skyra system (Siemens) and 32-channel head coil. The three MR sequences used 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). These observed changes demonstrate the potential of the three sequences as objective diagnostic and prognostic tools for mTBI events.

Poster 6.17

ATP13A2: Characterization of a novel human IPS cell model of Batten and Parkinson's disease

Oluwatobi Eboda[1], Indranil Basak[1], Michael Ward[2], Stephanie Hughes[1]

[1]University of Otago, Dunedin, New Zealand, [2]National Institute of Health, Bethesda, United States of America

ebool499@student.otago.ac.nz

Mutations in *ATP13A2* lead to the development of two distinct neurological disorders, Kufor-Rakeb Syndrome, a juvenile parkinsonism and CLN12 Batten disease, a lysosomal storage disorder. The underlying cause of Parkinson's Disease (PD) is unknown, though the accumulation of misfolded proteins suggests that improper disposal of aggregate-prone proteins plays an important role in the pathogenesis of disease. PD and Batten mutations have been modelled in animal and cell models, though none fully recapitulate the pathology seen in humans. Therefore, it is imperative to develop better models for disease study. The aim of this study is to establish new models for Parkinson's and Batten disease and assess pathological hallmarks. We have established a novel line of iPSC cultures to provide accurate modeling of human neuronal cell biology. CRISPRi was implemented to inhibit the endogenous ATP13A2 locus through lentiviral transduction of sgRNAs into neurons, achieving a 99% knockdown. Pathology was assayed by mitohealth kit, immunocytochemistry, western blot, and lysotracker, mitotracker and Magic Red assays. Knockdown of *ATP13A2* coincided with upregulation of SNCA, attenuated lysosomal trafficking and acidity, decreased mitochondrial health and cell viability, and indications of attenuated neurite projections. These findings establish an hiPSC model of ATP13A2 deficiency as viable tool for further research.

Poster 6.18

Secreted amyloid precursor protein alpha affects the transcriptome of IPSC derived human cortical neurons

Katie Peppercorn, Owen Jones, Stephanie Hughes, Warren Tate

University of Otago, Dunedin, New Zealand

katie.peppercorn@otago.ac.nz

Secreted amyloid precursor protein alpha (sAPPα) is a neuroprotective, neurogenic, memory enhancing molecule in the human brain. Isogenic human IPSC derived cortical neurons (iN's) were exposed to sAPPα in this study. RNA sequencing results indicate that the transcriptome of iNs is affected by sAPPα. sAPPα was expressed in and purified from genetically modified HEK cell cultures. iN cell cultures were characterised by electrophysiology and immunocytochemistry, using antibodies against neuronal markers. Following treatment of iN cells with 1 nM sAPPα for 30 min (n=3), total RNA was isolated and purified. The Otago Genomics facility (University of Otago) performed library construction and paired end sequencing across 4 lanes of HiSeq 2500 flow cells (Illumina). Trimmed FASTQ output files were aligned to the G38 human genome to identify differentially expressed genomic features. Six gene transcripts were upregulated after analysis with an adjusted p-value of 0.05, and 26 transcripts were down-regulated (log (fold change) criteria < -0.58 or > 0.58). Using a non-adjusted p-value of 0.05, 645 differentially expressed transcripts were identified which enabled network pathway analysis. Of the 241 protein coding genes, there were links to signal transduction (83), anatomical structure morphogenesis (44) and Wnt signalling (14). Selected transcripts will be validated by qPCR.

Poster 6.19

A model predictive control method for simulating the sympathetic/parasympathetic control of the circulatory system

Finbar Argus, Soroush Safaei, Gonzalo Maso Talou, Mahyar Osanlouy, Chris Bradley, Peter Hunter

University of Auckland, Auckland, New Zealand

farg967@aucklanduni.ac.nz

A combined local and global control model is developed for the local regulatory control of arterial smooth muscle tone with the global sympathetic/parasympathetic control of arterial and venous smooth muscle tone. The control model ensures sufficient cerebral blood flow while avoiding syncope during a stand-up manoeuvre. A local proportional integral derivative (PID) controller is implemented into a full body circulatory system model to approximate the vasodilator feedback effect caused by insufficient oxygen. The global control method approximates the control of the vasomotor centre. We create a forward-predicting model of the circulatory system and use it to optimise for efferent sympathetic/parasympathetic response. We propose that throughout one's lifetime, the vasomotor centre creates and improves a model of the circulatory system in order to more effectively optimise its efferent response to perturbations from homeostasis. A Koopman operator approach is used to identify a model that can be used to implement real-time, model predictive control. This Koopman forward-predicting model represents the proposed forward-predicting model of the vasomotor centre. This approach is easily extendable to more complex systems and control inputs, giving a control approach that can be used in models ranging from simple circulatory system models to full virtual human models.

Poster 6.20

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

Henry Liu, Amy Smith, Adelie Tan, Malvindar Singh-Bains, Nasim Mehrabi, Richard Faull, Mike Dragunow

University of Auckland, Auckland, New Zealand

henry.liu@auckland.ac.nz

Background: Alzheimer's disease (AD) is the most common neurodegenerative disease with no existing cure. Astrocytes and microglia have been implicated in AD. Previous *in vitro* and human transcriptomic studies in tissue have identified key molecular pathways which may be associated with these cell types and AD progression. This project aims to characterize the significance of these alterations in the middle temporal gyrus (MTG) of the AD human brain using immunohistochemistry on human brain tissue microarrays (TMAs) – a technique that utilizes up to 60 tissue core samples from control and AD donors. Methods: Immunohistochemistry with astrocytic (GFAP, Kir4.1, AQP-4, GLT-1, GS, and ALDH1L1) and microglial (STARD13, ATG7, ASAH1, and MYO1E) antibodies was used to investigate protein expression in the control and AD brain. Image acquisition was conducted using the V-slide automated scanning microscope, and the software MetaMorph will be used for quantitative analysis to assess cell number, protein expression and cellular morphology. Results: We have optimized the various astrocytic and microglial antibodies for IHC on human brain TMAs and have identified novel features which will be investigated in future studies. Significance/conclusion: Using TMAs, preliminary results demonstrate interesting and novel astrocytic and microglial protein targets of therapeutic relevance for human AD.

Poster 6.21

Dietary Zinc supplementation rescues autism-associated behaviours and synaptic deficits in the Tbr1 haploinsufficiency mouse model of autism spectrum disorders

Yewon Jung[1], Kevin Lee[1], Yuktiben Vyas[1], Yi-Ping Hsueh[2], Johanna M Montgomery[1]

[1]University of Auckland, Auckland, New Zealand, [2]Academica Sinica, Taipei, Taiwan

y.jung@auckland.ac.nz

Autism spectrum disorder (ASD) is a neurodevelopmental disease characterised by reduced social interaction, communication deficits, repetitive patterns of behaviour and cognitive impairments. Multiple studies have demonstrated that low levels of zinc, a prevalent metal in the brain that regulates synapse function, occur in the ASD population. Previously, we have shown that feeding *Shank3* deletion mouse model of ASD with zinc supplemented diet prevented autistic behaviours, in part, by normalising cortico-striatal synapse dysfunction. Here, we have taken a step forward to assess the efficacy of dietary zinc supplementation by testing its therapeutic potential in another mouse model of ASD, T-box brain protein 1 (Tbr1) haploinsufficiency mice ($Tbr1^{+/-}$). Our data revealed that zinc supplemented diet prevents social interaction deficit and reduced fear conditioned memory apparent in $Tbr1^{+/-}$ mice. Moreover, our electrophysiology analysis exhibited that the weakening of glutamatergic synaptic transmission observed at amygdala of $Tbr1^{+/-}$ mice was protected by dietary zinc supplementation. This was, in part, mediated by restoring the number of N-methyl-D-aspartate (NMDA) receptor-containing synapses in the amygdala. Together, our study suggests that therapeutic effects of dietary zinc is not limited to ASD-associated mutations in zinc-sensitive Shank synaptic proteins, signifying the effectiveness and breadth of dietary zinc supplementation as a treatment strategy.

Poster 6.22

The validity of magnetic resonance spectroscopy combined with echo-planar spectroscopic imaging for the measurement of human neuroinflammation

Julia Plank, Joanne Lin, Suresh Muthukumaraswamy

University of Auckland, Auckland, New Zealand

j.plank@auckland.ac.nz

Psychiatric disorders affect a significant percentage of the New Zealand population. These disorders are associated with educational difficulties, decreased productivity, and reduced quality of life, yet their pathophysiological mechanisms are not fully elucidated. Recent studies support the pathogenic role of neuroinflammation; however, there are no accepted methods that can reliably measure these inflammatory processes in patients. Magnetic resonance imaging (MRI) is a versatile, non-invasive neuroimaging technique that demonstrates sensitivity to neuroinflammation. Magnetic resonance spectroscopy in conjunction with echo-planar spectroscopic imaging (MRS/EPSI) measures brain metabolites relative to a temperature-dependent water reference to estimate brain temperature. There is evidence of increased whole-brain and regional temperatures in cases of chronic neuroinflammation. The validity of MRS/EPSI was tested using an experimental model of neuroinflammation – intramuscular administration of typhoid vaccine. Healthy volunteers (n=20) participated in a double-blind, placebo-controlled crossover study including MRI scans before and after vaccine/placebo administration. Whole-brain analysis suggests no effect of vaccine on temperature compared to placebo; regional analysis is in progress. Non-invasive methods for the measurement of neuroinflammation may be vital in identifying subgroups of psychiatric patients with neuroinflammation who would be most likely to respond favourably to certain classes of treatments, and to improve monitoring of neuroinflammatory-related disease activity.

Poster 6.23

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

Janelle Chong[1], James F Cheeseman[1], Matthew D M Pawley[2], Andrea Kwakowsky[1], Guy R Warman[1]

[1]University of Auckland, [2]Massey University, Auckland, New Zealand

janelle.chong@auckland.ac.nz

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 suprachiasmatic nucleus (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 6.24

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

Christine Arasaratnam[1], Helen Murray[1], Blake Highet[1], Ann Graybiel[2], Henry Waldvogel[1], Richard Faull[1]

[1]University of Auckland, Auckland, New Zealand, [2]Massachusetts Institute of Technology, Cambridge, United States of America

c.arasaratnam@auckland.ac.nz

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 have 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 6.25

The upregulation of SMAD2/3 signalling in GBM stromal cells in response to inflammatory stimuli

Jena Macapagal Foliaki[1], Richard L M Faull[1], Patrick Schweder[1,2], Thomas I-H Park[1], Mike Dragunow[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

jena.macapagal@auckland.ac.nz

Glioblastoma (GBM) is an aggressive and fatal brain malignancy characterised by a highly immunosuppressive tumour microenvironment (TME). The contribution of pericytes, an important neurovascular mural cell that forms the blood-brain barrier, towards GBM TME immunosuppression has been inadequately studied compared to other cells within the microenvironment. TGFβ signalling through the activation of SMAD2/3 is associated with anti-inflammatory effects and has been shown to regulate pericyte inflammatory responses. We hypothesise that aberrant SMAD2/3 signalling in GBM stromal cells may play a role in establishing the GBMs immunosuppressive phenotype. Primary patient-matched human brain stromal cells (BSCs) were isolated from both the tumour mass and normal cortical tissue from resections requiring normal cortex removal for tumour access. BSCs were treated with IL-1β, IFN-γ, TNFα & TGFβ for 1 hour and up to 24 hours. SMAD2/3 is classically only activated by TGFB superfamily ligands. As expected, normal BSCs only display nuclear translocation of SMAD2/3 in response to TGFβ. However, GBM BSCs upregulated SMAD2/3 expression and nuclear translocation when treated with classically pro-inflammatory molecules not observed in their normal counterparts. This novel finding of abnormal SMAD2/3 activation highlights GBM's potential use of an anti-inflammatory pathway in response to pro-inflammatory stimuli to maintain its immunosuppressive phenotype.

Poster 6.26

The role of glia in the Parkinson's disease striatum

Jessica Crockett, Christine Arasaratna, Malvindar Singh-Bains, Henry Waldvogel, Richard Faull

University of Auckland, Auckland, New Zealand

jessica.crockett@auckland.ac.nz

Parkinson's disease (PD) is a neurodegenerative disorder characterized by neuronal loss in the substantia nigra, resulting in decreased dopaminergic innervation in the striatum. Investigating non-neuronal cells such as microglia and astrocytes has become increasingly important due to their role in maintaining the neuronal environment and the role of microglia and astrocytes in the PD striatum remains to be fully elucidated. This study aimed to investigate microglia and astrocytes in the PD striatum by characterizing glial immunoreactivity patterns and cell morphology. *Post-mortem* human striatal sections (*n=8* PD, *n*=8 control cases) were stained for microglia using anti- Human Leukocyte Antigen-DR (HLA-DR) and anti-Ionized calcium-binding adaptor molecule-1 (Iba-1) and for astrocytes using anti-glial fibrillary acidic protein (GFAP) and imaged with the V-slide automated microscope. Automated image-analysis software Metamorph was used to determine protein expression, cell count and morphology measurements for each marker. A significant increase in the number of HLA-DR processes was found, suggesting hyperactive/ hyper-ramified microglia morphology. Trending increases were seen in HLA-DR and GFAP immunoreactivity patterns and morphology in PD. However, high case variability within the PD cohort requires further investigation. These findings suggest evidence of changes to microglia in the PD striatum, contributing to the neuropathological processes in PD.

Poster 6.27

Non-spatial memory and the anterior thalamic nuclei

Jennifer J Hamilton, John C Dalrymple-Alford

University of Canterbury, Christchurch, New Zealand

jjh75@uclive.ac.nz

The anterior thalamic nuclei (ATN), a central node in a complex memory system, are associated with spatial and temporal memory. 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 trace between these non-spatial stimuli. If ATN lesions recapitulate hippocampal function, specifically CA1 function, then they should disrupt acquisition only when an explicit delay (i.e., a 10-second trace) is inserted between the stimuli. Acquisition was completely abolished by ATN lesions, however, irrespective of the presence of the temporal trace (Lesion, $F=151.24$, $df=1,27$, $p<0.001$), and despite extended training (50x12-trial sessions). Faster acquisition with the 10-second trace was found in the sham rats (Lesion by Trace Condition, $F=3.51$, $df=1,27$, $p=0.07$). During recall, 5 days after reaching criterion, sham rats showed elevated Zif268 expression in hippocampal CA1 for the trace compared to no-trace condition. ATN-lesion rats showed reduced Zif268 expression in prefrontal and retrosplenial cortex. This is the first evidence that ATN lesions impair non-spatial paired-associate tasks. The findings suggest that the ATN are associated with memory beyond time and space, and are critical for learning arbitrary associations.

Poster 6.28

Scopolamine: A potential new pharmacotherapy for depression?

Joseph Chen[1], Rachael Sumner[1], Venkat Krishnamurthy Naga[2], Nicholas Hoeh[1,3], Hafis Adetokunbo Ayeni[3], Vikrant Singh[3], Andrew Wilson[3], Douglas Campbell[3], Frederick Sundram[1,2], Suresh Muthukumaraswamy[1]

[1]University of Auckland, [2]Waitemata District Health Board, [3]Auckland District Health Board, Auckland, New Zealand

joseph.chen@auckland.ac.nz

Background: Depressive disorders are leading causes of disability, but current pharmacotherapies and psychotherapies typically take several weeks before achieving efficacy. Comparatively, prior studies involving intravenous scopolamine infusions reduced depressive symptomologies compared to saline placebo infusions within days. However, several parameters of scopolamine's antidepressant effect remain unknown, such as the dose-response profile and washout period. Glycopyrronium was chosen as the active placebo as it has antimuscarinic properties similar to scopolamine but is unable to cross the blood-brain barrier. Methods: The present clinical trial recruits depressed individuals and randomises participants to receive single intravenous doses of either scopolamine hydrobromide (4-6µg/kg) or glycopyrronium bromide (4µg/kg). The primary mood outcome measure for detecting depression severity was the Montgomery–Åsberg Depression Rating Scale, which was administered from pre-infusion and 1, 3, 7, 14, 28, 42 days post-infusion. Results: Both scopolamine and glycopyrronium reduce depressive symptomologies within a day of drug administration and maintain such antidepressant effect until 1-week post-drug administration. No significant mood difference was detected between the two drugs. Conclusion: The results show scopolamine has no more antidepressant effects than the active placebo glycopyrronium. This raises questions about the magnitude of the placebo response and the central and peripheral antimuscarinic contributions to depression.

Poster 6.29

Parkinson's disease non-motor symptoms did not worsen during COVID-19 lockdown

Kyla-Louise Horne[1,2], Maddie Pascoe[1], Leslie Livingston[1,2], Beth Elias[1], Marie Goulden[1,2], Sophie Grenfell[1], Bob Young[1], Rebekah Blakemore[1,3], Campbell Le Heron[1,2,4], Toni Pitcher[1,2], Daniel Myall[1], Reza Shoorangiz[1,2,5], Roeline Kuijer[5], Michael MacAskill[1,2], John Dalrymple-Alford[1,2,5], Tim Anderson[1,2,4]

[1]New Zealand Brain Research Institute (NZBRI), [2]University of Otago, Christchurch, New Zealand, [3]University of Otago, Dunedin, New Zealand, [4]Christchurch Hospital, [5]University of Canterbury, Christchurch, New Zealand

kyla.horne@nzbri.org

European and Middle Eastern Parkinson's disease patients reported increased non-motor symptoms during COVID-19 lockdowns. These symptoms, however, were already elavated in Parkinson's populations prior to lockdowns, and direct comparisons with pre-lockdown evidence is lacking. During New Zealand's brief but stringent lockdown, 171 Parkinson's and 49 control NZBRI research participants gave self-reports of neuropsychiatric symptoms and everyday function via online surveys and telephone interviews. Bayesian mixed-effects models compared pre-lockdown and lockdown assessments. Caregiver burden was also assessed. Relative to pre-lockdown, everyday functional impairment increased in Parkinson's participants with mild cognitive impairment (93% posterior probability). There was no change in everyday functional impairment in the Parkinson's participants with dementia (77% posterior probability), which could be due to high pre-lockdown levels of impairment. There was no evidence of increased anxiety, depression and neuropsychiatric symptoms during lockdown (all <87% posterior probability). During lockdown, caregiver burden was greater for carers of Parkinson's participants with dementia and mild cognitive impairment compared to those with normal cognition (>99% posterior probability) and controls (90% posterior probability); the latter two groups did not differ (25% posterior probablity). We speculate that the low COVID-19 incidence and the nature of Government policy and response contributed to this lack of symptom aggravation.

Poster 6.30

Pūnaha Io: The New Zealand NeuroGenetic Research Bank

Miriam J Rodrigues[1], Christina Buchanan[1], Gina O'Grady[2], James Cleland[3], Richard H Roxburgh[1]

[1]Auckland City Hospital, [2]Starship Child Health, Auckland, New Zealand, [3]Bay of Plenty District Health Board, Tauranga, New Zealand

mrodrigues@adhb.govt.nz

Pūnaha Io, the New Zealand Neuro-Genetic Research Bank, is intended to be an easily accessible repository of clinical data linked to biological samples donated from patients with rare neurogenetic disorders. In collaboration with Te Ira Kawai, the Auckland Regional Biobank, it will provide infrastructure aimed at translational research. Extensive consultation with key stakeholders – including Maori and non-Maori participants with neurogenetic conditions, pharmaceutical companies, Pharmac, and scientists – led to the formation of the Research Bank. It 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. Here we describe the study population, the datasets, and the planned tissue sample collection.

Poster 6.31

Ryanodine Receptor: The next target for Alzheimer's disease

Ruben Vergara, Shane Ohline, Michelle Munro, Peter Jones

University of Otago, Dunedin, New Zealand

verru146@student.otago.ac.nz

Alzheimer's disease (AD) is the most common form of dementia. A major goal is to determine a pharmacological treatment since no clinical trial has been able to produce a new therapy for >20 years. 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. Here super-resolution microscopy (dSTORM) was used to analyse the structure of RyR2 clusters in the soma and synaptic regions of hippocampal CA1 neurons from wild type and AD (APPswe/PS1ΔE9) mouse brains. The results show a clear formation of RyR2 clusters in CA1 neurons. More excitingly, the data indicate that RyR2 clusters become fragmented in the APPswe/PS1ΔE9 brain in a manner consistent with those associated with altered calcium release in heart disease. This data suggests a novel pathway underlying the pathological calcium leak observed in AD, highlighting RyR2 as a potential therapeutic target. Supported by the Health Research Council (20/370).

Poster 6.32

The role of the dopamine D1 receptor in the negative symptoms of schizophrenia

Katherine Witt, Bart Ellenbroek

Victoria University of Wellington, Wellington, New Zealand

kate.witt@vuw.ac.nz

Schizophrenia is a psychiatric disorder that affects 1% of the world population. Current pharmacological treatment alleviates the positive symptoms (e.g., hallucinations, delusions) while the negative symptoms (e.g., anhedonia, amotivation, asociality) remain unresponsive. The negative symptoms are associated with poor occupation and social outcomes; therefore, it is critical to understand the neurobiological mechanisms of these symptoms in order to develop pharmacological treatment. Dopamine plays a critical role in anticipatory pleasure, social behaviour, and effort-based learning, and pharmacological studies suggest the D1 receptor mediates this effect. The current study utilises rats with a genetic reduction in the D1 receptor (Drd1 mutants) to examine the role of the D1 receptor in anticipatory pleasure, social behaviour, and effort-based learning. This presentation will specifically explore preliminary results in effort-based learning between wildtype rats and Drd1 mutants. Across various operant chamber experiments, Drd1 mutants exerted significantly less effort compared to wildtypes, suggesting that the D1 receptor mediates dopamine's role in effort and motivation.

Poster 6.33

Postpartum changes of the amygdala

Eileen Luders[1], Christian Gaser[2], Malin Gingnell[3], Jonas Engman[3], Inger Sundström Poromaa[3], Florian Kurth[1]

[1]University of Auckland, Auckland, New Zealand, [2]Jena University Hospital, Jena, Germany, [3]Uppsala University, Uppsala, Sweden

e.lueders@auckland.ac.nz

Research exploring the underlying neuroanatomical correlates of early motherhood seems to suggest that the period after giving birth is marked by tissue increases in the mother's brain. While some studies point to the amygdala as one of the areas undergoing postpartum changes, existing analyses did not discriminate between the different subregions of this functionally heterogeneous structure. Thus, to further extend this understudied field of research and to better understand the potential role of the amygdala when transitioning to motherhood, we applied an advanced region-of-interest technique that enabled us to analyse the amygdala as a whole as well as its different subareas, specifically the left and right centromedian (CM), laterobasal (LB) and superficial (SF) regions. Comparing the brains of 14 healthy women between immediate postpartum (within 1-2 days of childbirth) and late postpartum (at 4-6 weeks after childbirth), we revealed increases of the amygdala. However, effects manifested differentially across subareas, with particularly strong effects for the SF region, moderate effects for the CM region, and no effects for the LB region. These findings might reflect region-specific adaptations of the mother's brain tuning into the distinct and ever-changing needs of a newborn.

Poster 6.34

Understanding the expression of oligodendrocyte-specific ADAMTS4 following an SCI and its role as a potential modulator of oligodendrocyte maturation

Jerram P Sheehan, Connor A Clemett, Simon J O'Carroll

University of Auckland, Auckland, New Zealand

jshe969@aucklanduni.ac.nz

Following a spinal cord injury (SCI), chondroitin sulfate proteoglycans (CSPGs) become highly deposited and inhibit cellular regeneration. Oligodendrocytes suffer rapid cell death following an injury, with CSPGs acting as key inhibitors of their regeneration and remyelination. A disintegrin and metalloproteinase with thrombospondin motifs 4 (ADAMTS4) is an endogenous proteinase that can degrade CSPGs. ADAMTS4 is shown to be expressed by oligodendrocytes during development and is important for maturation and myelination. However, the role of ADAMTS4s in oligodendrocytes post-injury remains unclear. Immunohistochemistry was used to investigate ADAMTS4 expression in uninjured and contused rat spinal cord tissue, co-staining with markers such as myelin basic protein (MBP) for mature oligodendrocytes. Perilesional MBP + immunoreactive areas demonstrated an initial loss and recovery of ADAMTS4 over 28-days post-injury, indicating a co-response between oligodendrocytes and ADAMTS4. *In vitro* primary cell experiments are currently underway to investigate the regulatory mechanisms of ADAMTS4 expression, focusing on the activation of the Calcineurin / Nfat transcriptional pathway. Further, the role ADAMTS4 upregulation may play in promoting oligodendrocyte maturation post-injury is being explored by treating oligodendrocytes with TGFβ and CSPGs. These studies will inform future research into targeting and upregulating endogenous ADAMTS4 to aid cellular regeneration as a treatment for SCI.

Poster 6.35

Whodunnit: Inferring ALS Genotype from archival tissue

Miran Mrkela, Kyrah M Thumbadoo, Laura R Nementzik, Molly E V Swanson, Emma L Scotter

University of Auckland, Auckland, New Zealand

miran.mrkela@auckland.ac.nz

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by the progressive degeneration of motor neurons. Approximately 90% of ALS cases are classified as sporadic while the remaining are familial, indicating family history of the disease. While over 30 different genes have been linked to ALS, DNA-based genotyping requires access to high quality DNA which is not always accessible from archived fixed tissue. We propose an immunohistochemical neuropathology panel which can discriminate, in fixed brain tissue, between four ALS-causative genes: *C9ORF72*, *FUS*, *SOD1*, and *UBQLN2*. These account for 56% of causation in familial cases and 10% in sporadic cases. A systematic search was conducted of literature on ALS post-mortem human brain tissue, to examine the morphological and anatomical distribution of common protein aggregates and to correlate ALS genotype with neuropathology. We identified unique signatures of aggregating proteins in specific brain regions for each genotype. Based on those signatures we devised a single immunohistochemistry panel that could discriminate between the genotypes, and validated the panel on a cohort of ALS cases (including n=1 known case of each genotype, n=7 cases of unknown genotype). This panel will be of utility to researchers and brain banks with archived ALS brain tissue of unknown genotype.

Poster 6.36

Decreased salience network fMRI functional connectivity following a course of repetitive transcranial magnetic stimulation for treatment-resistant depression

Kate E M Godfrey, Suresh D Muthukumaraswamy, Cathy M Stinear, Nicholas Hoeh

University of Auckland, Auckland, New Zealand

k.godfrey@auckland.ac.nz

Repetitive transcranial magnetic stimulation (rTMS) is a treatment shown to be effective in treating major depressive disorder (MDD). However, the effect of rTMS on functional connectivity within the brain remains poorly understood. Few studies have investigated the effects of a course of rTMS on resting state network activity. In an open-label naturalistic study, resting state fMRI was collected prior to and following a four-week course of rTMS in 26 participants with MDD. Montgomery-Asberg depression rating scale scores showed a response rate of 42%. Clinical response to rTMS was correlated with reduced functional connectivity from baseline to post-rTMS within the salience network (SN), indicating reduced SN connectivity may be functionally relevant to how rTMS produces antidepressant effects. In an exploratory inter-network analysis, connectivity between the SN and posterior default mode network (pDMN) was lower following treatment, however this difference was not correlated with the antidepressant response. Local activity within these networks was also assessed using BOLD fractional amplitude of low frequency fluctuations (fALFF). Local activity increased in both the SN and pDMN following rTMS, however this increase was also not correlated with antidepressant response. Together these results provide evidence for the involvement of the SN in the antidepressant response to rTMS treatment.

Poster 6.37

The role of CD44 in neurodevelopment: Interactions with hyaluronan during neurite outgrowth within the rat hippocampus

Natasha G Lust, Rashi N Karunasinghe, Molly Abraham, Jaya Prasad, Justin M Dean

University of Auckland, Auckland, New Zealand

natasha.lust@aucklanduni.ac.nz

Within the last decade, the importance of successful neuronal development within the hippocampus has been extensively highlighted. This literature posits a link between molecular and structural abnormalities and several prevalent neurodevelopmental disorders that show common patterns in dysregulated development of neuronal processes. Recent work suggests that hyaluronan (a major component of the extracellular matrix) is critical for regulating the development of neurites. Naturally, the principal receptor of hyaluronan, CD44, is now proposed to be involved in early neurodevelopment, and is the main hypothesis for this Honours project. CD44 is a cell-surface glycoprotein, regulating several cellular processes throughout the body. Hyaluronan's involvement in cellular growth has sparked much interest in CD44 as a potential therapeutic target for neurodevelopmental disorders. Therefore, the aim of this study is to elucidate the contribution of CD44 to hippocampal neurite outgrowth. Dissociated hippocampal neuron cultures (E18 rats) were transfected using Lipofectamine3000, with DNA constructs containing short-hairpin loop RNA-interference sequences that knockdown CD44 receptor expression, and were compared with scrambled sequences. mApple Fluorescent reporter expression was used to identify transfected cells, and trace neuronal morphology, using Neurolucida 360. Preliminary datasets were blinded and traced, with findings intended towards clarifying an underlying role of CD44-hyaluronan signalling in neurodevelopment.

Poster 6.38

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

Nikita Lyons, Lucia Schoderboeck, Hollie Wicky, Stephanie Hughes

University of Otago, Dunedin, New Zealand

nikita.lyons@otago.ac.nz

Neurons were traditionally viewed as the key determinants of brain health and disease. Yet they do not exist in isolation, relying on glia for support and synaptic modulation through both direct, proximity-dependant interactions, and the release of secreted factors. Functional 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 glial activation. Additionally, late onset neurodegenerative disorders including Alzheimer's and Parkinson's disease show lysosomal defects and glial activation. However, the specific role of glial lysosomal dysfunction in these disorders is, as yet, unknown. Disruption of the cellular recycling system in astrocytes or microglia is hypothesised to impair glial function, and thus incite deterioration of neurons. We have optimised a method to produce primary cultures of astrocytes and microglia (~80% purity) from mice with a CLN6 mutation that disrupts lysosomal function. Lysosomal and mitochondrial phenotypes of pure glia cultures, and their effect on the morphology and lysosomal function of co-cultured, healthy human induced pluripotent stem cell derived cortical neurons are now being assessed. This research is interrogating the cellular drivers of neurodegeneration to help advise future treatment options for neurodegenerative diseases.

Poster 6.39

RyR2 trafficking and its role in Alzheimer's disease

Luke Phillips, Shane Ohline, Peter P Jones

University of Otago, Dunedin, New Zealand

philu654@student.otago.ac.nz

Alzheimer's Disease (AD) is an age-associated neurodegenerative disease that is the most common form of dementia in NZ. An emerging hypothesis is that the dysregulation of calcium (Ca^{2+}) signalling driving synaptic transmission can cause AD. Ca^{2+} plays an important role in the pre- and post-synaptic cell to initiate presynaptic neurotransmitter release and postsynaptic signal amplification. A protein critical in intracellular Ca^{2+} release on both sides of the synapse is the ryanodine receptor (RyR). Inappropriate release, or 'leak' of Ca^{2+} through RyR shows association with AD, however why this occurs is unknown. Ca^{2+} leak in cardiomyocytes has been attributed to the inappropriate ultrastructural placement of RyR within the cell. Whether inappropriate trafficking of RyR also occurs at the synapse in AD neurons is not known. Using spinning-disk confocal microscopy we will analyse single protein movement determining if there is increased RyR trafficking towards the synapse in AD culture neurons. Preliminary results will be presented tracking GFP- labelled RyR motion in HEK293 cells. Future work will include tracking labelled RyR in cultured neurons in a amyloid-beta treatment model of AD. This work is the first to determine how RyR is trafficked within a cell and whether this is altered in AD.

Poster 6.40

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

Rebecca M Lee[1,2], Lana Cleland[2], James A Foulds[2], Reza Shoorangiz[1,2,5], Mustafa M Almuqbel[1,3], Campbell Le Heron[1,2,4], Ross Keenan[3], Roger Mulder[2], Richard Porter[2], Giles Newton-Howes[6], Katie Douglas[2], Anthony Butler[2], Joseph M Boden[2], Tracy R Melzer[1,2]

[1]New Zealand Brain Research Institute, [2]University of Otago, [3]Pacific Radiology Group, [4]Canterbury District Health Board, [5]University of Canterbury, Christchurch, New Zealand, [6]University of Otago, Wellington, New Zealand

rebecca.lee@nzbri.org

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 forties, we explored the impacts of past heavy cannabis exposure on brain structure using MRI, with particular focus on brain atrophy, cerebral perfusion, function, and white matter structure. Between cannabis users (n=25) and non-using controls (n=25, matched for sex and tobacco use), we identified no significant atrophy in *a priori* regions of interest, including the hippocampus and amygdala, nor across the entire brain. 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 as they age.

Poster 6.41

The University of Auckland, Centre for Brain Research, Neurogenetics Research Clinic: An opportunity for translational research collaboration

Richard H Roxburgh, Julie Rope, Christine Tooke, Nicola Merrilees, Kay Yeoman, Tony Antunovich, Sian Hewetson, Luciana Pelosi, Rachael Taylor, Ashleigh Baker, Miriam Rodrigues

University of Auckland, Auckland, New Zealand

richard.roxburgh@auckland.ac.nz

The University of Auckland, CBR, Neurogenetic Research Clinic was established in 2019 to promote translational and clinical research in patients with neurogenetic conditions. These individually rare conditions are caused by pathological variants in single genes. The team is made up of a neurologist, study doctors, research nurses, study coordinators and a valued collaboration with the Duncan Foundation provides phsyios, occupational, and speech language therapists. We are undertaking pharma-sponsored drug trials in Pompe disease, Friedreich's ataxia, and mitochondrial myopathy as well as investigator-led therapeutic interventions in patients with inherited ataxias. We are collaborating with international natural history studies in myotonic dystrophy, spinal muscular atrophy and inherited ataxias and also undertaking local observational studies with muscle and nerve ultrasound and comprehensive vestibular testing. Patients enrolled in natural history studies receive clinical advice based on their assessments. We plan to receive and biobank samples (see presentation on Pūnaha Io – the New Zealand Neuro-Genetic Research Bank) on these patients annually. We are looking for basic science collaborators, throughout New Zealand and overseas, who would be interested in working on biomarkers, mechanisms of disease or developing treatments for these patients.

Poster 6.42

Paternal alcohol consumption causes reduced sensitivity to the motor coordination deficits of ethanol in offspring

Sahir Hussain[1], Heidi M D Lesscher[2], Darren J Day[1], Bart A Ellenbroek[1]

[1]Victoria University of Wellington, Wellington, New Zealand, [2]University of Utrecht, Utrecht, Netherlands

sahir.hussain@vuw.ac.nz

Alcohol use disorder (AUD) is known to run in families. One gene that has been associated with AUD is SLC6A4 (solute carrier family 6 member A4) which codes for the serotonin transporter (SERT). This study assessed serotonin dysfunction on adolescent ethanol consumption and subsequent intergenerational effects of drinking using a rat model: $SERT^{+/+}$ (regular functioning transporter), $SERT^{+/-}$ (50% reduction) and $SERT^{-/-}$ (complete reduction). Using an intermittent access two-bottle choice paradigm, F0 adolescent Wistar rats developed ethanol seeking behaviour with no SERT genotype differences in males. However, females consumed higher volumes of ethanol compared to males, with $SERT^{-/-}$ females showing the highest intake, indicating differences in the way genetic factors may act across sexes. Highest drinking males were mated to alcohol naïve females and offspring were compared with offspring of alcohol naïve parents. A clearer genotype effect was seen in the F1 generation with a genetic reduction in SERT activity leading to enhanced ethanol intake in both sexes. Importantly, paternal exposure to ethanol significantly reduced the ethanol- induced motor side effects in offspring as measured on the rotatord, an effect which was independent of genotype and sex. This suggests the involvement of epigenetic mechanisms in the intergenerational effects of alcohol.

Poster 6.43

Evaluation of evoked versus non-evoked behavioural responses in a preclinical model of demyelination mimicking multiple sclerosis

Sheein Hong, Kelly Paton, Andrew Biggerstaff, Bronwyn Kivell

Victoria University of Wellington, Wellington, New Zealand

sheein.hong@vuw.ac.nz

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system, affecting 2.5 million people globally. While current pharmacotherapies modulate the immune system, none promote myelin repair or restore function. The toxin-induced cuprizone model of demyelination is a preclinical model used to study non-immune mediated demyelination to model more progressive forms of MS. In this study, we quantified anxiety-like behaviours using the elevated-zero maze and non-evoked activity utilising home-cage activity and the murine motor skill sequence (MOSS) wheel. We show cuprizone-intoxicated male mice exhibited significantly more anxiety-like behaviours than healthy mice ($t(18)=4.48$, $p<0.001$), but significant differences were not seen in female mice ($t(27)=1.395$, $p=0.174$), suggesting that male and female mice may exhibit differences in anxiety-like behaviour induced by cuprizone. In the MOSS wheel, male ($F(1,16)=22.84$, $p<0.001$) and female ($F(1,14)=30.95$, $p<0.001$) mice both displayed significant decreases in accumulated distance travelled on the complex wheel, showing deficits in motor coordination in both sexes. This data supports growing evidence that non-evoked measures of home-cage activity are sensitive measures that show a wide window of locomotor deficits following cuprizone-induced demyelination. We conclude that this is a robust model for investigating the effects of therapeutic drugs that promote recovery in MS.

Poster 6.44

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

Sheryl Tan[1], Helen Murray[1,2], Simon J O'Carroll[1]

[1]University of Auckland, Auckland, New Zealand, [2]National Institutes of Health, Bethesda, United States of America

sheryl.tan@auckland.ac.nz

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. Single-label, chromogenic immunohistochemistry on fixed human spinal cord tissue revealed distinct patterns of labelling for calretinin, parvalbumin, and calbindin within C5, T5, and L1 segments. Further, multiplex immunohistochemistry revealed their relationships with key neuroimmune mediators microglia (IBA-1) and astrocytes (GFAP). Significance: 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 neuroimmune mediators in relation to the distribution of CaBPs and identify potential areas of vulnerability in SCI.

Poster 6.45

Mechanisms of astrocyte-mediated regulation of synaptic plasticity in the hippocampus

Shruthi Sateesh, Anurag Singh, Owen D Jones, Wickliffe C Abraham

University of Otago, Dunedin, New Zealand

shruthi.sateesh@postgrad.otago.ac.nz

Synaptic plasticity such as long-term potentiation (LTP) and long-term depression is fundamental to the neural processes underlying learning and memory. Interestingly, synaptic plasticity itself can be dynamically regulated by prior activity, by processes termed 'metaplasticity' which can be expressed both homosynaptically and heterosynaptically. Here we tested a novel heterosynaptic metaplastic effect by undertaking field potential recordings in rodent hippocampal slices. Remarkably, a strong preconditioning stimulation (''priming'') to the afferents of stratum oriens in CA1 inhibited LTP induced 30 minutes later at perforant path synapses onto granule cells in the dentate gyrus (DG), a neighboring region ~800 µm away. This priming-induced LTP inhibition does not require canonical neuronal triggers such as the release of the transmitters glutamate or GABA. However, this inhibition of LTP was blocked by clamping astrocytic Ca^{2+} during priming. The involvement of astrocytes was further confirmed using $IP3R2^{-/-}$ mice that do not display Ca^{2+} release from IP3R2-dependent stores located specifically in astrocytes. Additionally, we have confirmed the cytokine tumour necrosis factor alpha (TNFα) acting on TNFα receptor-1 as a critical signaling molecule. This long-range, trans-regional inhibition of LTP mediated by astrocytes may play a vital role in hippocampal information processing while also homeostatically adjusting plasticity thresholds to avoid excitotoxicity.

Poster 6.46

Measuring hippocampal activity in conjunction with behaviour utilising head-mounted miniaturised microscopes

Skylar Pollack, Yukti Vyas, Zahra Laouby, Yewon Jung, Johanna M Montgomery, Juliette E Cheyne

University of Auckland, Auckland, New Zealand

skylar.pollack@aucklanduni.ac.nz

Alzheimer's disease is a neurodegenerative disorder which produces atrophy and subsequent dysfunction with a marked reduction in the cerebral cortex and hippocampus. To date, nearly all human brain studies are post-mortem and very few studies have examined neuronal activity during animal behaviour in Alzheimer's transgenic models *in vivo*. Therefore, the aim of our research is to investigate neuronal function with simultaneous behavioural testing in $APP_{swe}/PS1_{dE9}$ mice utilising head-mountable miniaturised microscopes (miniscopes). Mice were injected with a genetically encoded activity reporter (GCaMP7 AAV1) and implanted with a gradient-refractive index (GRIN) lens and cranial baseplate, to allow attachment of the miniscope. $APP_{swe}/PS1_{dE9}$ and wildtype mice were subject to open field, y-maze, and novel object recognition tests to measure behaviour deficits in learning and memory, while neuron dynamics were simultaneously recorded by *in vivo* imaging of GCaMP7 expressing hippocampal CA1 neurons with miniscopes. We confirmed that $APP_{swe}/PS1_{dE9}$ mice show increased anxiety, as well as deficits in spatial memory. We have optimised our image processing and analysis routines to extract neuronal firing data and relate this to behaviour. This study is enabling us to link differences in neuronal firing activity to behavioural deficits in memory and anxiety in Alzheimer's Disease.

Poster 6.47

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

Christopher Erb[1], Matthew Welhaf[2], Bridget Smeekens[2], David Moreau[1], Michael Kane[2], Stuart Marcovitch[2]

[1]University of Auckland, Auckland, New Zealand, [2]University of North Carolina at Greensboro, Greensboro, United States of America

christopher.erb@auckland.ac.nz

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 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 6.48

Investigating platelet-derived growth factor signalling in primary human brain cells for elucidation of physiological function and GBM disease mechanism

Susan Y S Li[1], Rebecca Johnson[1], Patrick Schweder[1,2], Edward Mee[1,2], Thomas I-H Park[1], Michael Dragunow[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

susan.li@auckland.ac.nz

Platelet-derived growth factor (PDGF) is a powerful mitogen for mesenchymal cells in the brain. Physiologically, PDGF signalling is integral to the recruitment and maintenance of pericytes, an important mural cell for blood-brain barrier formation and function. Aberrance in this pathway is implicated in diseases such as glioblastoma (GBM), a highly malignant and invasive grade IV primary brain tumour, where overexpression of the receptor is commonly found. Despite evidence of receptor amplification, pharmacological targeting of this pathway has largely failed. Therefore, it is imperative to gain a better understanding of the signalling mechanism driven by this receptor. Surgically resected epilepsy pericyte and GBM tumour cell lines were established to characterise PDGF signalling using a number of *in vitro* assays. Treatment of pericytes with PDGF ligands including PDGF-AA/BB/CC/DD lead to activation of MAPK and PI3K/Akt pathways and subsequently increases pericyte proliferation. Comparatively, GBM cells display differential responses to ligand stimulation. This suggests that aside from receptor overexpression, aberrance in the signalling pathway itself could contribute to pathogenesis. These findings enhance the understanding of GBM disease mechanism and help inform therapeutic development.

Poster 6.49

Preparation of human brain tissue for studies of neurodegenerative diseases

Phoebe Anscombe, Remai Parker, E Marika Eszes, Henry J Waldvogel, Maurice A Curtis, Richard L M Faul

University of Auckland, Auckland, New Zealand

p.anscombe@auckland.ac.nz

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 6.50

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

Svenja Meissner, Brad Raos, Darren Svirskis

University of Auckland, Auckland, New Zealand

svenja.meissner@auckland.ac.nz

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 the potential for off-target effects. These challenges could be overcome by the temporal and spatial control of NFs delivery to its target site. Therefore, a delivery system where release can be stimulated via external triggers, like ultrasound, might improve the therapeutic efficacy of NFs. A model drug (FITC-lysozyme) was loaded into hydrogel-based drug delivery systems and the efficacy of active and passive loading was explored. The release of the model drug was compared with and without stimulation. The results show that active loading has a higher loading efficacy in gelatin methacryoyl (GelMA) and poly(N-isopropylacrylamide) (pNIPAM) compared to passive loading. The release of FITC-lysozyme from the hydrogels was increased by ultrasound stimulation. In the future, these hydrogel-based ultrasound-triggered delivery systems will be loaded with NFs and NFs will be released in a controlled manner to support the regrowth of nerve cells.

Poster 6.51

Microglial and astrocytic changes in the human cingulate cortex in Huntington's disease

Thulani Palpagama[1], Clinton Turner[1,2], Henry Waldvogel[1], Richard Faull[1], Andrea Kwakowsky[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

t.palpagama@auckland.ac.nz

Huntington's disease (HD) is a genetic neurodegenerative disease in which patients present with a number of symptoms including the loss of motor control, behavioural and psychiatric symptoms, and cognitive decline. The cingulate cortex plays a vital role in learning, memory and emotion processing. Previous research in our laboratory suggests that the cingulate cortex is affected in HD, and mood symptoms in HD cases are linked with major cell loss in the anterior cingulate cortex. Significant evidence of neuroinflammatory changes in HD is evident in the literature and has been hypothesised to promote cell death. Microglia and astrocytes are non-neuronal cells which contribute to an inflammatory response. Our study examined microglial and astrocytic changes in the middle cingulate cortex in human HD post-mortem tissue using immunohistochemistry. We identified the presence of morphological changes in microglia and astrocytes in HD and quantitative analysis of these alterations are in progress. Understanding the role of astrocytes and microglia in the human cingulate cortex and how they correlate to cell death and symptomology may help us understand the underlying mechanisms of cell death in HD. Ultimately, a better understanding of the inflammatory environment in HD will aid the development of targeted therapies for the disease.

Poster 6.52

Dense sampling to enable precision mapping in systems neuroscience

Kristina Wiebels, David Moreau
University of Auckland, Auckland, New Zealand
k.wiebels@auckland.ac.nz

Research in neuroscience has long relied on average-based estimates to further our knowledge about neural systems. For these estimates to be reliable and generalisable—and thus for findings to be replicable—both adequate statistical power and sufficient individual-level data are required. In recent years, a number of functional MRI (fMRI) studies have begun to focus on intensive assessments of single or a small number of individuals, starting to provide important insights about the reliability and stability of functional architectures of the human brain. Here, we present findings from studies that have used this emerging dense sampling approach, and reflect on the significant advances in our understanding of brain function gained thus far. Specifically, we discuss the advantages of dense sampling, and consider how it can complement more traditional approaches, both with regard to theoretical understanding and methodological advancements. We also point out limitations that need to be considered for the field to integrate this approach in an effective manner. We further examine how dense sampling could be extended to other techniques in systems neuroscience, and conclude with a discussion of possible applications, particularly in the context of personalized interventions—for both healthy and clinical populations—that go beyond group characteristics to instead target individuals.

Poster 6.53

Development of a large animal model of Fragile X syndrome for therapeutic testing

Victoria Hawkins, Jessie Jacobsen, Renee Handley, Kimiora Henare, Russell Snell
University of Auckland, Auckland, New Zealand
victoria.hawkins@auckland.ac.nz

Fragile X syndrome (FXS) is a neurodevelopmental disorder (1:4000 males, 1:8000 females) caused by an expanded triplet repeat in the 5'UTR of the FRM1 gene. The hypermethylation of the expanded repeat leads to silencing of the gene, a lack of FMR1 protein (FMRP), and the condition's onset. There is currently no effective treatment addressing the cause of FXS. New treatments are traditionally developed using preclinical testing in a model organisms, most commonly rodents. Unfortunately, FXS rodent models have been unable to predict the efficacy of drugs in humans. To help improve drug development for FXS, we are developing a novel ovine model that will better represent the human condition in brain size and structure and neurodevelopmental rate. Because a lack of FMRP causes FXS, we have chosen a knockout approach to model the condition. We have developed the tools to target the ovine FMR1 gene using a pair of guide RNAs for CRISPR-Cas9 mediated cleavage that disrupt the FMR1 Met codon and removes the first exon. This targeted deletion approach works at a remarkable 80% efficiency in cultured cells with a concomitant reduction of FMRP production in edited cells. We will present these results and further progress towards the model.

Poster 6.54

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

Rashi N Karunasinghe[1,2], Molly Abraham[1], Tania M Fowke[1], Tomomi Tani[2], Justin M Dean[1]

[1]University of Auckland, Auckland, New Zealand, [2]Marine Biological Laboratory, Woods Hole, United States of America

rashika.karunasinghe@auckland.ac.nz

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 the 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 cornerstone deposition of hyaluronan regulates early hippocampal neurite outgrowth.

Poster 6.55

Investigating the subcellular roles of *HDAC4* in *Drosophila* neuronal development

Wei Jun Tan, Helen L Fitzsimons

Massey University, Palmerston North, New Zealand

w.j.tan@massey.ac.nz

Histone deacetylase 4 is a Class IIa HDAC that regulates transcription and itself is regulated by nucleocytoplasmic shuttling. In neurons, nuclear and cytoplasmic pools of HDAC4 have been shown to promote neurodegeneration and neuroprotection respectively, however, the mechanisms through which HDAC4 acts in each subcellular compartment are not well understood. To investigate the subcellular roles, fly lines expressing nuclear (3A) or cytoplasmic (dMEF2 and dNLS) restricted mutants were generated and assessed for their impact on development of the mushroom body, a region important for learning and memory. Expression of wild-type HDAC4 (n=18 brains) or the 3A mutant (n=26) resulted in 100% malformed mushroom bodies (Fisher's Exact, $p<0.01$). While the dMEF2 mutation reduced the defects to ~20% (n=24, Fisher's Exact $p<0.01$), expression of the dNLS mutant resulted in similar penetrance to wild-type HDAC4 albeit with morphologies that were less pronounced. Together, these data indicate that the detrimental effects of overexpressing HDAC4 in subcellular compartments may be dependent on MEF2 binding. In support of this hypothesis, mutation of the MEF2 binding site in the 3A mutant reduced the defects to ~27% (n=22, Fisher's Exact $p<0.01$). Therefore, these data provide insight into the mechanism through which nuclear accumulation of HDAC4 impairs brain development.

7.1

Excising the lesion: A history of surgery for brain tumours in New Zealand

Edward Mee[1,2]

[1]Previous Consultant for Auckland District Health Board, [2]University of Auckland, Auckland, New Zealand

edward.mee@xtra.co.nz

From the pioneering efforts of general surgeons in the 1880s to the computer guided resections of cortically mapped lesions in awake patients, the history of neurosurgery for brain tumours will be outlined. The importance of the laboratory review of the resected specimens and the local research efforts to understand the clinical implications of the tumour biology will be discussed.

7.2

Finding the NEURO in neuro-oncology

Thomas I-H Park[1], Patrick Schweder[1,2], Edward Mee[1,2], Maurice A Curtis[1], Richard L M Faull[1], Mike Dragunow[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

thomas.park@auckland.ac.nz

Glioblastoma (GBM) is the most common and fatal form of a brain tumour in adults. The last 20 years have seen major advances in curative therapies for numerous peripheral tumours; however, failures to replicate these in GBM has left patients with a dismal survival time of 15 months. Many attribute this high attrition rate to the field approaching these tumours as just another high-grade tumour in the brain. However, after multiple clinical trial failures to repurpose high-profile anticancer agents for GBM, there has been a growing appreciation that primary brain tumours are unique neoplasms that arise *from* the brain and are heavily influenced or even aided by the brain's microenvironment. This talk will present work from our lab that sheds light on aspects of GBM tumour biology, which appear to hijack our brain's machinery to migrate, evade our immune system, and become resistant to current modes of therapy. These include the neuromigratory and neuroimmunoregulatory mechanisms, as well as the specific cellular populations and drugs transporters present in our brain. This presentation will focus on stimulating ideas and discussions in the neuroscience community to find brain-specific therapeutic targets for this incurable NEURO-oncological disease.

7.3

Ultrasmall superparamagnetic iron oxide MRI to distinguish brain tumours with a high-content of tumour associated macrophages

Tania Slatter[1,2], Jean Zhou[3,4], Louisa Lim[3], Ahmad Taha[1,3], Michael Reddy[3], Ben Wilson[3], Stephen Delvisco[4], Janice Royds[1], Noelyn Hung[1]

[1]University of Otago, Dunedin, New Zealand, [2]Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand, [3]Southern District Health Board, New Zealand, [4]TRG Imaging, Milford, Auckland, New Zealand

tania.slatter@otago.ac.nz

Tumour associated macrophages (TAMs) promote tumour progression. Gliomas with a high content of TAMs are associated with worse patient outcomes. Here, we investigated the effectiveness of using ultrasmall superparamagnetic iron oxide (USPIO) as an MRI contrast agent for predicting tumours with a high content of TAMs to improve surgical resection. Twelve patients, as part of a pilot study, with high-grade glioma were administered USPIO followed by MRI after an optimised time period. Immunohistochemistry was used to distinguish tumours with a high content of TAMs. Tumours from four individuals showed increased enhancement with USPIO compared to standard gadolinium contrast. These tumours had a high content of TAMs and showed aberrant tumour vessels with USPIO MRI. Patients receiving USPIO with a high content of macrophages in their tumours also had improved survival. In summary, USPIO MRI predicted gliomas with a high TAM content identifying additional regions for surgical resection. USPIO may also have therapeutic benefits.

7.4

Glioblastoma's incredible ability to suppress and evade anti-tumour immunity: How does glioblastoma do it?

E Scott Graham[1,3], Laverne Robilliard[1,3], Jane Yu[1,3], Graeme Finlay[2,3], Akshata Anchan[1,3], Kate Angel[3]

[1]Centre for Brain Research, [2]Auckland Cancer Society Research Centre, [3]University of Auckland, Auckland, New Zealand

s.graham@auckland.ac.nz

Glioblastoma is the most common and most deadly primary brain tumour, with a devastating median survival time of <15 months. Inevitable post de-bulking recurrence and no effective therapies lead to less than 5% of patients alive after 5 years of disease progression. Notably, glioblastoma has seen limited benefits from immunotherapy intervention despite promising outcomes in other cancer types. Further complicating therapeutic strategies are the presence of therapy-resistant cancer stem-like cell populations within the glioblastoma micro-environment. Therefore, we seek to understand the differential regulation of the immune system by glioblastoma cellular subtypes; particularly by the cancer stem-like population. Patient derived glioblastoma serum-derived and cancer stem-like models express numerous inhibitory immune-checkpoint ligands, with elevated expression detected on the cancer stem-like populations. Inhibitory checkpoint ligands engage with checkpoint receptors to negatively regulate effector T-cell function promoting an immune-suppressed microenvironment. While immunotherapies such as Nivolumab and Ipilimumab have shown significant clinical benefits in other cancers, in glioblastoma there have been limited responses. This talk will highlight some of our checkpoint expression data along with other potential molecular mechanisms of immune manipulation by the glioblastoma cells. These data reveal pronounced differences between the different glioblastoma cellular subtypes and how they potentially control the tumour microenvironment.

7.5

Mechanisms of therapy resistance in glioblastoma

Melanie McConnell[1,2,3], Anna Tribe[2,3], Devlin Forsythe[2,3], Paul Teesdale-Spittle[2,3]

[1]The Malaghan Institute of Medical Research, [2]The Centre for Biodiscovery, [3]Victoria University of Wellington, Wellington, New Zealand

melanie.mcconnell@vuw.ac.nz

Glioblastoma is the most aggressive and most common of the primary brain tumours, and a diagnosis of glioblastoma is inevitably fatal. Most people diagnosed with this neurological malignancy will not survive more than 2 years, even with the best treatments medical science can offer. There are several reasons for this. Surgical resection can only be used to reduce tumour burden; tumour cells migrate beyond the margins of the tumour and out of reach of radiotherapy; and glioblastoma cells are intrinsically resistant to DNA damaging chemotherapy, through a variety of mechanisms. Our research has focused on these resistance mechanisms, including a pathway where intervention appears to mitigate resistance. This talk will summarise our recent findings in this area, and describe the tools that we have generated to carry out this research. The aim of this is to stimulate the exchange of ideas and resources, and to build effective research collaborations that will lead to better outcomes for people diagnosed with this incurable neurological malignancy.

Poster 8.1

Towards an *in vitro* model to investigate the effects of neurotrophic gradients on neuronal cells

Anusha Dravid, Brad Raos, Simon J O'Carroll, Darren Svirskis

University of Auckland, Auckland, New Zealand

a.dravid@auckland.ac.nz

Neurotrophins are chemotrophic molecules known to support the outgrowth and navigation of regenerating axons towards functional targets after traumatic injury. *In vitro* assays of gradient-generation are crucial tools for evaluating the potential of therapeutic compounds prior to investigation within the complex *in vivo* environment. In the present work, we describe the design and fabrication of a novel compartmentalised gradient-generator to examine the effects of neurotrophic gradients on neuronal cells. Hydrogels were loaded into the center chamber, separating outer source and sink reservoirs. Sodium fluorescein (NaFl), FITC-Dextran 10 kDa (FD-10) and FITC-Dextran 40 kDa (FD-40) were used as model molecules to quantify the gradient. The fabricated gradient-generator is capable of rapidly establishing concentration gradients of within 1-hour, sustained over a period of 3 days. Biocompatibility studies demonstrated high cell viability (>96%) within the platform. Additionally, we compared the effects of different detachment reagents and report a new protocol to successfully replate differentiated SH-SY5Y neuron-like cells. These findings suggest that differentiated SH-SY5Y cells may be applied for use as a human cell model of axonal guidance, helping inform the development of new *in vivo* therapies.

Poster 8.2

EAAT2 expression in the Alzheimer's disease hippocampus, subiculum, entorhinal cortex and superior temporal gyrus

Oliver Wood[1], Jason Yeung[1], Thulani Palpagama[1], Clinton Turner[2], Henry Waldvogel[1], Richard Faull[1], Andrea Kwakowsky[1].

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

oliver.wood@auckland.ac.nz

Alzheimer's Disease (AD) is a neuropathological disorder characterized by the presence and accumulation of amyloid beta plaques and neurofibrillary tangles. Glutamate dysregulation and the concept of glutamatergic excitotoxicity is postulated to play a major role in the progression of AD. Alterations in glutamate uptake have been implicated in AD, with dysfunction of the excitatory amino acid transporter 2 (EAAT2), the main glutamate uptake transporter, reported. Several animal and few human studies have examined EAAT2 expression in multiple brain regions in AD but studies of the hippocampus, the most severely affected brain region, are scarce. As such, this study aims to investigate expression of EAAT2 qualitatively and quantitatively through DAB immunohistochemistry and immunofluorescence within the hippocampus, subiculum, entorhinal cortex and superior temporal gyrus regions, between human AD and control cases. Although no significant EAAT2 density changes were observed between control and AD cases, there was a significant translocation of transporter expression, with reduced immunoreactivity along astrocytic cell bodies, and increased diffuse staining in the neuropil. These spatial expression changes may contribute to glutamatergic dysfunction and subsequent neuronal damage in AD. Our findings warrant further investigation into the potential of this glutamate transporter as a therapeutic target.

Poster 8.3

Connexin hemichannel mimetic peptide attenuates cortical interneuron loss and perineuronal net disruption following cerebral ischemia in near-term foetal sheep

Panzao Yang[1], Joanne O Davidson[1], Tania M Fowke[1], Robert Galinsky[2], Guido Wassink[1], Rashika N Karunasinghe[1], Jaya D Prasad[1], Sumudu Ranasinghe[1], Colin R Green[1], Laura Bennet[1], Alistair J Gunn[1], Justin M Dean[1]

[1]University of Auckland, Auckland, New Zealand, [2]Hudson Institute of Medical Research, Melbourne, Australia

p.yang@auckland.ac.nz

Background: Perinatal hypoxia-ischemia is associated with disruption of cortical gamma-aminobutyric acid (GABA)ergic interneurons and their surrounding perineuronal nets, which may contribute to persisting neurological deficits. Blockade of connexin43 hemichannels using a mimetic peptide can alleviate seizures and injury after hypoxia-ischemia. In this study, we tested the hypothesis that connexin43 hemichannel blockade improves the integrity of cortical interneurons and perineuronal nets. Methodology: Term-equivalent foetal sheep received 30min of bilateral carotid artery occlusion, recovery for 90min, followed by a 25h intracerebroventricular infusion of vehicle or a mimetic peptide that blocks connexin hemichannels or by a sham ischemia + vehicle infusion. Brain tissues were stained for interneuronal markers or perineuronal nets. Results: Cerebral ischemia was associated with loss of cortical interneurons and perineuronal nets. The mimetic peptide infusion reduced loss of glutamic acid decarboxylase-, calretinin-, and parvalbumin-expressing interneurons and perineuronal nets. The interneuron and perineuronal net densities were negatively correlated with total seizure burden after ischemia. Conclusions: These data suggest that the opening of connexin43 hemichannels after perinatal hypoxia-ischemia causes loss of cortical interneurons and perineuronal nets and that this exacerbates seizures. Connexin43 hemichannel blockade may be an effective strategy to attenuate seizures and may improve long-term neurological outcomes after perinatal hypoxia-ischemia.

Poster 8.4

Task-based fMRI activation predicts intelligence better than resting-state functional connectivity and structural MRI

Alina Tetereva, Narun Pornpattananangkul

University of Otago, Dunedin, New Zealand

alina.tetereva@postgrad.otago.ac.nz

Human intelligence is associated with important life achievements, including educational success, wellness and income. Accordingly, understanding brain differences in intelligence is of great interest. Neuroscientists have used multiple brain-MRI modalities, including cortical thickness, brain volume and resting-state functional connectivity, to predict intelligence. Yet most studies have ignored the predictive ability of task-based activation, or the neural activity in response to events in cognitive tasks. Our aim is to determine if task-based activation improves prediction of intelligence over and above other brain-MRI modalities. Using the Human Connectome Project dataset (N=840 after exclusions), we applied Elastic Net and stacking to predict intelligence from the combination of different brain-MRI images: task-based activation from seven different tasks, cortical thickness, brain volume and resting-state functional connectivity. The final model predicted 32.3% of the variance in intelligence based on cross-validation. Importantly, the model based solely on task-based activation from seven different tasks had a comparable performance with the model with all brain-MRI modalities and had a much better performance than the model without task-based activation. Moreover, task-based activation from some tasks (working-memory, relational, language) performed better than other tasks. This suggests that important information about intelligence is selectively encoded in brain activation during specific cognitive processes.

Poster 8.5

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

Bhavya Chawdhary[1], Antonio de Souza[1], Emily Meyer[1], Stanley Stylli[2], Andrea Kwakowsky[1], Colin Green[1], Helen Danesh-Meyer[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Melbourne, Melbourne, Australia

b.chawdhary@auckland.ac.nz

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. Behavioral analysis showed a significant improvement in the behavioral 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 8.6

Dietary zinc supplementation partially rescues autism-associated behavioural deficits but not synaptic dysfunction in Shank2 knock-out mice

Kevin Lee[1], Yewon Jung[1], Yuktiben Vyas[1], Eunjoon Kim[2], Johanna M Montgomery[1]

[1]University of Auckland, Auckland, New Zealand, [2]Korean Institute of Advanced Science and Technology, Daejeon, South Korea

kevin.lee@auckland.ac.nz

SHANK2 is a member of SHANK family of synaptic proteins (SHANK1-3) that play a pivotal role in the structure and function of excitatory glutamatergic synapses in the brain. Mutations in *SHANK* genes have been found in people with autism spectrum disorder (ASD), a neurodevelopmental disorder characterised by social interaction and communication deficits, excessive repetitive behaiviouar and cognitive dysfunction. As synaptic localisation and structural stability of SHANKs are highly regulated by zinc, we have developed and tested zinc supplementation diet as a treatment strategy for Shank-associated mouse models of ASD. Here, we investigated the effectiveness of dietary zinc supplementation on behavioural and synaptic deficits that occur in a *Shank2* knock-out mouse model of ASD (Shank2$^{-/-}$). We performed behavioural tests, *ex vivo* hippocampal slice electrophysiology, and immunohistochemistry on Shank2$^{-/-}$ mice. We found that supplementing zinc in diets for 6 weeks prevented social interaction deficits and partially, but significantly, reduced hyperactive behaviours in Shank2$^{-/-}$ mice. However, short term spatial working memory deficit, as well as abnormal hippocampal glutamatergic synapse structure and function found in Shank2$^{-/-}$ mice, were not rescued by zinc supplemented diet. Together, we demonstrate that the zinc supplementation diet has a therapeutic potential for social interaction deficits in Shank2 ASD deletion.

Poster 8.7

Evaluating the effects of novel mixed opioid agonists on respiratory depression

Brittany Scouller[1], Diana Atigari[1], Amy Alder[1], Susruta Majumdar[2], Bronwyn Kivell[1]

[1]Victoria University of Wellington, New Zealand, [2]St Louis College of Pharmacy and Washington University School of Medicine, St Louis, United States of America

brittany.scouller@vuw.ac.nz

Mu Opioid Receptor (MOPr) analgesics are commonly prescribed for the treatment of moderate to severe pain, cancer pain and chronic pain by inhibiting ascending nociceptive pathways, producing analgesia. However, MOPr activation also causes constipation, addiction and respiratory depression. Stimulation of MOPrs in the respiratory control centres of the brain lead to respiratory failure. In 2018, over 46 thousand people in the United States died from opioid overdose. In an attempt to develop safer opioid-pain medications we investigated the effects of a novel mixed opioid agonist MP1104. MP1104 shows potent long-lasting effects in the tail-withdrawal assay in mice, a measure of thermal nociception. These effects are due to dual activation of kappa and delta opioid receptors *in vivo*. Using whole-body plethysmography measures of respiration in unrestrained awake C57BL/6J mice we showed that MP1104, in contrast to MOPr agonist morphine, possessed no respiratory depressive effects. Morphine significantly decreased minute volume, tidal volume, and inspiratory flow, whereas MP1104 ($p<0.01$), and active metabolites, SC71 ($p<0.001$) and SC52 ($p<0.01$) had no significant effects on these respiratory measures (n=6-7). This data provides promising evidence that mixed opioid agonists hold potential for the development of safer opioid pain medications in light of the global opioid epidemic.

Poster 8.8

The therapeutic efficacy of psilocybin in a rodent model of depressive- and anxiety-like symptomology

Henry Chafee, Bart Ellenbroek

Victoria University of Wellington, Wellington, New Zealand

chafeehe@vuw.ac.nz

Recent clinical research suggests that the serotonergic hallucinogen psilocybin may be an effective pharmacological adjunct to psychotherapy in the context of multiple psychiatric disorders, including depression and anxiety associated with terminal illness, treatment-resistant depression, and various forms of substance use disorder, among others. Although the results are promising, few attempts have been made to replicate them in preclinical models of psychopathology. This underdeveloped line of inquiry is critical in elucidating the neurobiological and behavioural mechanisms by which psilocybin might exert a therapeutic effect. The aim of the present study is to determine whether psilocybin reduces depressive- and anxiety-like symptomology that is environmentally induced with the early maternal separation paradigm. The short- and long-term effects of psilocybin will be assessed using the Affective Disorders Test. This newly developed behavioural assay not only allows for the simultaneous measurement of aspects of depression and anxiety in the same animal but can also be used to measure trait rather than just state anxiety. The results will shed light on whether the psychiatric benefits of psilocybin are exerted pharmacologically or are dependent on the context of psychotherapy and unique facets of human cognition.

Poster 8.9

The Salvinorin A analogue, EOM Salvinorin B, promotes remyelination in preclinical models of multiple sclerosis

Kelly Paton[1], Nikki Templeton[1], Afnan Al Abadey[1], Lisa Denny[1], Katharina Robichon[1], Thomas Prisinzano[2], Anne La Flamme[1,3], Bronwyn Kivell[1]

[1]Victoria University of Wellington, Wellington, New Zealand, [2]University of Kentucky, Lexington, United States of America, [3]Malaghan Institute of Medical Research, Wellington, New Zealand

kelly.paton@vuw.ac.nz

Multiple sclerosis (MS) is a devastating autoimmune disease caused by the immune system attacking and destroying the protective myelin coating nerve cells. There is no cure for MS and current disease-modifying treatments target the immune system and reduce damage by limiting the immune attack. Our approach is different, we aim to evaluate the ability of our novel kappa opioid receptor drugs to repair and restore myelin levels. We have discovered that the Salvinorin A analogue, ethoxymethyl ether Salvinorin B (EOM SalB), is highly effective at promoting functional recovery and remyelination in two models of MS. Following therapeutic administration in the experimental autoimmune encephalomyelitis model, EOM SalB significantly reduced disease score in treated mice and increased the percentage of mice recovered. This effect was reversed with the kappa opioid receptor antagonist nor-binaltorphimine. In the cuprizone-induced model of demyelination, administration of EOM SalB leads to improved health measure, as evidence by a restoration of body weight. Transmission electron microscopy of the corpus callosum showed that EOM SalB increased the number of myelinated axons and significantly increased myelin thickness. Overall, our findings show the potential of EOM SalB to promote recovery and remyelination in two preclinical models of MS, suggesting promise for clinical development.

Poster 8.10

Stepping outside the cell: Establishing the secretome as a marker of CLN6 Batten Disease

Kirstin McDonald, Hannah Best, Alison Clare, Hollie Wicky, Stephanie Hughes

University of Otago, Dunedin, New Zealand

kirstin.mcdonald@otago.ac.nz

CLN6 Batten Disease is a progressive neurodegenerative disease caused by mutations in the *CLN6* gene. CLN6, an endoplasmic reticulum membrane bound protein, regulates the secretion of proteins into the extracellular space. We tested the changes in the secreted protein profile of cells isolated from CLN6 Batten Disease mice ($Cln6^{nclf}$) and control heterozygous mice ($Cln6^{\pm}$). Neurons and glia isolated from $Cln6^{nclf}$ or $Cln6^{\pm}$ mice were co-cultured, media collected, and mass spectrometry was used to compare protein profiles. The cathepsin enzyme secretome profile was investigated further via immunoblotting and enzyme activity assays, and showed differences between control and $Cln6^{nclf}$ conditioned media. Viral-mediated gene therapy rescued the disease phenotype and restored the secretome, both in co-cultures and in mouse plasma. Within $Cln6^{nclf}$ cells, proteomics showed an increase in catabolic and cytoskeletal-associated proteins. These changes were partially corrected by gene therapy, suggesting these proteins as candidate *in vitro* biomarkers. Importantly, these *in vitro* changes showed promise for *in vivo* translation, with Cathepsin L activity reduced in both co-cultures and $Cln6^{nclf}$ plasma samples post gene-therapy. This work highlights the significance of the secretome as an *in vitro* model to study CLN6 pathogenesis. Furthermore, proteomic changes present a list of identifiers for monitoring disease progression and assessing potential therapeutics.

Poster 8.11

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

Sahan Jayatissa, Yihan Wu, Thomas Park, Iain Anderson, Vickie Shim, Samuel Rosset

University of Auckland, Auckland, New Zealand

cjay511@aucklanduni.ac.nz

Mild Traumatic Brain Injury (mTBI) is a leading cause of 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 a 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 8.12

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

Conor Nelson, Angela Wu, Alexandre Mouravlev, Dahna Fong, Deborah Young

University of Auckland, Auckland, New Zealand

conor.nelson@auckland.ac.nz

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 8.13

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

Denise Neumann, Sarah Herbert, Elizabeth Peterson, Lisa Underwood, Susan Morton, Karen Waldie

University of Auckland, Auckland, New Zealand

d.neumann@auckland.ac.nz

Poor maternal mental and physical health 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, perinatal and maternal health characteristics and early childhood receptive language and executive control. 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 and education during pregnancy may reduce the potential deleterious impact of adverse antenatal and perinatal conditions on children's early cognitive development.

Poster 8.14

Immunohistochemical mapping of huntingtin protein distribution using human brain tissue microarrays

Florence Layburn, Adelie Tan, Nasim Mehrabi, Richard Faull, Mike Dragunow, Malvindar Singh-Bains

University of Auckland, Auckland, New Zealand

florence.layburn@auckland.ac.nz

Huntington's Disease (HD) is a hereditary neurodegenerative disease caused by a mutation in the huntingtin gene resulting in the production and accumulation of mutant huntingtin (HTT). Despite being one of the pathological hallmarks of HD, there are limited studies characterising protein distribution, expression, and localization of either normal or mutant HTT. This study provides a comprehensive profile of HTT protein immunoreactivity in human brain tissue microarrays (HBTMAs) by utilising a range of antibodies specific to various regions along the HTT protein sequence. Through successful immunohistochemical staining of 9 HTT antibodies (2B7, 2E10, 4C9, EPR5526, MAB2168, MAB5490, MAB5492, MW1, MW8), this investigation illustrates the complexity of HTT expression throughout both healthy control and HD human brains. All antibodies resulted in diffuse, cytoplasmic HTT staining throughout both cohorts. Punctate HTT aggregates were more clearly labelled with antibodies MAB5492, MW8, MAB5490, MAB2168, and 4C9 and plaque-like inclusions were labelled with 2E10 and MW1. EPR5526 appeared to more cell-specific, staining pyramidal cells while 2B7 demonstrated neuropil immunoreactivity. Gaining a better understanding of the complex expression patterns of HTT protein as well as how to best identify its various forms will serve to advance our understanding of HD disease pathology towards a potential treatment.

Poster 8.15

Long-term meditators show reduced age-related grey matter loss in areas of the subgenual cingulate cortex

Florian Kurth[1], Sára Zsadanyi[1], Eileen Luders[1,2]

[1]University of Auckland, Auckland, New Zealand, [2]University of Southern California, Los Angeles, United States of America

f.kurth@auckland.ac.nz

Accumulating evidence suggests that meditation practices have positive effects on brain ageing overall. The anterior cingulate – particularly its four subgenual subregions which are involved in emotional regulation, cognition, and autonomic as well as endocrine functions – is well-known to be recruited during meditation. However, research into the possible effects of meditation on anterior cingulate ageing is currently missing. Here, we investigated differences in age-related grey matter loss between 50 long-term meditation practitioners (28 male, 22 female), aged between 24 and 77, and 50 age- and sex-matched controls. We applied an advanced region-of-interest technique that enabled a targeted analysis of age effects on the subgenual cingulate's four subregions (areas 25, 33, s24, and s32). The analysis revealed a significant age-related decline in all subregions in both meditators and controls, but with significantly lower rates of annual tissue loss in area s32 (left and right) and area 25 (right) in meditators. These regions have been shown to play a role in mood regulation, autonomic processing, and the integration of emotion and cognitive processes, which are all involved in and impacted by meditation. Overall, the results add further evidence to the emerging notion that meditation may slow the effects of ageing on the brain.

Poster 8.16

The New Zealand motor neurone disease registry: Four years on

Dympna Mulroy[1], Claire Reilly[2], Emma Scotter[3], James Cleland[4], Janet Turnbull[5], Julian Bauer[1], Melanie Glenn[2], Miriam Rodrigues[1], Richard Roxburgh[1,3]

[1]Auckland City Hospital, [2]Motor Neurone Disease New Zealand, [3]University of Auckland, Auckland, New Zealand, [4]Tauranga Hospital, Tauranga, New Zealand, [5]Capital and Coast District Health Board, Wellington, New Zealand

dympnam@adhb.govt.nz

Motor neurone disease (MND) is a rare, terminal, neuromuscular disease for which there are few treatments available, each with only modest benefits. However, there is a large amount of research and drug discovery underway. The New Zealand Motor Neurone Disease Registry facilitates participation in research for people in New Zealand with MND, and aids researchers in planning and recruitment for studies. This opt-in patient registry collects personal, demographic and clinical data. We report anonymised amalgamated data and outcomes since its inception. To date 296 participants have enrolled. Gender distribution reflects the demographics reported worldwide. 88.5% of participants identify as New Zealand European. 85% of participants are diagnosed with sporadic MND and 4% have familial MND. The remainder have not been diagnosed but have a family history. 6% have a positive result for an MND-causing genetic mutation. This data is important given the increasing number of genetic clinical studies. Levels of disability indicate the majority of participants are within the higher range of the ALSFRS-R scale. The registry has facilitated entry of participants into eight studies. The role of patient registries is ever changing, but with clear utility at every point along the pathway in support of research and drug discovery.

Poster 8.17

Overexpression of nutrient transporters for targeted drug-delivery of anti-cancer agents: Conjugation with heptamethine cyanine dyes

Elizabeth Cooper[1], Peter J Choi[1], Patrick Schweder[1,2], Edward Mee[1,2], Clinton Turner[2], Richard Faull[1], William A Denny[1], Mike Dragunow[1], Jiney Jose[1], Thomas I-H Park[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

e.cooper@auckland.ac.nz

Glioblastoma is the most common and aggressive primary brain tumour in adults. The development of anti-cancer agents for brain tumours is challenged by the blood-brain barrier and the resistance conferred by the local tumour microenvironment. Heptamethine cyanine dyes (HMCDs) are a class of near-infrared fluorescence compounds that have recently emerged as promising agents for drug delivery. The reported mechanism of uptake of HMCDs in peripheral tumours is through a hypoxia-inducible factor 1-alpha (HIF1α)-organic anion-transporting polypeptide (OATP) signalling axis. However, the expression and regulation of these transporters in glioblastoma is not well studied. We sought to establish the expression profile of OATPs in human glioblastoma patients *in situ* and *in vitro*, and the reliance of HMCDs on OATPs for tumour uptake. Surgically resected glioblastoma and epilepsy tissue samples were co-labelled for OATP isoforms in addition to cell-type-specific markers. Primary patient-derived glioblastoma cell lines were used to validate OATP-HIF1α signalling axis *in vitro*. We report overexpression of OATPs glioblastoma compared to non-tumour samples, *in situ* and *in vitro*. HMCDs used a combination of OATPs and endocytosis mechanisms for accumulation into GBM cells. These results highlight the opportunity for targeting OATPs and endocytosis mechanisms for the delivery of anti-neoplastic agents in glioblastoma.

Poster 8.18

Emergence of functional connectivity networks on a brain-inspired spiking neural network model

Gurleen Singh[1], Nikola Kasabov[1,2], Gonzalo Maso Talou[1], Mahyar Osanlouy[1]

[1]University of Auckland, [2]Auckland University of Technology, Auckland, New Zealand

gsin255@aucklanduni.ac.nz

Understanding the true nature of neural changes underlying brain function requires an integrated systems-level approach. Great effort has gone into the investigation of functional connectivity networks (FCNs) which represent brain regions that correlate in activation during resting-state or task. Such investigations have unveiled the scale-free, small-world, modular and rich-club organization of brain function. The model presented here aims to create FCNs derived from simulated spiking neuronal networks (SNNs). These SNNs learn patterns of association present in simultaneously recorded EEG and fMRI data through principals of Hebbian learning. The connections formed are spatially restricted to projections of axonal bundles observed in the averaged DTI across individuals. Traditionally, brain networks are investigated by graph representation derived from the correlation between regionally-averaged time courses. In contrast, the networks of function that emerge in our model are a product of Hebbian learning and are restricted by biological plausibility provided by our multimodal approach. This biologically-restricted emergence of FCNs allows the investigation into the causal mechanisms by which such networks are shown to be disrupted in neurological disorders.

Poster 8.19

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

Hannah Hawley, Helen Fitzsimons

Massey University, Palmerston North, New Zealand

h.hawley@massey.ac.nz

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 tetramerization. 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 8.20

Blood-brain barrier pathology in the Huntington's disease human brain

Ieuan Sargent, Adelie Tan, Malvindar Singh-Bains, Nassim Mehrabi, Richard Faull, Mike Dragunow

University of Auckland, Auckland, New Zealand

ieuan.sargent@auckland.ac.nz

Although there are no current disease-modifying treatments for Huntington's disease (HD), clinical trials have targeted the brain through intrathecal injections of Huntington protein- lowering therapies. Whilst this is one approach to deliver potential therapeutics to the brain, other delivery pathways exist. In healthy individuals, the blood-brain-barrier (BBB) serves as a highly selective barrier, protecting the brain from foreign matter. However, during disease, the BBB may become dysfunctional and problematic for drug delivery. In HD, evidence surrounding BBB dysfunction is emerging and has been linked to disease pathogenesis. Furthermore, recent studies have suggested that pericytes, a key component of the BBB, are a promising therapeutic target due to the role of these cells in maintaining BBB integrity and mediating neuroinflammation. This study investigates key components of the BBB through immunohistochemical screens on human brain tissue microarrays, which contain up to 56 cortical samples from both control and HD brains. Mural, endothelial, extracellular matrix, and leakage markers will be quantified via automated high-throughput imaging and analysis. Preliminary results from initial screens have highlighted optimal markers for both pericytes and surrounding BBB components. Deducing the role of the BBB and its various cellular components in HD will unveil new targets for treatment strategies.

Poster 8.21

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

Helen Murray[1,2], Kory Johnson[2], Andrea Sedlock[2], Blake Highet[1], Birger Victor Dieriks[1], Praju Vikas Anekal[1], Richard L M Faull[1], Maurice A Curtis[1], Alan Koretsky[2], Dragan Maric[2]

[1]University of Auckland, Auckland, New Zealand, [2]National Institutes of Health, Bethesda, United States of America

h.murray@auckland.ac.nz

Multiplexed immunohistochemical (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 unbiased 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 8.22

Optogenetic modulation of beta amyloid-induced brain network changes in the mouse hippocampus

Isabella Lavas[1], Laura McNamara[1], Soo H Kim[1], Warren Tate[2], Katie Peppercorn[2], Stephanie Hughes[2], Louise Parr-Brownlie[2], Henry J Waldvogel[1], Richard L M Faull[1], Andrea Kwakowsky[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Otago, Dunedin, New Zealand

isabella.lavas@auckland.ac.nz

Alzheimer's disease (AD) is a debilitating neurodegenerative disorder and a global health concern due to the lack of efficacious treatments and a growing aging population. The aim of this study was to investigate the behavioural and cellular effects of optogenetically increasing GABA release via GABAergic interneurons within the CA1 hippocampal subregion following beta-amyloid (Aβ) hippocampal injection. C57BL/6 male mice received bilateral hippocampal stereotaxic injections of a lentiviral vector (LV-GAD67-ChR2-mCherry), inducing GABAergic interneuron-specific expression of channelrhodopsin-2 which conducts a depolarising cation influx upon blue light (470nm) exposure. Mice were also stereotaxically injected with $A\beta_{1-42}$, implanted with a wireless optogenetic device, and blue light stimulus was administered. One week later, mice were subjected to novel object alteration and recognition (NOA and NOR) tests to examine hippocampal function. Hippocampal cells were stained with NeuN/Hoechst, Iba-1 and GFAP and further analysed via fluorescence immunohistochemistry. Optogenetic activation of GABAergic interneurons in $A\beta_{1-42}$-injected mice improved NOR outcomes and reduced neurotoxicity within the CA1 stratum pyramidale indicating that elevated GABA release exerted a neuroprotective effect which likely ameliorated cognitive and memory function as demonstrated by improved NOR scores. Understanding GABAergic network changes in AD can identify novel therapeutic targets and treatment for AD.

Poster 8.23

Identification and characterisation of distinct α-synuclein strains in different human α-synucleinopathies

James Wiseman, Helen Murray, Victor Dieriks, Maurice Curtis

University of Auckland, Auckland, New Zealand

j.wiseman@auckland.ac.nz

α-synucleinopathies are a class of pathologically and phenotypically heterogeneous neurodegenerative disorders that are characterised by the aggregation of insoluble α-synuclein. Currently, the exact mechanisms that underlie this heterogeneity remain elusive. α-synuclein aggregates in a microenvironment-dependent manner and is capable of forming several distinct 3D-conformations, called strains. It is hypothesised that distinct α-synuclein strains precipitate the clinical and pathological heterogeneity of α-synucleinopathies. To interrogate this, we sought to identify and characterise distinct strain differences and pathological variations across several pathologically significant regions of Parkinson's disease (PD) and cortical Lewy body disease (CLBD) brains, using 12 epitope-specific α-synuclein antibodies. Multiplex immunohistochemistry was conducted in the olfactory bulb, medulla oblongata, substantia nigra and middle temporal gyrus to determine an optimal combination of α-synuclein antibodies that collectively identify each of the well-defined structural domains and serine 129 phosphorylation status of α-synuclein. Our data suggest differential staining signatures for antibodies that detect the N-terminus and NAC-region of α-synuclein, comparative to those that detect the C-terminus and phosphorylated serine 129. These data will be combined with real-time quaking-induced conversion assays and subsequent electron microscopy data to allow the definitive identification of α-synuclein strains and delineation of distinct α-synucleinopathies based on epitope-specific staining signatures and strain variability.

Poster 8.24

Development of a unique set of human neuron knockdown models of Batten disease using human CRISPRi in derived neurons

Janet Boyu Xu, Indranil Basak, Stephanie Hughes

University of Otago, Dunedin, New Zealand

janet.xu@otago.ac.nz

Batten disease is a group of fatal inherited childhood brain disease manifesting symptoms like blindness, seizures and dementia. A key hallmark of Batten disease is the accumulation of auto fluorescent storage materials in dysfunctional lysosomes in neurons. To understand the pathophysiology underlying the childhood forms of Batten disease, we have developed induced pluripotent stem cell (iPSC)-derived human cortical neuronal cultures with inhibited expressions of *CLN* genes. Using a CRISPRi system with integrated deactivated Cas9, we inhibited the transcription of *CLN2*, *3* and *10*. We designed five small guide RNAs (sgRNAs) against *CLN2,* three sgRNAs against each of *CLN3* and *CLN10.* The sgRNAs were cloned into lentiviral vectors and iPSC-derived human neurons were transduced with the sgRNA lentiviruses individually. We confirmed that all sgRNAs against CLN2 and CLN3, and two out of three CLN10 sgRNAs show more than 90% inhibition of *CLN2, CLN3* and *CLN10* expression in the human neurons. Currently, we are assessing the phenotypic changes, including lysosomal, mitochondrial activity, and synaptic endocytosis, in neurons with inhibited expression of CLN2, CLN3, and CLN10. Our CLN inhibition models in human neurons will serve as a unique platform to screen potential therapeutic candidates to treat the three childhood forms of Batten disease.

Poster 8.25

Mapping the myeloid landscape of glioblastoma tumours

Zoe Woolf[1], Molly E V Swanson[1], Emma L Scotter[1], Patrick Schweder[1,2], Edward Mee[1,2], Richard L M Faull[1], Thomas I-H Park[1], Michael Dragunow[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand

z.woolf@auckland.ac.nz

Glioblastoma is the most aggressive form of brain tumour with a characteristically immunosuppressed microenvironment comprised of several different niches. Although these tumours contain a milieu of immune cells, the predominant populations comprise peripherally-derived tumour-associated macrophages (TAMs) and brain-resident microglia. Despite microglia and TAMs being two ontogenetically distinct populations, their distribution and potentially differing functions across the glioblastoma landscape are not well defined. Surgically resected glioblastoma tissue was immunofluorescently labelled to define tumour niches and infer myeloid-cell function. Single-cell image analysis was conducted to define microglia (P2RY12+ Iba1+) and TAMs (P2RY12- Iba1+) and to quantify protein expression across tumour niches delineated by Ki67, GFAP, and lectin immunoreactivity. We found that microglia predominantly reside in the tumour periphery, displaying higher expression of activation markers CD163, CD14, and CD68 towards the tumour core. TAMs predominantly resided in the tumour core and perivascular niche, in close proximity to blood vessels and areas of vascular leakage. These findings demonstrate that microglia and TAMs reside in distinct tumour niches and express different proteins that may differentially drive tumour growth and malignancy. Understanding this myeloid landscape will be critical in informing potential niche-targeted immune therapies.

Poster 8.26

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

Jordan Lloyd[1], Andrew Yee[2], Pang Ying Cheung[1], Kathryn Todd[1], Anower Jabed[1], Rashika Karunasinghe[1], Srdjan Vlajkovic[1], Peter Freestone[1], Prasanna Kallingappa[1], Janusz Lipski[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Colorado, Denver, United States of America

jt.lloyd@auckland.ac.nz

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 wild-type 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.

Poster 8.27

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

Ruth Monk, Blake Highet, Taylor Stevenson, Ryan Dixon, Jonathan Sperry, Maurice A Curtis

University of Auckland, Auckland, New Zealand

r.monk@auckland.ac.nz

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 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 pre-formed, recombinant human α-synuclein fibrils and low-dose proteasome inhibition on proteasome function in differentiated SH-SY5Y neurons to establish a model of impaired protein processing that occurs in PD. 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 8.28

Environmental Sensitivity and its impact on learning for higher education students

Kaaryn Cater

Whitireia Weltec, Wellington, New Zealand

kaaryn.cater@whitireia.ac.nz

People differ in their levels of sensitivity to internal, external, social and emotional stimuli and generally fit into three sensitivity groups of low, medium and high on the sensitivity spectrum 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 benefit disproportionately from positive experiences than less sensitive people. Further, high sensitivity is associated with deep cognitive functioning, creativity, memory and metacognition. This study (n=365) explored the associations between levels of sensitivity as measured by the short form Highly Sensitive Person Scale and success-promoting attitudes and strategies as measured by the Perceived Success in Study Survey for post-secondary 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 the first study investigating the impact of environmental sensitivity on learning for higher education students and highlights interesting educational implications for students at either end of the sensitivity spectrum.

Poster 8.29

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

Kyrah M Thumbadoo[1], Birger V Dieriks[1], Helen C Murray[1], Molly E V Swanson[1], Ji Hun Yoo[1], Nasim Mehrabi[1], Beth J L Synek[1,2], Clinton Turner[1,2], Richard L M Faull[1], Michael Dragunow[1], Henry J Waldvogel[1], Maurice A Curtis[1], Teepu Siddique[3], Christopher E Shaw[4], Garth Nicholson[5,6,7], and Emma L Scotter[1]

[1]University of Auckland, [2]Auckland City Hospital, Auckland, New Zealand, [3]Northwestern University, Chicago, United States of America, [4]Kings College London, London, United Kingdom, [5]Australian and New Zealand Army Corps (ANZAC) Research Institute, Concord, Australia, [6]University of Sydney, Sydney, Australia, [7]Concord Repatriation General Hospital, Concord, Australia

k.thumbadoo@auckland.ac.nz

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 8.30

Identification of treatment-specific biomarkers in mood disorder research: The problem of placebo variance

Suresh Muthukumaraswamy, Kate Godfrey, Joanne Lin, Rachael Sumner

University of Auckland, Auckland New Zealand

sd.muthu@auckland.ac.nz

A key goal in neuropsychopharmacology research is to relate the clinical outcomes that follow therapeutic interventions with objectively measured biomarkers. A main aim being to differentiate the mechanism of action of a therapy from placebo response or an alternative treatment option. Candidate biomarkers are often derived from, for example, neuroimaging, electrophysiological and blood-based measurements. In these studies statistical relationships observed between outcomes and biomarkers are generally interpreted as reflecting treatment-specific mechanisms. However, subjective clinical outcomes are known to be heavily contaminated with placebo responses. Due to the fundamental problem of causal inference, it is impossible to measure the effect of both treatment and a counterfactual control condition in any individual patient. Hence, the relative contribution of placebo and treatment responses to any individual clinical score is not-identifiable. We demonstrate in numerical simulations how observed correlations between biomarkers and clinical outcomes most likely indicate general clinical response rather than reflecting treatment-specific therapeutic mechanisms. Further, we show most uncontrolled studies are under-powered to detect treatment-specific mechanisms when placebo variance is modelled. We suggest two approaches to address this. Firstly, the addition of a treated healthy control arm to randomised controlled trials allows treatment-specific biomarkers to be identified. Secondly, differences in regression model coefficients between treatment and control interventions suggests treatment-specificity.

Poster 8.31

The effect of S107 on RyR2 clustering in AD-like neuronal cells

Joan Chan, Pete P Jones

University of Otago, Dunedin, New Zealand

chajo611@student.otago.ac.nz

Alzheimer's disease (AD), characterised by memory and cognitive deficits, is a progressive, irreversible neurodegenerative disease. A rising theory addressing AD development and progression is the Ca^{2+} hypothesis, suggesting that Ca^{2+} dyshomeostasis can result in neuropathological lesions observed in AD patients. Previous studies have shown that ryanodine type II receptors (RyR2), predominantly expressed in the heart, have a high expression in hippocampal neurons, and that Ca^{2+} leak through RyR2 leads to AD-like symptoms. FKBP12.6, a regulatory protein bound to RyR2, modulates its Ca^{2+} release activity. In the heart, it has been shown to reduce abnormal Ca^{2+} leak upon forming a complex with RyR2, by manipulating RyR2 ultrastructural organisation. Current treatment for AD is limited. S107, a RyR2-specific Rycal, has shown to prevent FKBP12.6 depletion, therefore reducing Ca^{2+} leak by stabilizing the RyR2-FKBP12.6 interaction. We propose to determine how S107 alters ultrastructural RyR2 and FKBP12.6 arrangement in HEK293 cells and AD culture neurons by performing real-time Ca^{2+} imaging and super-resolution microscopy. If S107 acts in a similar manner as it does in the heart, this may provide a novel treatment for preventing Ca^{2+} leak in AD. We expect our assay results to demonstrate reduced Ca^{2+} leak and more organised RyR2 channels.

Poster 8.32

Moving beyond response times: A simple solution for capturing the dynamics of cognitive control

Katie A Smith, Samara Morris, Annette M E Henderson, Christopher D Erb

University of Auckland, Auckland, New Zealand

ksmi944@aucklanduni.ac.nz

The Gratton effect (the observation that response time is enhanced in congruency tasks when the current trial repeats the congruency of the previous trial) has been influential in recent debates surrounding the processes underlying cognitive control. Recently, hand-tracking techniques have been used to deconstruct response time into *initiation time* (time elapsed between stimulus onset and movement initiation) and *movement time* (time elapsed between movement initiation and response completion). Initiation and movement time reveal distinct and separable patterns, the sum of which gives the Gratton effect. Despite the efficacy of hand-tracking, widespread adoption of the technique is hindered by a range of factors. The current study therefore investigated the extent to which the dynamics of cognitive control observed with motion-tracking equipment can be captured with an affordable and easy-to-assemble three-button response box. Six-to-8-year olds and adults (N=90) completed a computerised version of the Flanker task by pressing and holding a central button to initiate each trial and responding using two lateralised response buttons. Consistent with previous research, initiation times and movement times revealed distinct patterns of effects, indicating that a simple response box can be used to capture the functioning of dissociable processes underlying cognitive control.

Poster 8.33

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

D Samuel Schwarzkopf[1], Alex Puckett[2], Poutasi W B Urale[1], Derek Arnold[2]

[1]University of Auckland, Auckland, New Zealand, [2]University of Queensland, Brisbane, Australia

s.schwarzkopf@auckland.ac.nz

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 degrees of visual angle) centred on the observer's blind spot. 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. Additional analyses revealed that data-driven approach is far superior to conventional model-based pRF analysis. Thus, our method has exciting potential for studying plasticity of receptive fields in visual field loss, and investigating the neural mechanisms underlying filling-in in human observers.

Poster 8.34

A spiking neural network model of motor cortex circuits and responses to TMS simulation

Lysea Haggie[1], Thor Besier[1], Mark Sagar[2], Angus McMorland[1]

[1]University of Auckland, [2]Soul Machines Ltd, Auckland, New Zealand

imun373@aucklanduni.ac.nz

The motor cortex is involved in the control of muscle contraction but how motor cortical activity relates to muscle activation is still unclear. Transcranial Magnetic Stimulation (TMS) over the motor cortex results in a twitch in muscle associated with that region of cortex and high frequency bursts of 500-1000 Hz, known as I-waves, observable in the epidural space of the cervical spinal cord. A model of motor cortex circuitry was created using excitatory and inhibitory neuron populations representing Layer 2/3 and Layer 5 of the motor cortex with intralaminar and interlaminar connections and spontaneous thalamic input. Leaky-integrate and fire neuron models with sodium, potassium and leak currents were used to represent spiking activity, using the neural network simulator toolbox Brian2. This population-based computational model of motor cortex replicates the generation of I-waves in response to TMS as well as the experimental effects of $GABA_A$ activity enhancement and changes in TMS strength. The neuronal circuitry in this model supports the idea that recurrent corticocortical projections contribute to I-waves, furthering our understanding of the motor cortex and creating a platform for deeper investigation into the dynamics of cortical control of voluntary movement.

Poster 8.35

Combined effects of cannabidiol oil and gene therapy in a mouse model of Batten disease

Jasmine Lock[1], Madeline McIntyre Wilson[1], Ben Bolton[1], Becci Gadsby[1], Janet Boyu Xu[1], Hollie Wicky[1], Kirstin McDonald[1], Kathrin Meyer[2], Katherine White[3], Brandon Meyerink[3], Jill Weimer[3], Stephanie Hughes[1]

[1]University of Otago, Dunedin, New Zealand, [2]Nationwide Children's Hospital, Columbus, United States of America, [3]Sanford Research Center, Sioux Falls, United States of America

locja386@student.otago.ac.nz

CLN6 Batten disease is a rare autosomal recessive neurodegenerative disease that affects children. Caused by a mutation in CLN6, this disease is fatal in the second decade of life. Gene therapy using an adeno-associated viral (AAV) vector delivering a functional copy of the *CLN6* gene is in clinical trial. The initial results of this trial are promising, yet further investigation into combination treatments may improve outcomes. Our aim was to determine if cannabidiol oil (CBD) is an effective treatment in a mouse model of CLN6 disease, either alone or in combination with gene therapy. $Cln6^{nclf}$ mice were injected intracerebroventricularly with either scAAV9.CB.hCLN6 or saline, 1-2 days after birth. At weaning, mice were split into CBD or control treatment groups. Treatment was given by oral voluntary dosing. At 12 months behavioural outcomes were tested using the Morris water maze, ataxia scoring, and rotarod. RNAscope was conducted on post-mortem brain tissue to confirm the presence of hCLN6 from gene therapy. Autofluorescence, a pathological hallmark of CLN6 disease, was also analysed as a measure of disease state. The outcome of this study provides evidence that CBD can be used safely in combination with gene therapy and could improve affected children's quality of life.

Poster 8.36

Human brain cells derived from iPSCs – applications, tools and opportunities

Lucia Schweitzer, Jennifer Palmer, Nikita Lyons, Kirstin McDonald, Indranil Basak, Stephanie Hughes

University of Otago, Dunedin, New Zealand

lucia.schweitzer@otago.ac.nz

Ad libitum availability of human neurons to grow and engineer in cell culture is now reality. The efforts of many research groups cumulated in optimisation of protocols for human induced pluripotent stem cells (iPSCs), as well as reliable, reproducible, and manageable procedures to differentiate iPSCs into different cell types. Integration of inducible, fate-determining transcription factors provides a scalable system to generate enough cells even for material-intensive molecular biological and biochemical applications. We use an integrated, inducible, and isogenic system that utilises the transcription factor *neurogenin-2* to differentiate iPSCs into cortical glutamatergic neurons (i3Ns). We are working on the derivation of dopaminergic neurons (i3DNs) and astrocytes (i3As) from iPSCs using a CRISPR/Cas9 strategy. We are using the i3N system to study the lysosome/autophagy pathway, critical for brain health and often impaired in neurological diseases. Two of our proteins of interest are the ER protein CLN6 and the ubiquitin ligase RNF167, both regulating lysosomal biology. Using CRISPRi, we can reduce CLN6 levels by 75%, and RNF167 levels by 74%. We are assessing resulting phenotypes using enzyme assays, morphological characterisation, and lysosome-specific readouts including tracking of lysosome movements. Established phenotypes in these iPSC-derived neurons will provide a platform to screen for disease-modifying drugs.

Poster 8.37

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

Victor Birger Dieriks[1], Luc Bousset[2], Brigid Ryan[1], Richard Faull[1], Ronald Melki[2], Maurice A Curtis[1], Mike Dragunow[1]

[1]University of Auckland, Auckland, New Zealand, [2]National Center for Scientific Research, Fontenay- Aux-Roses, France

v.dieriks@auckland.ac.nz

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 are perivascular cells that 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 phagocytose and degrade α-synuclein aggregates. Using RNAseq, we identified 622 significantly modified genes after treating pericytes with different α-synuclein strains (Fibrils, Ribbons, P65, P91, and P110). 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.

Poster 8.38

Evaluating the use of primary mouse glial cultures to model oligodendrocyte maturation as a screening tool to identify drugs that promote remyelination

Rabia Bibi[1], Anne La Flamme[1,2], Bronwyn Kivell[1]

[1]Victoria University of Wellington, [2]Malaghan Institute of Medical Research, Wellington, New Zealand

rabia.bibi@vuw.ac.nz

Demyelination is a pathological event occurring in many diseases including multiple sclerosis. Lack of myelin repair is largely due to the failure of oligodendrocyte precursor cells (OPCs) to differentiate into myelin-forming oligodendrocytes (OLs). To identify compounds that promote differentiation of OPCs, we have optimized an *in vitro* high-throughput screening assay using mixed glial cultures from wild-type mice and transgenic mice expressing eGFP on OPCs (PDGFRα-eGFP). We have shown that 5 days treatment with thyroid hormone, a known promoter of differentiation, caused OPCs to differentiate into mature myelinating myelin basic protein positive (MBP+) OLs. We found our mixed glial cultures contained 40% OPC-lineage cells (SOX10+). Ten percent were OPCs (PDGFRα-eGFP+), 8% were premature OLs expressing NG2 and 3% were mature MBP+ OLs. Using Sholl analysis to evaluate cell morphology we showed MBP+ cells were more complex, possessing more intersections (Int=30), with longer branching (distance from soma; S=10 µm) and covered a larger area (A=450 mm^2) compared to immature OLs (Int=15; S=3.5 µm; A=400 mm^2) and OPCs (Int=10; S=2.5 µm; A=350 mm^2). This mixed glial culture model provides a simplified and reliable *in vitro* method for drug screening and quantifying changes in OPC maturation using morphology and immunohistochemical markers.

Poster 8.39

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

Meyrick Kidwell, Bart Ellenbroek

Victoria University of Wellington, Wellington, New Zealand

meyrick.kidwell@vuw.ac.nz

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 forced swim test, and the one trial tolerance 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 an 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 8.40

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

Nidhi Aggarwal, Jeffrey Ham, Barry Hughes
University of Auckland, Auckland, New Zealand
nidhi.aggarwal@auckland.ac.nz

Cortical plasticity has been observed in visually-impaired individuals, particularly the involvement of occipital cortex in blind individuals during a variety of tactile and auditory tasks. However, most of the research is focused on understanding the mechanism and functional relevance of this plasticity based on spatial differences i.e., "where the plasticity occurred?". We aim to understand these differences by focusing on the time course of this plasticity. Here, we investigated differences in the 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 the 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. This was done to ensure same task difficulty for the EEG task for each participant. We found high N1 and P2 amplitude for blind compared to sighted, and P2 was more frontal in blind and centrally distributed in sighted. These findings demonstrate both spatial and temporal cortical response in blind is different.

Poster 8.41

Muscle synergy expression is influenced by motor impairment after stroke and task context

Pablo Ortega-Auriol, Winston D Byblow, Thor F Besier, Angus J C McMorland
University of Auckland, Auckland, New Zealand
p.ortegaauriol@auckland.ac.nz

Muscle synergies (MSs) have been proposed as markers for musculoskeletal and neurological disorders. To transfer the theory of MSs to practice, better insight is needed regarding the correlation between motor function and synergy expression. EMG data were recorded from 16 muscles of the upper extremity of nine chronic stroke and fifteen age-similar non-stroke participants. Participants executed four different upper-limb tasks: an isometric contraction, reaching, the Fugl-Meyer (FM) assessment, and a finger pinch. The stroke group showed fewer MSs and stereotypical changes in MS structure despite similar motor behaviours. Greater impairment was correlated with a reduction in the number of MSs ($m = 0.09$, $R^2 = 0.5$) but we did not find a relationship between impairment and intermuscular coherence, which was lower in the stroke group. Additionally, task constraints influenced the number of identified MSs across tasks, with the FM task identifying the most synergies. The FM task, by exploring a higher spatial volume, is able to recruit a broader repertoire of MSs than other more constrained tasks. Task and methodological designs should be a major consideration in the interpretation of MS analysis.

Poster 8.42

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

Giovanni Pedone, Ryan Ward, John Reynolds

University of Otago, Dunedin, New Zealand

pedgi962@student.otago.ac.nz

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 happens 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. This region of the brain is 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 8.43

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

Julia Newland[1], Clinton Turner[1,2], Henry J Waldvogel[1], Richard L M Faull[1], Andrea Kwakowsky[1]

[1]*University of Auckland,* [2]*Auckland City Hospital, Auckland, New Zealand*

julia.newland@auckland.ac.nz

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 that altered neuronal KCC2 and NKCC1 expression 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 8.44

Spatial relationship between microglial activation and pathological TDP-43 deposition in Amyotrophic Lateral Sclerosis

Molly E V Swanson, Helen C Murray, Miran Mrkela, Maize C Cao, Richard L M Faull, Maurice A Curtis, Emma L Scotter

University of Auckland, Auckland, New Zealand

m.swanson@auckland.ac.nz

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 8.45

Reward and loss anticipation during ambiguous risk

Abby Sabrini[1], Joanne Lin[1], Grace Wang[2], Bruce Russell[3], Rob Hester[4], Ian Kirk[1], Louise Curley[1]

[1]University of Auckland, [2]Auckland University of Technology, Auckland, New Zealand, [3]University of Otago, Dunedin, New Zealand, [4]University of Melbourne, Melbourne, Australia

s.sabrini@auckland.ac.nz

According to Mohr et al. (2010), risk processing is context dependent. During non-choice situations or when a choice has already been made (anticipation risk), risky stimuli are proposed to be evaluated by the anterior insula (aINS) and dorsomedial prefrontal cortex (dmPFC). No study, however, has specifically looked into risk in the loss domain. Here, we used a modified monetary incentive delay task that aimed to separately investigate anticipation risk (ambiguous risk) during trials with potential monetary gains and losses. Sixteen healthy adults (age 23.4 ± 1.4) were included in the study. During both reward and loss prospect (cue presentation), bilateral aINS was activated (corrected, $p < 0.05$). In addition, putamen/pallidum was activated during reward but not loss prospect. During both reward and loss anticipation (target presentation), a significant activation was observed in the right aINS and left caudate. In addition, superior frontal gyrus was activated during reward anticipation, while inferior frontal gyrus was activated during loss anticipation. In this study, we have confirmed the aINS as being involved in anticipation risk in both gain and loss conditions, after an ambiguous decision was made. In addition, anticipation of reward activated dmPFC while anticipation of loss activated ventrolateral prefrontal cortex.

Poster 8.46

Optogenetic modulation of GABAergic systems improves Aβ-induced memory deficits

Soo H Kim[1], Warren P Tate[2], Katie Peppercorn[2], Stephanie Hughes[2], Louise Parr-Brownlie[2], Henry J Waldvogel[1], Richard L M Faull[1], and Andrea Kwakowsky[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Otago, Dunedin, New Zealand

soo.kim@auckland.ac.nz

Accumulation of beta amyloid (Aβ), neurofibrillary tangles, and disrupted excitatory neurotransmission are considered the major factors underlying the cognitive deficits observed in Alzheimer's disease (AD). Recent evidence indicates that remodelling of the inhibitory y-aminobutyric acid (GABA) signalling system, resulting in excitatory/inhibitory imbalance, also contributes to cognitive impairments in AD; in particular, Aβ-induced elevation of extracellular GABA level and disruption of inhibitory function in the hippocampus. However, how GABAergic modulation affects AD pathogenesis is still not fully understood. Through optogenetic modulation of GABAergic interneurons in the hippocampus using a novel wireless implantable optogenetics device, we examined if modulation of GABAergic inhibition can restore cognitive deficits in Aβ-injected mice. Animals were given optogenetic stimulus during learning and memory behavioural tasks, and long-term recognition and spatial memory were assessed. We found that continuous light stimulation during both the learning and recall phases of the behavioural tasks reversed memory deficits in Aβ-injected animals, including the inability to recognise object and location novelty. We also found that optogenetic modulation prior to developing AD symptoms also reversed cognitive deficits. These results support the critical role of GABAergic systems in AD pathogenesis and advance our understanding of the potential for GABAergic modulation as a therapy for AD.

Poster 8.47

Predictors of apathy in Parkinson's disease

Samuel J Harrison[1,2], Daniel J Myall[1], Kyla-Louise Horne[1,2], John C Dalrymple-Alford[1,3], Tim J Anderson[1,2,4], Michael R MacAskill[1,2], Campbell Le Heron[1,2,4]

[1]New Zealand Brain Research Institute, [2]University of Otago, [3]University of Canterbury, [4]Canterbury District Health Board (Neurology), Christchurch, New Zealand

sam.harrison@nzbri.org

Non-motor symptoms of Parkinson's disease (PD), including apathy, have a major impact on quality of life; however, relatively little is known about the onset and development of apathy over the course of PD. Here, we use data from 325 PD patients collected over 1,274 sessions as part of a longitudinal study at the New Zealand Brain Research Institute. Presence of apathy is inferred from caregiver responses to the Neuropsychiatric Inventory, and patients regularly undergo extensive neuropsychiatric and motor assessments. 42% of patients with PD (137/325) had apathy at least once during the study. Cross-sectionally, the prevalence of apathy is significantly lower in female patients (logistic regression, odds ratio: 0.32 [95% CI: 0.16 – 0.62]). However, there are no significant associations with either age at diagnosis, years since diagnosis, or UPDRS motor scores. Rather, reductions in global cognitive scores (aggregrated from 22 different tests) and depression (measured by the HADS) are both associated with apathy, and crucially also predict future onset of apathy (multi-state predictive model, hazard ratios: 0.46 [95% CI: 0.31 – 0.69] and 2.05 [95% CI: 1.19 – 3.52] respectively). These results suggest that apathy is primarily associated with poor cognitive status and depression, rather than simply increasing with duration of disease.

Poster 8.48

Inducing traumatic brain injury in human pericytes using dielectric elastomer actuators

Yihan Wu, Thomas Park, Samuel Rosset, Edward Mee, Mike Dragunow, Vickie Shim

University of Auckland, Auckland, New Zealand

yihan.wu@auckland.ac.nz

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 that 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 parkmechanical strain. Pericytes are mural cells found ubiquitously throughout the brain that are important for maintaining homeostasis and supporting blood-brain barrier integrity. Evidence suggests that pericytes are involved in brain scarring, a consequence of TBI that becomes a barrier to full recovery. We modelled TBI by plating 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 8.49

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

Sarah Wilson, Silvia Schwartz, Helen Fitzsimons

Massey University, Palmerston North, New Zealand

swilson3@massey.ac.nz

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 8.50

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

Victoria F Low[1], Mahyar Osanlouy[1], Gonzalo Maso Talou[1], Soroush Safaei[1], Chinchien Lin[1], Shan Su[1], Peter Mombaerts[2], Maurice A Curtis[1]

[1]University of Auckland, Auckland, New Zealand, [2]Max Planck Research Unit for Neurogenetics, Frankfurt, Germany

v.low@auckland.ac.nz

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 to develop a detailed three-dimensional anatomical map. This will be the first systematic study of the human olfactory system utilising rare human tissue resources. The resulting model is a graphical representation of the distribution and projection of human olfactory sensory neurons from the nose into the brain. 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 8.51

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

Poutasi W B Urale, D Samuel Schwarzkopf

University of Auckland, Auckland, New Zealand

tasi.watson@auckland.ac.nz

The Ebbinghaus and Delboeuf illusions are two similar illusions that affect the perceived size of a circle (target) depending on the size and proximity of circular inducers (Ebbinghaus) or an annulus (Delboeuf). Recent converging evidence has suggested that these illusions are driven by interactions between contours, which in turn may be mediated by cortical distance within the primary visual cortex. Here we tested the effect of cortical distance on the Ebbinghaus and Delboeuf illusions using two methods. First, we manipulated the physical distance between inducers and annuli in a two-interval forced choice design with an adaptive staircase procedure. From this we targets appeared larger with closer surrounding inducers/annuli. 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. Finally, 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.

Poster 8.52

Selective inhibition of inflammatory but not homeostatic immune cell trafficking into the CNS in a model of multiple sclerosis

Tessa Peck[1], Olga Zubkova[1], Anne La Flamme[1,2]

[1]Victoria University of Wellington, [2]Malaghan Institute of Medical Research, Wellington, New Zealand

tessa.peck@vuw.ac.nz

Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system (CNS) where immune cells attack the protective myelin sheath surrounding axons, causing permanent neuronal damage. Targeting immune cell trafficking into the CNS is an effective treatment for MS. However, complete abolishment of immune surveillance can cause deadly side effects. Normally the tightly controlled blood brain barrier (BBB) protects the CNS from inflammation by restricting entrance of immune cells. In MS, enzymes released at the BBB contribute to its breakdown. One such enzyme, heparanase, has been suggested as a target for drug development in neuroinflammatory disorders and can be selectively inhibited by heparan sulfate mimetics. Our lab has found that therapeutic administration of heparan sulfate mimetics significantly reduces disease in an *in vivo* model of MS. By maintaining integrity of the BBB, entrance of immune cells into the CNS is significantly reduced. Importantly, this inhibition of inflammatory trafficking does not appear to affect homeostatic trafficking into the CNS quantified by flow cytometry. This suggests that the heparan sulfate mimetic selectively reduces neuroinflammation, whilst maintaining immune surveillance that is essential for the homeostasis of the CNS.

Poster 8.53

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

Sophie Mathiesen, Wickliffe C Abraham, Stephanie Hughes

University of Otago, Dunedin, New Zealand

matso768@student.otago.ac.nz

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 may contribute 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 mouse model. Via tail vein injection, male 13-month-old (n = 8) and 10-month-old (n = 4) APP/PS1 mice were administered with AAV-PHP.eB encoding a TFEB transgene, and 13-month-old APP/PS1 (n = 4) and C57BL/6 mice (n = 7) were administered with AAV-PHP.eB encoding a reporter protein, tdTomato. Unexpectedly, mice administered 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. Livers of animals administered TFEB showed abnormal cell masses near blood vessels, indicating that TFEB overexpression in peripheral organs may produce fatal toxicity, independent of expression in the brain. TFEB gene therapy for AD may be limited to methods that produce overexpression only in the brain.

Poster 8.54

Personalised brain-inspired AI technology, based on integrated neurological, clinical, and psychological data for prediction of an individual response to tinnitus therapy

Zohreh Doborjeh[1], Phil, Sanders[1], Mithila Durai[1], Maryam Doborjeh[2], Nikola Kasabov[1,2,3], Grace Wang[2], Alexander Sumich[4], Grant Searchfield[1]

[1]University of Auckland, [2]Auckland University of Technology, Auckland, New Zealand, [3]Ulster University, Derry/Londonderry, United Kingdom, [4]Nottingham Trent University, Nottingham, United Kingdom

zohreh.doborjeh@auckland.ac.nz

Tinnitus ("ear and head noise") is a highly prevalent condition affecting between 5-20 % of the world's population. Tinnitus can have a catastrophic effect on the quality of life and 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 "tinnitus distress" is possible. However, this treatment is complicated by the large variability in tinnitus, and response to treatments, amongst sufferers. The understanding of the underlying psychological and neural mechanisms of tinnitus subtypes and response to treatment is currently limited. This study used a behavioural case series, alongside Electroencephalography (EEG) and a computational brain-inspired Artificial Intelligence (AI) methodology, to evaluate the effect of three masking sounds on tinnitus and associated symptoms across 12 months. EEG was related to clinically significant changes in the behavioural data using the computational AI model. The AI framework was able to predict sound therapy responders (93% accuracy) from non-responders (100% accuracy) using baseline EEG recordings. The results will be 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.

9.1

Pericyte cell death and α-synuclein – a double hit

Taylor Stevenson, Victor Dieriks, Mike Draguno, Maurice A Curtis

University of Auckland, Auckland, New Zealand

t.stevenson@auckland.ac.nz

Parkinson's disease (PD) is caused by the accumulation of the misfolded protein α-synuclein (α-syn) where it leads to death of neurons and eventually the development of motor symptoms. Pericytes are found surrounding endothelial cells on capillaries and are important for maintaining the blood-brain barrier. Our recent work has shown that pericytes contain α-syn in the PD brain, however, not much is understood about their involvement in the disease. In this study, we investigated whether α-syn was toxic to pericytes *in vitro*. Primary human brain pericytes (n = 4) derived from human brains were treated with three different α-syn aggregates and exposed to different cell stressors. α-syn exposure alone did not alter pericyte cell viability. However, co-treatment of α-syn with cellular stressors such as the proteasome inhibitor MG132, resulted in the induction of reactive oxygen species (ROS), release of superoxide from mitochondria and apoptotic cell death. Treatment with Vitamin C was associated with reduced cell death and ROS production. These results suggest that α-syn alone does not induce cell death in pericytes, rather, an additional insult is required. Additionally, treatment with an antioxidant can rescue pericytes from cell death after exposure to α-syn and cellular stressors.

9.2

Network dysfunction in the Alzheimer's disease hippocampus

Andrea Kwakowsky[1], Jason Yeung[1], Thulani Palpagama[1], Soo Hyun Kim[1], Joshua Walby[1], Oliver Wood[1], Warren Tate[2], Katie Peppercorn[2], Clinton Turner[3], Henry Waldvogel[1], Richard Faull[1]

[1]University of Auckland, Auckland, New Zealand, [2]University of Otago, Dunedin, New Zealand, [3]City Hospital, Auckland, New Zealand

a.kwakowsky@auckland.ac.nz

Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by the presence and accumulation of amyloid-beta (Aβ) plaques and neurofibrillary tangles. The balance between excitatory and inhibitory (E/I) neurotransmission is severely disrupted in AD. This imbalance has been associated with the development and progression of the disease and it could underlie the cognitive deficits that are characteristic of the condition. Current drugs for symptomatic treatment of AD are targeted towards the excitatory systems, but these provide only marginal clinical benefits. Further development of therapeutic options targeting the glutamatergic system and the main inhibitory gamma-aminobutyric acid (GABA) system could reduce neuronal vulnerability to excitotoxic damage by restoring the E/I balance. However, there is a need to better understand the remodelling of these E/I networks in the AD brain. We performed a comprehensive examination of the glutamatergic and GABAergic signalling components in the post-mortem human AD hippocampus and *in vitro* and *in vivo* mouse models of the disease. We identified an extensive remodelling of both neurotransmitter systems and demonstrated differences in acute and chronic effects of Aβ exposure. Here, we provide evidence that targeting these systems might enable us to ameliorate the E/I imbalance, prevent cell death, and potentially have a disease-modifying effect in AD.

9.3

A growing problem in Huntington's disease

Adelie Y S Tan, Malvindar K Singh-Bains, Nasim F Mehrabi, Richard L M Faull, Mike Dragunow

University of Auckland, Auckland, New Zealand

adelie.tan@auckland.ac.nz

Despite the significant advances in the understanding of Huntington's Disease (HD), there is still a lack of treatments available, highlighting the complexity of this monogenic disease. An approach that we propose which may aid in the understanding of HD is through human brain tissue microarrays (HBTMAs). As all human brain samples are located on the same glass slide, HBTMAs provides a time- and reagent-efficient method to screen for potential changes occurring within the disease. Using an HBTMA consisting of up to 28 control and 28 HD human brain cortical samples, we have identified the presence of ionised calcium-binding adapter molecule-1^{+} (IBA1) microglial proliferation in HD using two proliferative markers, Ki-67 ($p = 0.05$) and proliferative cell nuclear antigen (PCNA; $p = 0.005$). Furthermore, PCNA^{+} proliferation quantified in the TMA correlated ($r = 0.74$, $p = 0.03$) with whole tissue section quantification, thereby validating both the method and the presence of proliferation in HD. This study serves to highlight a significant and more nuanced role that microglia may play in the progression of HD, thereby advancing our understanding of this tragic disease.

9.4

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

Emma Deeney, Mohamed Ibrahim, Kay Potapov, Stephanie Hughes, Ruth Empson

University of Otago, Dunedin, New Zealand

emma.deeney@postgrad.otago.ac.nz

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. Four-week-old SCA1 and wild-type (WT) mice were separated into exercising (E) and non-exercising (NE) group (n=13-14/group), and individually housed with/without a running wheel for 4 weeks, then tested on an accelerating rotarod. Inhibitory basket cells (BC) synapse onto the cerebellar sole output neuron (Purkinje neuron: PN), and control the regularity of PN firing. PN firing is disrupted in SCA1 mice hence we assessed BC synapses onto PNs using confocal fluorescent immunohistochemistry. We show clear failure of coordinated motor performance and learning on the accelerating rotarod in SCA1 NE mice, which was rescued by voluntary exercise, as SCA1 E mice improved their latency-to-fall to match WT NE mice (two-way ANOVA). SCA1 NE mice BC expression tended to be increased compared with WT NE mice (P=0.056), and was also restored to WT NE levels following exercise (unpaired t-tests, n=4-5/group). These exciting findings indicate that voluntary exercise may restore motor coordination in SCA1 mice by normalising BC expression levels and restoring PN firing fidelity.

9.5

Uncovering new trafficking routes in axons

Macarena Pavez, Laura F Gumy

University of Otago, Dunedin, New Zealand

macarena.pavez@otago.ac.nz

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 associate 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 and 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.

9.6

Septin 2 stabilises the axonal initial segment of induced pluripotent stem cell derived neurons

Deanna Barwick, Macarena Pavez, Zandra Jenkins, Laura Gumy, Stephen Robertson

University of Otago, Dunedin, New Zealand

deanna.barwick@otago.ac.nz

The axon initial segment (AIS) is the neuronal structure that separates the somatodendritic and axonal domains. Organisation of the AIS is achieved by the localisation of the scaffold protein Ankyrin G, in conjunction with cytoskeletal actin filaments and microtubules at the base of the axon. Despite the critical importance of the AIS for normal neuronal functioning, little is known about AIS assembly and maintenance. To identify novel proteins with a role in AIS formation, we screened human induced pluripotent stem cell (iPSC) derived neurons and identified Septin 2 as a novel protein specifically located at the AIS. Given that Septins interact with actin and microtubules we hypothesised that Septin 2 might function in AIS assembly and/or maintenance. To test our hypothesis, we used gene editing tools, immunocytochemistry and confocal microscopy to knock down or overexpress Septin 2 in human iPSC-derived neurons. We found that perturbations of Septin 2 expression affected Ankyrin G localisation at the AIS. Furthermore, our results revealed that Septin 2 is required for proper neuronal morphology. Thus, Septin 2 is crucial for the functioning of human-derived neurons.

10.1

Potential PINK1 founder effect in Polynesia causing early onset Parkinson's disease

Christina M Buchanan[1], Shilpan G Patel[1], Eoin Mulroy[1,2], Mark Simpson[1], Hannah A Reid[3], Kylie M Drake[3], Marilyn E Merriman[4], Amanda Phipps-Green[4], Murray Cadzow[4], Tony R Merriman[4,5], Neil E Anderson[1], Nicholas Child[1], P Alan Barber[1], Richard H Roxburgh[1,6]

[1]Auckland City Hospital, Auckland, New Zealand, [2]UCL Queen Square Institute of Neurology, London, United Kingdom, [3]Canterbury Health Laboratories, Christchurch, New Zealand, [4]University of Otago, Dunedin, New Zealand, [5]University of Alabama, Birmingham, United States of America, [6]University of Auckland, Auckland, New Zealand

c.buchanan@adhb.govt.nz

BACKGROUND: Patients with early-onset Parkinson's disease (EOPD) are more likely to have a genetic cause of disease. Two patients with EOPD, one Samoan, one Tongan, were found to be homozygous for the rare pathogenic *PINK1* variant, NM_032409.3(*PINK1*):c.1040T>C p.(Leu347Pro). OBJECTIVES: To determine whether *PINK1*:c.1040T>C is a common cause of EOPD in Māori and Pacific patients. METHODS: We recruited Māori and Pacific patients with EOPD and late-onset disease. We sequenced their *PINK1* gene. We also determined the carrier-frequency of *PINK1*:c.1040T>C variant in a control population of Māori and Pacific people. RESULTS: Seventeen unrelated patients with PD were recruited; 14 with EOPD and 3 with late-onset PD. Of the 14 patients with EOPD, 12 were homozygous for *PINK1*:c.1040T>C; the three late-onset patients were *PINK1*-wildtype. In a control population of 273 Māori and Pacific people the allele-frequency for *PINK1*:c.1040T>C was 1.5%; a higher allele-frequency (2.8%) was found in Western Polynesian sub-populations. CONCLUSIONS: *PINK1*:c.1040T>C homozygosity appears to be a common cause of EOPD in patients of West Polynesian ethnicities; carrier-frequencies in Western Polynesian populations indicate a homozygosity rate of 1 in 5000. Māori and Pacific patients with EOPD should be tested for *PINK1* variants; if gene positive, family members can be referred to Genetic Services.

10.2

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

Zahra Laouby, Yukti Vyas, Johanna Montgomery, Juliette Cheyne, Simon J O'Carroll

University of Auckland, Auckland, New Zealand

zlao031@aucklanduni.ac.nz

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 the 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 act as neuronal activity indicators. 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 that transverse sinus injection allows chronic *in vivo* imaging of neurons in unrestrained rats with miniscopes. We are now applying this technology to investigate the dialog between the motor cortex and spinal cord following spinal cord injury.

10.3

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

Rachael L Sumner[1], Meg J Spriggs[2], Alexander D Shaw[3]

[1]University of Auckland, Auckland, New Zealand, [2]Imperial College London, London, United Kingdom, [3]Cardiff University, Cardiff, United Kingdom

r.sumner@auckland.ac.nz

Background: 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. Methods: 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. Results: 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. Discussion: 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.

10.4

Cell-type specific responses to neuroinflammation in human leptomeninges

Serey Naidoo, Sheryl Feng, Molly Swanson, Victor Birger Dieriks, Maurice Curtis, Richard Faull, Michael Dragunow, Emma Scotter

University of Auckland, Auckland, New Zealand

s.naidoo@auckland.ac.nz

The meninges – three layers of membranes that surround the central nervous system – were until recently thought of as solely a protective layer. The meninges have been shown to harbour a rich repertoire of immune cells, suggesting a contribution to neuroinflammation in health and disease. However, the cytokine responses in humans of specific meningeal cell types are poorly characterised. Leptomeningeal explants (LME) were cultured from post-mortem human meninges by removing and sectioning the pia and arachnoid mater and culturing *ex vivo*, allowing structurally conserved tissue to be probed pharmacologically. Neuroinflammatory responses of LME were assessed following pro-inflammatory stimulation with IL-1β, IFNγ, or TNFα for 24 h. Cytokine expression was quantified using multiplex cytometric bead array (secreted cytokines) and analyzed alongside immunohistochemistry (intracellular cytokines and cell-type markers) to investigate the specific cellular contribution to the inflammatory response. IL-6 and IL-8 were the most induced cytokines following stimulation, followed by ICAM-1, VCAM-1, MCP-1 and GM-CSF. Vascular cells and meningeal macrophages were the predominant cell types in the LME, and were responsive to inflammation. The release of cytokines by specific cell types of the meninges in response to various pro-inflammatory cytokines highlights the likely contribution of meninges to neuroinflammation in health and disease.

11.1

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

Narun Pat[1], Yue Wang[1], Argyris Stringaris[2]

[1]*University of Otago, Dunedin, New Zealand,* [2]*National Institute of Mental Health, Bethesda, United States of America*

narun.pat@otago.ac.nz

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.

11.2

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

Rebekah Blakemore[1,2], Michael MacAskill[1,3], Daniel Myall[1], and Tim Anderson[1,3,4]

[1]New Zealand Brain Research Institute, Christchurch, New Zealand, [2]University of Otago Dunedin, New Zealand, [3]University of Otago, [4]Christchurch Hospital, Christchurch, New Zealand

rebekah.blakemore@otago.ac.nz

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 may interfere with tremor circuitry, thereby diminishing tremor impact.

11.3

Zebrafish on "P": Behavioural effects of methamphetamine

Susan Schenk[1], Julia Horsfield[2], Sheri Johnson[2]

[1]Victoria University of Wellington, Wellington, New Zealand, [2]University of Otago, Dunedin, New Zealand

susan.schenk@vuw.ac.nz

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 100 ml beaker containing 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.

11.4

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

Sonja Seeger-Armbruster, Aisya Ahmad Zamri, Mandy Wang, Rebecca E Campbell, Brian I Hyland

University of Otago, Dunedin, New Zealand

sonja.seeger-armbruster@otago.ac.nz

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 an 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.