13th Australasian Neurotrauma Symposium

30th November - 1st December 2024
Perth, Western Australia

THE AUSTRALASIAN
NEUROTRAUMA
NETWORK

The 13th Australasian Neurotrauma Symposium is proudly sponsored by:

Connectivity
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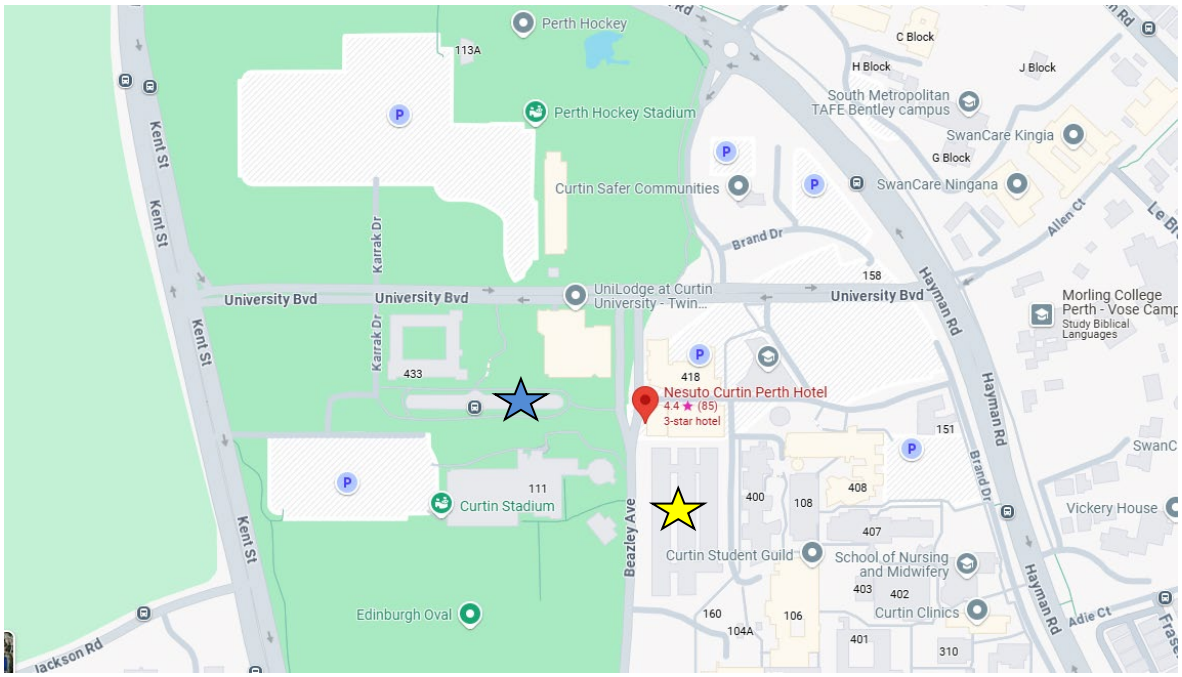
The Australasian Neurotrauma Symposium is an official Satellite Meeting of ANS 2024

The Symposium will be held in the Bentley Grand function space at Nesuto Curtin Perth Hotel, corner Koorliny Way and Beazley Avenue within the Curtin University campus.

Take the stairs opposite reception or the lift to level 1.



Getting to the Symposium

By Car
Enter the campus via University Boulevard from Kent Street or Hayman Road. Take Beazley Avenue and Park in the multistory car park next to Nesuto (marked with a yellow star on the map). Parking is free for this car park on weekends.

By Bus
There are many bus routes to Curtin University. Download the Transperth app for directions and live bus tracking. A bus from the city will take around 25 minutes.
Disembark at Curtin University **Central** Bus Station - there are two stations, Central is across the road from Nesuto.
You can pay cash ($3.50 from the CBD/nearby suburbs, no change given so bring exact fare) or buy a SmartRider card $10) from a newsagent.

By Uber/rideshare
From the CBD will take 15-20 minutes and cost $15-20.

Getting to the social event at the Old Tea Pavillion, Kings Park

By Car
Enter Kings Park via Fraser Avenue and turn right into Kattidj Close. There's a large car park with free parking behind the pavilion, though parking will be limited due to a concert. Other parking options can be found on Kings Park Road.

By Foot
A ~20 minute walk from the CBD. Follow St Georges Terrace as it turns into Malcolm Street and enter the park via Fraser Avenue.

By Bus
A ~5 minute bus trip from the CBD. Many buses travel along Kings Park Road (get off at the Kings Park Road/Dumas House stop) or go directly into Kings Park via Frazer Avenue, and stop directly outside the Old Tea Pavillion. The purple and blue CAT buses are free, no ticket required.

By Uber/rideshare
Apps should recognise "Old Tea Pavillion" as a destination. There's a set-down zone on Kattidj Close.

ANTS Special Guests

Kai Sakakibara

Ambassador, Connectivity Traumatic Brain Injury Australia

Resilience Reimagined

Half Japanese, half British but self described as 100% Australian… Connectivity ambassador Kai Sakakibara has a story like few others. Kai was a consistent Top 10 in the world BMX Racer on a pathway to the Olympics with his Sister and World Number 1, Saya Sakakibara and now Gold Medallist by his side on the journey.

Tragically in the lead up to the 2020 Olympics, Kai suffered a traumatic brain injury in a crash that nearly proved fatal when attempting to qualify for Tokyo. He was a certainty to make the Olympic squad and was pushing his limits to represent his Country.

Kai has since become an inspiration to many as he rebounds from this accident which included 8 weeks in a coma during the outbreak of COVID. Kai had to have lockdowns explained to him as he tried to make sense of the new world he woke up to. He hopes to one day compete at the Paralympic Games for his new sport of Rowing. Kai is one of Australia's most sought after Public Speakers now in his new phase of life, which he uses to fund his Paralympic dream.

Paul Scanlan

Vigil Australia

Blast Overpressure and Brain Health: Addressing the Invisible Injuries of Service

Paul Scanlan is a retired Australian Army Special Forces Officer with a background spanning operational, training, policy, capability development, and more recently, social impact start-up environments. For 25 years, he led teams in uncertain, complex, and dynamic environments – 15 of them working in counter-terrorism-related roles in the National Security Community. In one of his final roles, as the Director of 'Diggerworks,' he led a specialised team comprising combat-experienced servicemen and women, scientists, and engineers. Their primary objective was not only to address the evolving needs of close combatants but also to enhance or develop combat capabilities, akin to the US Marine Corps' Gruntworks initiative. Here he became aware of mTBI, Impulse Noise, and Blast Overpressure. Paul is the Founder of Vigil Australia, a no-fee-for-service social enterprise dedicated to raising awareness of mTBI and Blast Overpressure within the Australian Defence Force (ADF), Veteran, and Police communities. Vigil Australia seeks to address the gap in recognition, research, and treatment of these injuries, advocating for systemic change and greater understanding of the impact of repetitive low-level blast exposure on the brain. The organisation works to connect stakeholders and experts across commercial, academic, government, and research sectors to drive change. Paul has been supporting the Australian Royal Commission into Defence and Veteran Suicide to raise awareness of mTBI in the ADF and Veteran communities. Paul holds a Master's in International Relations from the Australian National University and an MBA from the University of Melbourne Business School. He was awarded the Distinguished Service Medal for Leadership in Action in Afghanistan in 2013.

Antonio Vecchio

Spinal Research Institute

Identifying and engaging with consumers

Antonio Vecchio is currently the Community and Consumer engagement manager at the Spinal Research Institute in Melbourne. Antonio has a background in psychological science and sociology with particular interest areas been social psychology and developmental psychology. He is vastly experienced and program development as well as having experience working in the community with various community groups and community-based organisations.

Dr Lily Toomey

Pitch Science

Painting the Picture of Your Science: Branding & Online Media

Lily is a science communicator, neuroscientist, and founder of Pitch Science. Armed with experience in scientific research and digital marketing, Lily helps scientists and science organisations actively use their work as a tool for change. At Pitch Science, she turns science into stories through both her content creation services and her science branding and web design packages. Lily is also empowering scientists to do science communication and extend their reach beyond traditional academic channels with The Pitch Lab. Because whether you fund science, do science, or teach science, effective communication is critical for building support, awareness, and impact in the wider community.

PROGRAM

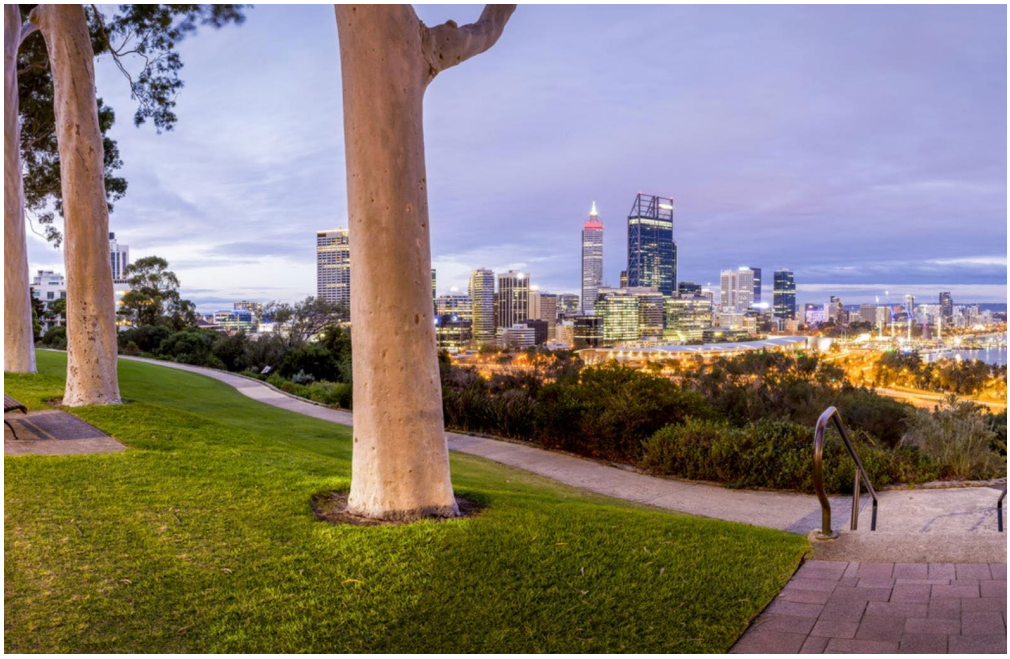
DAY 1 - SATURDAY, NOVEMBER 30

8:20	**Registration**		
8:50	**Welcome and housekeeping**		
Session 1 - Neuroinflammation and Neuroprotection ***Chair: Chidozie Anyaegbu***			
9:00	Mark Ruitenberg (*The University of Queensland)*	Dissecting inflammation in spinal cord injury through single-cell and spatial transcriptomics (*Keynote*)	Page 18
9:30	Samantha Edwards *(The University of Adelaide)*	Development of PD-like pathology in a novel rodent model of LPS-induced intranasal inflammation and traumatic brain injury	Page 19
9:50	Helen Murray *(University of Auckland)*	Focal perivascular glial reactivity is a feature of the tau lesions in Chronic Traumatic Encephalopathy	Page 20
10:10	Josh Allen *(Vancouver Island University / University of Victoria)*	Psilocybin ameliorates chronic behavioral deficits and alterations in 5-HT2A receptor density in a rat model of traumatic brain injury	Page 21
10:30	Shannon Stuckey *(The University of Adelaide)*	Chronic Neuroinflammation and Functional Decline: Decoding Secondary Neurodegeneration Following Photothrombotic Stroke in Rats	Page 22
10:50	**Morning tea**		
Session 2 - Insights from the patient and clinician perspective ***Chair: Sarah Hellewell***			
11:30	Rachel Singer *(Curtin University)*	Understanding the challenges of concussion recovery: Perspectives from individuals with delayed recovery after mild traumatic brain injury	Page 24
11:50	Gill Cowen *(Curtin University)*	Heads Up on Concussion: Aboriginal and Torres Strait Islander Peoples' Knowledge and Understanding of Mild Traumatic Brain Injury	Page 25
12:10	Jacinta Thorne *(Curtin University)*	Persisting symptoms, quality of life and return to work following mTBI in an Australian community-based cohort: results from the Concussion Recovery Study (CREST)	Page 26
12:30	Madeleine Homes-Vickers *(The University of Adelaide)*	Changing the Game – The Impact of Serious Games-Based Cognitive Training on Cognitive Function in Parkinson's disease	Page 28

12:50	Rachel Buckingham *(University of Notre Dame)*	"Rock on technology": Perspectives on robot-assisted lower limb and gait neurorehabilitation from people with neurological conditions	Page 29
13:10	Matthew Bagg *(University of Notre Dame)*	'Reaching for Robotics' : A mixed methods study of clinician perspectives on robot-assisted lower limb rehabilitation in Western Australia	Page 31
13:30	**Lunch and poster viewing**		
Session 3 - Engaging with end users and communicating your message: who, what, when and why ***Chair: Aleksandra (Ola) Gozt***			
14:30	Kai Sakakibara *(Connectivity TBI Ambassador)*	Resilience Reimagined	
15:00	Paul Scanlan *(Vigil Australia)*	Blast Overpressure and Brain Health: Addressing the Invisible Injuries of Service	
15:20	Antonio Vecchio *(Spinal Research Institute)*	Identifying and Engaging with Consumers	
15:40	Lily Toomey *(Pitch Science)*	Painting the Picture of Your Science: Branding & Online Media	
16:00	**Afternoon tea**		
Session 4 - Poster Blitz 1			
16:30	Andre Avila *(Curtin University)*	Neurofeedback Intervention for Persistent Post-Concussion Symptoms: A Case Series on Functional Connectivity in the Salience Network	Page 34
16:33	Glenn Yamakawa *(Monash University)*	Altered visual function as a biomarker for repetitive mild traumatic brain injury in adolescent rats	Page 35
16:36	Taylor Snowden *(University of Victoria)*	The Long Road: Using a Multi-Dimensional Approach to Examine the Relationship Between History of Concussion and Neurodegeneration in Adults over 50 years old	Page 36
16:39	Isabella Drew *(University of Western Australia)*	A novel, minimally invasive mode of photobiomodulation delivery to the injured rat spinal cord	Page 37
16:42	Rachel Singer *(Curtin University)*	AUS-mTBI: designing and implementing novel health informatics approaches to improve outcomes for people with mild TBI across Australia	Page 38

16:45	Jamie Morrison *(University of Victoria)*	Patient-Oriented Cognitive Rehabilitation: Effects of Three-Dimensional Multiple-Object Tracking on Cognitive and Functional Outcomes in Traumatic Brain Injury Survivors	Page 41
16:48	Zara van Zijl *(University of Western Australia)*	The effect of contralateral cortex injection of AAV1-CRMP2 on C6/7 hemi-contusion spinal cord injury repair in Fischer rats	Page 42
16:51	Melinda Fitzgerald *(Curtin University)*	AUS-mTBI Extend: An extended, innovative data collection to predict recovery for people with mild traumatic brain injury	Page 43
16:54	Elaina Vlassopoulos *(Monash University)*	Investigating the Role of the Circadian System in Traumatic Brain Injury within Adolescent Rats	Page 45
16:57	Marissa Sgro *(Monash University)*	Exposure to Perinatal Trauma Modifies Nociception and Gene Expression in the Prefrontal Cortex and Hypothalamus of Adolescent Rats	Page 46

18:00 Social function: Old Tea Pavillion, Kings Park



PROGRAM

DAY 2 - SUNDAY, DECEMBER 1

9:00	**Registration**		
Session 5 - Biomarkers of Injury ***Chair: Brittney Lins***			
9:20	Stuart McDonald (*Monash University)*	Next-Day Serum Glial Fibrillary Acidic Protein Levels to Aid Diagnosis of Sport-Related Concussion	Page 48
9:40	James Hickey (*Monash University)*	Instrumented Mouthguard Head Kinematics as Predictors of Concussion and Elevated Biomarkers of Astroglial and Axonal Injury in Amateur Australian Football Players	Page 49
10:00	Grace Bliesner *(Curtin University)*	Biological Resilience in Stress Environments: The impact of Mild Traumatic Brain Injuries on Saliva Biomarkers	Page 50
10:20	**Morning tea**		
Session 6: Neuroimaging ***Chair: Jacinta Thorne***			
10:50	Georgia Symons *(Monash University)*	White matter microstructure in women who have experienced intimate partner violence related mild traumatic brain injury	Page 52
11:10	Caerwen Ellery *(Curtin University)*	Quantitative electroencephalography reveals regional brain dysfunction in mild traumatic brain injury	Page 53
11:30	Jake Mitchell *(Monash University)*	Parsing Cortical Thickness Heterogeneity in TBI: A Normative Modelling Approach	Page 55
Session 7: Preclinical models and Behaviour ***Chair: May Majimbi***			
11:50	Sydney Harris *(Monash University)*	Acute and chronic brain and behavioural pathology produced in a neonatal mouse model of repetitive abusive head trauma	Page 57
12:10	Eleanor Bowley-Schubert *(The University of Adelaide)*	Does pre-existing brainstem tau pathology exacerbate Alzheimer's-related behavioural deficits following a mild traumatic brain injury?	Page 58
12:30	Crystal Li *(Monash University)*	Changes to nociception and inhibitory neurotransmission in the cerebellum following a traumatic peripheral nerve injury in adolescent	Page 59

		female rats	
12:50	Parth Patel *(Curtin University)*	Machine learning based segmentation and classification of axons following optic nerve injury	Page 60
13:10	**Lunch and poster viewing**		
Session 8 - Mental Health Consequences of Injury ***Chair: Grace Bliesner***			
14:10	Amanda Jefferson *(Curtin University)*	Mental health, personality and quality of life factors affecting mTBI recovery in an Australian cohort	Page 62
14:30	Abigail Astridge Clarke *(Monash University)*	The relationship between early-life trauma and mental health outcome among women IPV victim-survivors	Page 63
14:50	Melissa Papini *(Curtin University)*	Moderation Effects of Resilience and Coping Style on Relationships Between Psychological Health and Symptom Severity after Mild Traumatic Brain Injury	Page 64
15:10	Charlotte Copas *(Monash University)*	Characterising the neurological consequences of intimate partner violence within a community-based sample of women victim-survivors	Page 66
15:30	**Afternoon tea**		
Session 9 - Poster Blitz 2			
16:00	Carl Hooper *(University of Adelaide)*	Evaluating Cognitive and Motor Behavioural Changes within a Gyrencephalic Ferret Model of Mild Traumatic Brain Injury	Page 68
16:03	Rosie Costigan-Dwyer *(University of Adelaide)*	Exploring the long-term blood-brain-barrier alterations associated with secondary neurodegeneration in Ischaemic stroke.	Page 69
16:09	Kinta Pinchin-Yamada *(Curtin University)*	Tracking the temporal development of cellular hallmarks of neurodegenerative disease following repeated mild traumatic brain injuries in a rat model	Page 70
16:12	Ryan Dorrian *(University of Adelaide)*	Connecting the spots: Adapting the void spot assay as a non-invasive bladder assessment for rats with spinal cord injury	Page 71

16:15	Sarah Hellewell *(Curtin University)*	Alteration of Brain White Matter Tracts and Plasma Free Fatty Acid Concentrations following Mild Traumatic Brain Injury	Page 72
16:18	Bruce Harland *(University of Auckland)*	Intrathecal administration of a neurotrophin-3-delivering hydrogel in rat spinal contusion injury model	Page 74
16:24	Paul Marciano *(University of Adelaide)*	Changes in radiological biomarkers of the distal femur following concomitant spinal cord injury and traumatic brain injury	Page 75
16:27	Srisankavi Sivasankar *(University of Adelaide)*	Perceived and measured chronic cognitive function after traumatic spinal cord injury: insights from a clinical survey and testing approach	Page 76
16:30	**Prizes, concluding remarks and farewell**		

DAY 1 – SESSION I

Neuroinflammation & Neuroprotection

Dissecting inflammation in spinal cord injury through single-cell and spatial transcriptomics

MJ Ruitenberg[1], LF Grice[1,2], ER Gillespie[1], Courtney IG[1], T Lao[1], M Haritopoulou-Sinanidou[1], D Pham[2], and QH Nguyen[2,3]

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2. Institute for Molecular Bioscience, The University of Queensland, Brisbane, Australia

3. QIMR Berghofer Medical Research Institute, Brisbane, Australia

Background: Traumatic spinal cord injury (SCI) acutely induces a temporally orchestrated recruitment of immune cell subsets to the lesion site. At least some elements of this inflammatory response negatively interfere with recovery. Myeloid cells are of particular interest here as they dominate the inflammatory infiltrate in both human SCI patients and experimental animal models of SCI. Here we used single-cell and spatial omics approaches to better understand myeloid cell diversity and function following SCI, along with the transcriptional networks that are regulated by immunomodulatory therapy to improve recovery.

Methods and Findings: Adult female Scl-CreERT2 x R26-ZsGreen inducible reporter mice with and without immunomodulatory intervention (IVIG) were subjected to severe thoracic level 9 (T9) contusive SCI, followed by sorting of the $CD45^{pos}$ inflammatory infiltrate at 1, 3 and 7 days post-injury (n=3 per time point and condition) for single-cell RNA sequencing. A separate cohort of C57BL/6J SCI mice was processed for Visium spatial transcriptomics at matching time points (n=6 in total). Bioinformatics pipelines were then employed to demonstrate the presence of >30 immune cell (sub-) types and/or states at the site of SCI, and how their transcriptional signatures changed with time and/or treatment.

Significance and Conclusions: Our findings provide new insights into the complexity of the inflammatory response to SCI, with a particular focus on myeloid cell biology. We posit that better understanding the spatiotemporal activity of distinct myeloid subsets (or states) will assist the development of new strategies to promote improved recovery and the resolution of inflammation during spinal cord wound healing.

Funding: Wings for Life Spinal Cord Research Foundation & SpinalCure Australia.

Development of PD-like pathology in a novel rodent model of LPS-induced intranasal inflammation and traumatic brain injury

Samantha Edwards (B.Hlth & Med. Sc, PhD Candidate)[1,a], Eleanor Bowley-Schubert (B.Hlth & Med. Sc, PhD Candidate)[1], Charlotte Loipersberger (B.Hlth & Med. Sc)[1], Dr Rebecca George[1] A/Prof Lyndsey Collins-Praino (PhD)[1], A/Prof Frances Corrigan[1]

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Background: Parkinson's Disease (PD) is diagnosed based on hallmark motor symptoms, however additionally presents with a long prodromal phase characterised by symptoms such as gastrointestinal and olfactory dysfunction. PD is a complex neurodegenerative disorder with a multifactorial aetiology encompassing multiple risk factors. Traumatic brain injury (TBI) and olfactory inflammation, resulting from viral and other intranasal exposures, have been associated with olfactory and motor dysfunction, and independently linked with increased risk of PD. However, the role these risk factors play on the development of prodromal PD symptoms remains poorly understood.

Methods: Here, we assess synergistic effects of concomitant TBI and olfactory inflammation on the development of PD-like pathology. 8–10-week-old male Sprague-Dawley rats were randomly allocated to receive intranasal lipopolysaccharide (LPS; 1µg/uL, 50µL/naris) or saline as a control, followed by moderate-severe diffuse TBI or sham surgery seven days later. 3-months post-injury, animals underwent behavioural testing encompassing prodromal and motor symptoms.

Findings: LPS exposure worsened performance on the buried pellet test ($p=0.01$), indicating olfactory dysfunction, but TBI had no effect on olfaction independently or in combination with LPS. Gastrointestinal function, indicated by faecal water content, was not affected by injury, LPS or the two in combination. Gross motor function on open field and grip strength tests was also unchanged, while coordination, assessed by faults on the ledged beam task, was decreased in injured animals specifically ($p=0.0086$).

Interpretation: These results indicate persistent effects of injury and olfactory inflammation individually on specific functional domains, but no synergistic effect on PD symptom development. However, 3-months post-injury is an early time-point that does not represent the usual time course of neurodegeneration development. Furthermore, symptom presentation requires significant cellular pathology, while these exposures may cause subthreshold pathology that continues to worsen over time. Histochemical analysis is underway to further characterise synergistic effects of injury and inflammation in this model.

This project was funded by the Neurosurgical Research Foundation

Approved by the University of Adelaide Animal Ethics Committee, ethics number M-2023-020

Focal perivascular glial reactivity is a feature of the tau lesions in Chronic Traumatic Encephalopathy.

Helen Murray[1], Chelsie Osterman*[1], Danica Hamlin*[1], Catherine M. Suter[2,3], Andrew J. Affleck[2,3], Brian S. Gloss[4], Clinton P. Turner[1,5], Richard L. M. Faull[1], Thor D. Stein,[6,7], Ann McKee[6,7], Michael E. Buckland[2,3], Maurice A. Curtis[1].

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[4]Westmead Research Hub, Westmead Institute for Medical Research, Westmead, NSW, Australia
[5]Department of Anatomical Pathology, Pathology and Laboratory Medicine, Auckland City Hospital, 2 Park Road, Grafton 1023, Auckland, New Zealand.
[6]Department of Pathology and Laboratory Medicine, VA Boston Healthcare System, Boston, Massachusetts
[7]Department of Pathology, Boston University Chobanian & Avedisian School of Medicine, Boston, Massachusetts

Background: Chronic Traumatic Encephalopathy (CTE) is a neurodegenerative disease associated with repetitive head trauma and is characterised by the perivascular accumulation of hyperphosphorylated tau in the depths of cortical sulci. While the majority of CTE literature focuses on tau pathology, other pathological features such as glial reactivity, vascular damage, and axonal damage are relatively unexplored. We sought to investigate whether these pathological features are present within the CTE lesion using postmortem human brain tissue.

Methods: We examined frontal gyrus sections from 15 CTE, seven control, and eight Alzheimer's disease cases. Each section was labelled with 32 antibodies using multiplex immunohistochemistry to identify reactive gliosis, neuronal populations, axonal proteins, vasculature, ubiquitination, and tau. Images from the sequential rounds of labelling were aligned to create composite images of all 32 antibodies on the same tissue section, establishing microscopic resolution of the whole lesion microenvironment. The area of labelling for each antibody within the CTE perivascular lesion was compared to non-lesion vessels, and to Alzheimer's disease and control cases.

Results: Proteins associated with reactive gliosis (NQO1, CHI3L1, L-ferritin, GFAP, CD68, and aquaporin IV) were differentially expressed between CTE lesion and non-lesion vessels and between CTE, Alzheimer's disease and control cases. We observed focal expression of these reactive astrocyte and microglia markers around the tau lesion vessels in CTE, compared to a more ubiquitous distribution in Alzheimer's disease. No changes in axonal or vascular markers were observed.

Conclusion: The distribution of glial reactivity markers may be a neuropathological hallmark of CTE and suggests that repeated head trauma leads to a chronic and localised neuroinflammatory environment around blood vessels in the cortical sulci.

Psilocybin ameliorates chronic behavioral deficits and alterations in 5-HT$_{2A}$ receptor density in a rat model of traumatic brain injury

Josh Allen, PhD[1,4], Bianca Jupp, PhD[1], Mujun Sun, PhD [1], Robert Brkljača, PhD [1], Tamara Baker, PhD[1], Mohammad B Haskali, PhD[2,3], Rhys D Brady, PhD[1], Stuart J McDonald, PhD[1], Terence J O'Brien, PhD[1], Pablo M Casillas-Espinosa, PhD[1], Sandy R Shultz, PhD[1,4]

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2) Department of Radiopharmaceutical Sciences, Cancer Imaging, The Peter MacCallum Cancer Centre, Victoria 3000, Australia
3) Sir Peter MacCallum Department of Oncology, The University of Melbourne, Victoria 3010, Australia
4) Health Sciences, Vancouver Island University, Nanaimo, Canada

Background: Traumatic brain injury (TBI) is a significant global health concern that leads to persistent neurobehavioral sequela and an increased susceptibility to psychiatric disorders, such as depression, anxiety, and cognitive impairment. These issues are associated with deficient neuroplasticity, neuroinflammation, and impaired serotonergic neurotransmission. Presently, there are no approved effective pharmacotherapies that improve chronic TBI recovery. However, psilocybin, which targets several serotonin receptors, including the 5-HT$_{2A}$ receptor, has emerged as a promising candidate due to its rapid neuroplastic, anti-inflammatory, antidepressant, anxiolytic, and pro-cognitive effects. The aim of this study was to evaluate the effects of psilocybin for chronic TBI.

Methods: Male rats were subjected to an isolated severe fluid-percussion TBI or a sham injury. After a 1-year recovery period, rats received an intraperitoneal injection of either psilocybin (1 mg/kg) or saline. Motor ability, cognition, social function, and anxiety- and depression-like behaviours were assessed beginning 24 hours after treatment. Two weeks post-treatment, positron emission tomography (PET) scans were conducted to assess 5-HT$_{2A}$ receptor binding. Finally, brain tissue was processed to assess neuroinflammation and 5-HT$_{2A}$ receptor expression in the prefrontal cortex and hippocampus.

Findings: We found that psilocybin recovered sensorimotor, cognitive, and emotional impairments induced by TBI. Psilocybin also recovered deficits in 5-HT$_{2A}$ receptor binding availability and decreased the number of microglia cells.

Interpretation: Our PET data indicates that the beneficial effects of psilocybin are associated with the restoration of 5-HT$_{2A}$ receptor binding availability and psilocybin's anti-inflammatory properties. However, further research is necessary to elucidate whether psilocybin's therapeutic effects are dependent on the 5-HT$_{2A}$ receptor and/or other mechanisms of action.

Chronic Neuroinflammation and Functional Decline: Decoding Secondary Neurodegeneration Following Photothrombotic Stroke in Rats

Shannon M. Stuckey[1*#], Lyndsey E. Collins-Praino[2^], Rosie A. Costigan-Dwyer[1*], Isabella M. Bilecki[1*], Madeleine A. Homes-Vickers[2*], Amy J. Poyzer[1*], Rebecca J. Hood[1^], Lin Kooi Ong[3^], Renée J. Turner[1^]

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[*]Bachelor of Health and Medical Sciences (Hons); [^] PhD; [#]Corresponding Author

Background: Secondary neurodegeneration (SND), characterised by delayed neuronal death distal to the infarct site, is linked to long-term functional deficits after stroke. Neuroinflammation is implicated in SND, yet its long-term role remains underexplored, essential for understanding disease progression, identifying novel treatment targets and the potential window for intervention.

Aim: Investigate the spatiotemporal profile of neuroinflammation, neurodegeneration, and related functional changes post-stroke.

Method: Male Sprague-Dawley rats (n=88; 12-weeks) underwent photothrombotic stroke or sham surgery. Motor outcomes (open field and step test), anxiety (open field), and cognitive decline (Barnes maze and paired associated learning task) were assessed throughout the post-stroke period, with brain tissue and serum collected (n=30/stroke gp; n=14/sham gp) at 12- or 15-months post-stroke. Peripheral (serum) and neuroinflammation (SND regions: peri-infract, thalamus, hippocampus and basal ganglia) were analysed using a cytokine multiplex (Millipore). Data were analysed using mixed model ANOVAs, with Tukey's post-hoc test.

Findings: Motor activity significantly decreased 7-days post-stroke versus sham in the 15-month group ($p=0.0004$) but recovered by endpoint. Motor initiation was significantly impaired at 15-months compared to 12-months (sham: $p=0.0142$, stroke: $p=0.0012$). Anxiety ($p=0.001$) and cognitive deficits ($p=0.03$) were more prominent at 12-months compared to 15-months post-stroke. Pro- and anti-inflammatory cytokines in SND regions (IL-1β, IL-6, TNF-α, IFN-γ, MCP-1, IL-10, IL-4) were lower in stroke rats at 15-months compared to shams ($p<0.05$), while sham animals showed higher levels at 15-months than 12-months ($p<0.05$). In contrast, serum IL-10 levels were elevated at 15-months post-stroke versus 12-months ($p=0.025$).

Interpretation: Age is likely impacting the decrease in motor decline seen at 15-months. Indeed, increased cytokines in the 15-month sham group indicates inflammageing, whilst the decrease in the stroke group suggests immunosuppression. Cognitive and neuropsychiatric recovery at 15-months suggests long-term neuroplastic remodelling may occur. These results highlight that stroke-associated changes are ongoing >12-months, highlighting a prolonged therapeutic window for intervention.

Funding and Ethics: The Neurosurgical Research Foundation and Perpetual funded this study, which was approved by the University of Adelaide Animal Ethics Committee (M-2020-072).

DAY 1 – SESSION 2

Insights from the patient and clinician perspective

Understanding the challenges of concussion recovery: Perspectives from individuals with delayed recovery after mild traumatic brain injury

Rachel Singer[1,2], Jemma Keeves[1,2,3], Sarah Hellewell[1,2], Amanda Jefferson[4], Jacinta Thorne[1,2,5], Shaun Markovic[6,7,8], Samar Aoun[2,9,10], Melinda Fitzgerald[1,2]

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Corresponding author: Ms Rachel Singer (Research Assistant): rachel.singer01@gmail.com

Background: Mild traumatic brain injury (mTBI) is a complex and heterogeneous condition characterised by a diverse array of symptoms. While many people recover well, a significant proportion may experience ongoing symptoms for months or years post-injury, affecting daily activities and quality of life. This study employed qualitative research to gain insight into the lived experience of individuals with mTBI, which could aid development of targeted approaches to treatment and care pathways.

Methods: An Australia-wide online retrospective survey was conducted for people aged 18 to 65 years who had experienced a self-reported 'concussion' (mTBI) from any mechanism within the previous 18 months. Qualitative thematic analysis was used to investigate responses to the question, "What was the most challenging thing for you about having a concussion injury?".

Results: 77 participants (33%) met the inclusion criteria, which included a recovery time of >4 weeks. This population had a median age of 35y (IQR 29-50), with 53% identifying as female. Participants described financial strains due to reduced work capacity, familial and social stressors from diminished ability to fulfill caregiving duties, and increased reliance on social support. A loss of independence and reduced capacity for regular activities were common challenges, and often associated with post-concussion headaches, fatigue, sleep disturbances, and persisting dizziness and nausea. Cognitive and emotional difficulties including reduced concentration, memory loss and confusion, increased irritability and anxiety were also consistently reported. Multiple participants perceived their lack of understanding about concussion recovery and prognosis to be a major challenge.

Interpretation: These qualitative findings offer valuable insights into the multi-faceted challenges experienced by individuals following mTBI. Our data indicates a need for holistic support systems to address the diverse challenges people encounter during recovery, and to ensure accurate and informed education about recovery and prognosis is provided to people after mTBI.

Heads Up on Concussion: Aboriginal and Torres Strait Islander Peoples' Knowledge and Understanding of Mild Traumatic Brain Injury: A qualitative study.

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Background: There is a lack of understanding of the level of awareness and knowledge relating to concussion among Indigenous Australians. Factors preventing presentation for assessment after a potential concussion injury are also unknown. This limits the ability to target education and implement early intervention strategies. Aim: to investigate the knowledge of concussion among Indigenous Australians residing in Perth, Western Australia (WA).

Study design: A qualitative study. Participants were 18-65 years, recruited via Facebook advertising and snowball sampling. A semi-structured interview guide was used to facilitate 1:1 or group interviews with eligible and consented participants. Interviews were audio-recorded, transcribed, and thematically analysed using Nvivo.

Findings: Twenty-four participants were recruited**.** A good knowledge of modes of concussion injury was identified, however, there was difficulty differentiating concussion and its clinical presentation from other head injuries or medical conditions. Multiple factors contributed to a reluctance to seek assessment and further management of a potential concussion. A wide range of strategies to enhance education and increase presentation for assessment and management after sustaining a possible concussion were identified.

Interpretation: This study increases understanding of concussion knowledge in Indigenous Australians. Investigators included Aboriginal researchers, however, data was collected and formally analysed by non-Indigenous researchers. We acknowledge the potential influence this may have on the development of research findings but have confidence that Aboriginal co-investigators supervision assisted to mitigate these limitations. Further research is required to compare findings with other regions of Australia. Indigenous Australian owned and led concussion education is the first step in enhancing understanding of this condition. Education must be coupled with improvements in the cultural safety of healthcare services, as without this, patients will continue to fail to present for assessment and management. Concussion education focused on its differentiation from other injuries and where and when to seek medical assessment is recommended.

Ethics approval: WAAHEC (HREC1012) and Curtin University (HRE2020-0690).

Funding information: Curtin Medical School, Curtin University

Persisting symptoms, quality of life and return to work following mTBI in an Australian community-based cohort: results from the Concussion Recovery Study (CREST)

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Background: Most people recover well following mild traumatic brain injury (mTBI), however some experience persisting post-concussion symptoms (PPCS) for months or years. In an Australian population, the incidence of PPCS, impact on quality of life (QoL) and ability to return to work (RTW) after mTBI is currently unknown. Our aim was to evaluate the presence of PPCS, QoL and RTW for Concussion Recovery Study (CREST) participants at 3- and 12-months after mTBI.

Methods: CREST is a prospective, longitudinal cohort study of adults aged 18-65 years who sustained mTBI from a range of mechanisms. Telephone interviews were conducted within seven days of injury to collect demographic, pre- and peri-injury data. Acute concussion symptoms were assessed using the Post-Concussion Symptom Scale. Primary outcome measures were PPCS (symptom severity score >6 for males; >7 for females), health-related QoL using the Quality of Life after Brain Injury–Overall Scale (QOLIBRI-OS); and RTW in some capacity at 3- and 12-months post mTBI.

Findings: 232 participants with median age 33 years (IQR 24-50 years), 101(43.5%) female, 74(31.9%) sports-related mTBI, were included in analysis. Of 164(70.7%) participants completing 3-month follow-up, 81(49.7%) had PPCS. At 3-months median QOLIBRI-OS score was 87.5% (IQR 67-96). Of those working pre-injury, 131(95.6%) had RTW. Notably, 59(43.1%) of people who had RTW at three months had PPCS. At 12-months, 137(59.1%) people completed follow-up; 62(45.3%) were experiencing PPCS and median QOLIBRI-OS score was 88.0% (IQR 71-96). Of those working pre-injury, 109(94.8%) had RTW, with 38.3% working with a degree of PPCS.

Interpretation: Of those participants who completed follow-up, almost half reported experiencing persisting symptoms at 12 months after mTBI. Over a third of participants are continuing to work while symptomatic. Outcomes for those lost to follow-up are unknown, representing potential response bias. Further investigation into the social, financial and economic burden of PPCS is warranted.

Changing the Game – The Impact of Serious Games-Based Cognitive Training on Cognitive Function in Parkinson's disease

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Background: While traditionally recognised as a motor condition, Parkinson's disease (PD) is associated with a significant risk of cognitive dysfunction, with approximately 26% of individuals with PD developing dementia within five years post-diagnosis. Cognitive decline in PD is often under-recognised, with limited disease-altering interventions available. Cognitive training (CT) has shown promise in maintaining cognition; however, traditional methods often require fine motor skills, making such methods less accessible for individuals with motor difficulties.

Aim: To assess cognitive function and evaluate the immediate impact of *NeuroOrb*, a novel serious games-based cognitive training platform, on individuals with PD over six-weeks.

Methods: 75 individuals diagnosed with PD were randomly assigned to three groups: NeuroOrb (n=25), CogCafe (n=25) or Control (n=25). Preliminary data were analysed from 44 participants who engaged with either the NeuroOrb system or CogCafe pack, which included puzzle-based activities, for three hours per week over six weeks. Cognitive function was assessed pre- and post-intervention using a comprehensive battery of assessments. Secondary outcomes included mood and quality of life measures.

Findings: Preliminary results indicated a significant reduction in total errors on an episodic memory task for the NeuroOrb group compared to the CogCafe group after the six-week intervention ($p=0.0169$). In the NeuroOrb group, mean total errors decreased from 34.64±3.58 to 27.63±3.02, representing an 8.3% reduction in errors. No adverse events or side effects were reported.

Interpretation: These findings suggest that the NeuroOrb system may improve cognitive function in individuals with PD, highlighting the potential of serious games-based interventions in addressing cognitive decline in PD. While limitations include a small sample size and short follow-up, the focus on accessibility may bridge the gap for individuals with motor difficulties, facilitating greater engagement in cognitive training.

Funding and Ethics: Funded bodies include Perpetual Impact Philanthropy Application Program and Lifetime Support Authority. Ethics approval was granted by the University of Adelaide's Human Research Ethics Committee (H-2020-214; H-2022-020).

"*Rock on technology*": Perspectives on robot-assisted lower limb and gait neurorehabilitation from people with neurological conditions

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WARRIor Investigators: Samuel Cooper, Emma Gee, Eric Gaitho.

Background: Robot-assisted rehabilitation (RAR) is a promising approach to improve function and quality of life in people living with neurological conditions. There are no studies of the perspectives of people with neurological conditions on RAR in Western Australia (WA). The aim is to explore the perspectives and lived experience of people living with neurological conditions on RAR in WA, whilst evaluating the need for RAR implementation in WA.

Methods

Study design

This was a co-designed, qualitative descriptive study. People expressed interest in participating via recruitment flyers. This project was approved by the University of Notre Dame Australia Human Research Ethics Committee (2023– 32F).

Participants

Twenty-four participants took part (54.2% female), of whom 13 had RAR experience. Participant median age was 50.5 (23-77). Eligible participants had experience of rehabilitation for a neurological condition, aged ≥18 years old, resided in WA and were able to participate in English. Three neurological conditions were represented among the participants [spinal cord injury n=11, stroke n=3, multiple sclerosis n=2, other n=8].

Interventions
Five face- to-face focus groups (FGs) took place at a private neurological outpatient clinic in Perth (WA). FGs were facilitated by a person with lived experience of stroke using a semi- structured interview guide.

Analysis
FGs were recorded, data transcribed, then thematically analysed using a reflexive approach.

Findings: Three main themes were established in relation to RAR in WA: perceived benefits (physiological, psychosocial, therapy, ambulation, independence and pain), barriers (lack of awareness, access, cost, psychological challenges and device limitations), and future implementation in WA (improved access, design and purpose of rehabilitation robotic devices).

Interpretation: Participants identified perceived benefits, barriers and considerations for future implementation of RAR in WA, but this can only be achieved through addressing barriers of cost, design limitations, improved access and awareness.

Funding: University of Notre Dame Australia; University of Newcastle.

'Reaching for Robotics' : A mixed methods study of clinician perspectives on robot-assisted lower limb rehabilitation in Western Australia.

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Background: Evidence supports the clinical use of robotic-assisted lower limb rehabilitation alongside conventional therapy for people with neurological conditions. Clinicians can strongly influence the first phase of change in implementing emerging technology. However, Western Australian (WA) clinician perspectives are yet to be explored. This study aims to investigate

the perspective of WA clinicians towards use of this technology and its optimal delivery to enhance neurorehabilitation.

Methods

Study Design: Clinicians working in neurorehabilitation in WA were recruited to participate in a survey and an optional interview. This project was approved by the University of Notre Dame Australia Human Research Ethics Committee (2023 – 132F).

Subjects/Participants: Fifty-six clinicians, working in a wide range of clinical settings, completed the survey. Eleven participated in an additional semi-structured interview, 6 (54.5%) of whom had prior clinical experience using robotic rehabilitation.

Analysis: Survey data were summarised descriptively. Interview data were thematically analysed using a reflexive approach.

Findings: The majority of clinicians were interested in upskilling in robotic rehabilitation (n=49, 87.5%) and incorporating robotics into their clinical practice (n=44, 78.6%). Lack of access to devices, limited clinician confidence, and varied attitudes towards device usability and funding were identified as the main limiting factors to robotic implementation. Comprehensive clinician upskilling and improved access to robotic knowledge and support services were reported as key facilitators to robotic use.

Interpretations: Clinician perspectives of robot-assisted lower limb rehabilitation are varied. However, findings of this survey indicate strong interest in the clinical adoption of robotics statewide. Addressing current barriers and embracing identified facilitators could inform the creation and delivery of robot-assisted neurorehabilitation services in WA, optimised for this state. A centralised robotic service was proposed as a way to improve clinical outcomes and quality of life for clients throughout WA and encourage clinicians to incorporate using robotic assistance into neurorehabilitation programs.

Funding : None

Acknowledgements: Bianca Haagman

DAY 1 – SESSION 4

Poster Blitz 1

Neurofeedback Intervention for Persistent Post-Concussion Symptoms: A Case Series on Functional Connectivity in the Salience Network

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Objectives: Persistent post-concussion symptoms (PPCS) may occur in up to 50% of concussion cases. There is no effective treatment for PPCS. The salience network (SN), involved in shifting between internally and externally directed cognitive states, can be altered in PPCS. This pilot study explores the utility of Z-score neurofeedback to attenuate PPCS and restore changes in functional connectivity within the SN.

Methods: Two participants with PPCS aged 36 (16m post-injury) and 26 (13m post-injury), were randomised to two intervention conditions: (1) 18 sessions of personalised qEEG-informed neurofeedback targeting frontoparietal hyperactivity over 6-weeks, (2) placebo-neurofeedback of the same quantity and duration to delineate effects of environment. The post-concussive symptom scale (PCSS) was used to assess pre- and post-intervention symptom severity. NeuroNavigator was used to measure SN functional connectivity, expressed as Z-score coherence and averaged to examine percentage change pre- and post-treatment.

Findings: Neurofeedback was associated with improvements in the SN across all frequency bands: delta (49.99%), theta (69.71%), alpha (62.57%), beta (63.35%), and high-beta (28.16%). In contrast, the placebo participant had minimal changes, with delta worsening by 1.29%, and modest improvements in theta (9.40%), alpha (18.43%), beta (9.68%), and high-beta (9.74%). The neurofeedback participant demonstrated a full (100%) resolution of PCSS severity, while the placebo participant endorsed only a 22% reduction in symptom severity.

Interpretation: These pilot findings suggest that, compared to placebo, neurofeedback may improve SN functional connectivity and abrogate PPCS. This data supports a larger ongoing study to validate these findings and further investigate the mechanisms underlying neurofeedback.

Funding: Bryant Stokes Neurological Research Fund, Western Australian Future Health Research and Innovation Fund Near Miss Award Ideas Grant, Perron Institute Internal Grant

Altered visual function as a biomarker for repetitive mild traumatic brain injury in adolescent rats

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Background: Visual dysfunction, such as photophobia or light sensitivity, is very common following repetitive mild traumatic brain injury (RmTBI). The aim of this study was to determine if electroretinography and/or visual evoked potential could be used as biomarkers for RmTBI. We hypothesized that electroretinography and visual evoked potential would be significantly altered following RmTBI.

Methods: Adolescent male Sprague Dawley rats (n=24) were implanted with visual cortex electrodes and visual evoked potentials were recorded. Another group of males and females were administered electroretinography (n=24). Rats then received three mild traumatic brain injuries and underwent a behavioural test battery to confirm injury induction. Rats were administered a follow-up visual evoked potential, or electroretinography procedure before being euthanized.

Analysis: The latency and amplitudes of the visual evoked potentials were measured at the positive peaks P2 and P3. The negative peaks and latencies were measured at N1 and N2. For the electroretinography, the amplitude of the a waves and b waves in addition to the oscillatory potentials OP1-5 were assessed. Data were analysed using repeated measures ANOVAs.

Findings: We found a significant effect of injury on time to right following the injury ($p=0.005$) and on footslips on the beamwalk task ($p<0.001$). The visual evoked potential showed a significantly decreased amplitude of the N2 component with injury ($p<0.01$). There were no significant effects of injury on any of the α waves, waves, or oscillatory potential amplitudes of the electroretinograph at any light intensity tested ($p's>0.05$).

Interpretation: The retina contralateral to injury showed no changes in electroretinography indicating this may be a less reliable means of diagnosis. Changes in the of the N2 component in the visual evoked potentials has been observed in migraine sufferers and these findings indicate potential utility in the diagnosis of RmTBI as well.

The Long Road: Using a Multi-Dimensional Approach to Examine the Relationship Between History of Concussion and Neurodegeneration in Adults over 50 years old

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Background: Concussions are a type of mild traumatic brain injury. While symptoms typically subside in two weeks, the long-term impact on brain health is uncertain. Research suggests concussion history nearly doubles the risk of later-life dementia, highlighting the need to discover biomarkers linking concussions to neurodegeneration.

Methods: 35 individuals aged 50+ with at least one prior concussion were age-matched to 12 individuals without histories of concussion (N = 47, mean age = 64.65 years, SD = 8.79 years). Participants underwent a background interview, standardized neuropsychological tests, and blood and saliva sampling. Additionally, a subset of 26 participants underwent magnetic resonance imaging.

Findings: Results from this pilot suggest that history of concussion may be subtly related to current cognitive, structural and biological functions. Adults with a history of concussion performed worse on some cognitive tasks including total digit span [$F(1,45)=6.743$, $p=0.0127$], and Trail Making B [$F(1,45)=4.13$, $p=0.048$]. A weak negative correlation was observed between total number of concussions and current telomere length ($r = -0.239$). In the cohort that received neuroimaging, we applied tract-based spatial statistics to investigate white matter integrity across the brain and general linear modeling to assess the relationship between concussion history and fractional anisotropy. This revealed regions of increased fractional anisotropy (i.e. left and right anterior thalamic radiations, left inferior frontal-occipital fasciculus, $p < 0.05$) in individuals with a history of concussion while controlling for age. Blood analyses are ongoing and expected to be completed by November 1, 2024. Once completed we plan to use regression modelling to explore how biological, structural and cognitive variables may be associated with a history of concussion.

Interpretations: This ongoing research suggests that some biological, structural and cognitive variables may be associated with a history of concussion.

Funding: This research is funded by Canadian Institute of Health Research, Brain Canada Foundation and Quebec Consortium for Drug Discovery

A novel, minimally invasive mode of photobiomodulation delivery to the injured rat spinal cord

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Background: Infra-red/near infra-red light therapy (or "photobiomodulation", "PBM") shows varied beneficial outcomes in diverse injury models. Currently, attempts to treat experimental spinal cord injury (SCI) using PBM involve the use of diffusion tip catheters, optic fibre cables or handheld devices. However, efficacy can be affected by dislodgment and/or infection, both leading to variable dosage absorbed at the injury site. These approaches also require restraint or anaesthesia during treatment sessions. To address these issues, we have developed a novel, wirelessly powered, hermetically sealed LED device (6x12mm) positioned directly over the lesion site in a rat thoracic (T10) SCI model. This allows animals to move freely during treatment, which promotes exercise induced benefits, and has the capability of being upscaled to a mobile device for human application.

Methods: In our safety pilot study, 12-week-old female Fischer rats (n=6) were subjected to a thoracic (T10) laminectomy, with the non-activated device sutured directly above the injury site. Weekly functional tests (open-field and ladder walk) were conducted for two months before euthanasia, and were analysed by three assessors (two blinded).

Findings: Kruskal-Wallis and post hoc Dunnett's multiple comparisons test revealed a significant difference in locomotion seven days post-surgery in BBB scores ($p=0.008$, 95% CI (-0.9, -0.1), and ladder-walk accuracy ($p=0.039$, 95% CI (0.05, 2.95), however this was not maintained. Implants remained in place and the morphology of the underlying spinal cords (toluidine blue-stained sections) appeared normal. IBA-1 immunostaining revealed low-level reactive changes in microglia but there was no evidence of altered astrocytic phenotype (GFAP immunoreactivity).

Interpretations: Despite our small sample size, evidence suggests our novel hermetically sealed implants only transiently affected locomotion, did not result in dislodgment, infection, or elicit a significant inflammatory response, and therefore may be of use as a first line, minimally invasive therapy for SCI repair.

Funding: Funded by Perron Institute for Neurological and Translational Science.

AUS-mTBI: designing and implementing novel health informatics approaches to improve outcomes for people with mild TBI across Australia

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Background

In Australia, approximately 180,000 mild traumatic brain injuries (mTBI) occur each year. These injuries can have long-lasting negative impacts on individuals, their families, and society. Management of mTBI is hindered by poor prediction of those at risk of delayed recovery, as well as inconsistent treatment and care. Previous longitudinal studies have faced limitations related to the logistics of data collection; primarily relying on pen-and-paper tests, with fewer time points assessed post-injury, and often relying on metropolitan populations for recruitment.

Methods

The AUS-mTBI national consortium will use web-based app technology to gather data to aid reliable prediction of outcome and improved management of mTBI. AUS-mTBI aims to recruit 5000 participants aged five years and above across Australia, who have experienced mTBI from various aetiologies. The study has received ethics approval via Alfred Health HREC [ID 95470]. Self-reported demographics, injury circumstances, health status, mTBI symptomatology, and care management data will be collected. The presence of persistent post-concussion symptoms will be assessed fortnightly for 3 months after injury and then monthly until symptom resolution using the Rivermead Post-Concussion Questionnaire (adults), or the Post-Concussion Symptom Inventory (5-18 years). Through the app, participants will also be provided with an evidence-based recovery program tailored to their circumstances, and can track their symptom changes over time.

Interpretation

AUS-mTBI is the first study globally to integrate best practice, cutting-edge research, and patient recovery experiences for people with mTBI. This integrated core dataset will be analysed using machine learning to develop prognostic algorithms that will determine the relative contribution of multiple factors predictive of outcome. Identification of factors that may be amendable to interventions will facilitate the enhancement of care pathways to reduce the public health burden of mTBI, ultimately improving care and management of those at risk of a delayed recovery.

Funding

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Patient-Oriented Cognitive Rehabilitation: Effects of Three-Dimensional Multiple-Object Tracking on Cognitive and Functional Outcomes in Traumatic Brain Injury Survivors

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Background: Traumatic brain injury (TBI) is a leading cause of disability worldwide, affecting an estimated 69 million individuals annually. However, accessible recovery tools are limited. Three-dimensional multiple object tracking (3D-MOT) is a visual-spatial cognitive training task that engages working memory, distributed attention, and complex motion integration. This study aimed to assess the effects of 3D-MOT on quality of life and cognitive function in TBI survivors.

Methods: In partnership with the Victoria Brain Injury Society, 20 adults with moderate to severe TBI, all more than one year post-injury, were recruited. Ethics approval was obtained from the University of Victoria Human Research Ethics Board, and participants provided written consent. Participants were randomized into the 3D-MOT intervention or waitlist control group. Pre- and post-intervention assessments involved neuropsychological testing and standardized self-report questionnaires, including the Mayo Portland Adaptability Inventory 4 and Sport Concussion Assessment Tool 5. The intervention group completed 3D-MOT training at home twice per week for five weeks. Estimation statistics were used for analysis, incorporating 5000 bootstrap samples with bias-corrected and accelerated confidence intervals. Results are presented as (pre-post intervention mean difference [95% CI]); (pre-post control period mean difference [95% CI]).

Findings: Fifteen participants (10 male, 5 female) completed the study. The 3D-MOT group showed a 38.1% reduction in daily life challenges (-20.28 [95% CI: -39.45, 0.11]); (-5.25 [95% CI: -23.57, 15.46]) and a 38.5% decrease in symptom severity (-25 [95% CI: -52.71, 10.71]); (-3.25 [95% CI: -26.37, 13.89]). Intervention participants also improved 33.2% in verbal fluency (12.43 [95% CI: 2.67, 22.47]); (0.625 [95% CI: -12.38, 11.00]).

Interpretation: These findings suggest 3D-MOT has potential as a therapeutic tool for improving quality of life and cognitive function in moderate to severe TBI survivors.

Funding: Mitacs Accelerate, Canadian Institutes of Health Research, Eldercare Foundation.

The effect of contralateral cortex injection of AAV1-CRMP2 on C6/7 hemi-contusion spinal cord injury repair in Fischer rats

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Background: Collapsin response mediator protein 2 (CRMP2) is a microtubule-associated phosphoprotein in the mammalian CNS. It has multifunctional properties and is known to influence neuronal cytoskeleton integrity, a function that is inhibited following phosphorylation after injury. Importantly, preventing phosphorylation is reported to stabilise axons and promote neuronal survival after trauma.

Methods: In this pilot study, CRMP2's neuroprotective capacity was investigated following a moderate cervical C6/7 hemi-lateral contusion spinal cord injury (SCI) in anaesthetised adult female F344 rats. Rats were randomly assigned to experimental groups and neurons in contralateral forelimb sensorimotor cortex were transduced immediately after SCI with four 0.5ml injections of bi-cistronic adeno-associated viral vectors (AAV1) expressing either a mutated phospho-resistant form of CRMP2 (mCRMP2GFP) (2.1×1013GC/ml) (n=4) or AAV1mCherry in control rats (n=4). Function was assessed for 8 weeks post-injury using various behavioural tests and independently scored by four 'blinded' reviewers.

Findings: Morphology of corticospinal tract (CST) axons was compared between treatment groups by injecting biotinylated dextran amine into the same previously transduced regions of cortex. Rats were perfused two weeks thereafter (56 days after SCI). There were significant functional deficits associated with CST impairment but there were no significant differences between treatment and control groups (two-way ANOVA). Qualitatively, we observed fewer degenerative CST (GFP-positive) axons, increased microglia infiltration and smaller cysts near the injury in mCRMP2 treated rats. However, there was considerable variability, presumably from inconsistent damage sustained by the CST during the injury.

Interpretation: Transduction of mCRMP2 with AAV1 into the sensorimotor cortex of the rat brain can successfully target corticospinal neurons and their axons, providing a potential avenue to further explore the neuroprotective effects of mCRMP2 after SCI. Experimental procedures were approved by the Animal Ethics Committee of The University of Western Australia (approval number 2021/ET000687).

Funding: This study was funded by the Neurotrauma Research Program.

AUS-mTBI Extend: An extended, innovative data collection to predict recovery for people with mild traumatic brain injury.

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Background
Understanding mild traumatic brain injury (mTBI) is a significant challenge in Australia and worldwide. At least one in five Australians will experience a mTBI over their lifetime, with approximately 180,000 cases reported each year. Although most individuals recover within a few weeks of their injury, 20-50% experience ongoing and persistent post-concussion symptoms. Similar large-scale consortia to-date have been limited by the use of outdated neuroimaging sequences, and insufficient follow-up time points of recovery, restricting the generalisability of findings.

Methods
AUS-mTBI Extend aims to recruit 200 participants via three metropolitan Emergency Departments (Melbourne; Brisbane; Perth), and has received ethics approval via Alfred Health HREC [ID 94655]. Demographic, injury circumstance, health status, mTBI symptomatology and care management data will be collected at the time of injury, with telephone follow-up for 12-months. Participants will provide blood and saliva samples within 12 hours of injury, and undergo a multimodal MRI scanning protocol to collect complementary aspects of brain structural and functional connectivity including blood-brain barrier integrity and white matter microstructure; vestibular/ocular motor screening; cognitive assessment; and balance assessment within 4 days of injury. This MRI protocol has the potential to set a world standard for imaging after mTBI. Follow-up assessment will be completed at 1-week, 2-weeks, 1-, 3-, 6- and 12-months after injury to assess post-concussion symptoms, using the Rivermead Post-Concussion Questionnaire (adults), or the Post-Concussion Symptom Inventory (14-18years), and quality of life using the Quality of Life after Brain Injury Overall Scale.

Interpretation
The collection and integration of longitudinal multimodal data including neuroimaging, biomarkers, social, health, clinical, and outcomes data will contribute to a detailed understanding of recovery following mTBI, ultimately improving care and management of those at risk of a delayed recovery.

Funding
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Investigating the Role of the Circadian System in Traumatic Brain Injury within Adolescent Rats

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Background: Patients with mild traumatic brain injury (mTBI) often suffer persistent post-concussive symptoms, and commonly exhibit sleep dysregulation. The suprachiasmatic nucleus (SCN) receives light, or photic, information from the external environment to generate circadian rhythms. Following mTBI, these rhythms may be disrupted, impairing sleep and mTBI recovery. Therefore we aimed to examine changes to the SCN following repeat mTBI (RmTBI) as this could provide an avenue to improve clinical outcomes.

Methods and Analysis: Adolescent male and female rats (n=64) were given three sham or RmTBI injuries, followed by behavioural testing. Colchicine was injected into the SCN to better visualize cell morphology prior to euthanasia. Immunohistochemical detection of substance P (SP), calbindin (CalB), vasopressin (VP), and glutamate decarboxylase (GAD), was conducted in the SCN to quantify changes in photic neurotransmitters. In a separate experiment, another group of sham and RmTBI animals (n=24) received a 15-minute light pulse in the early night and then were euthanized 90 min later to examine c-Fos expression. For both experiments, the anterior, middle, and posterior of both left and right SCN slices were analysed using two-way ANOVAs with sex and injury as factors.

Findings: There were no significant differences in SP cell counts ($p = 0.899$). Within CalB, a sex difference was found, with females having more CalB cells in the SCN than males ($p<0.001$). VP cell counts displayed an injury by sex interaction ($p=0.036$). The relative optical density of GAD exhibited an injury effect ($p=0.001$), with an increase seen in RmTBI groups, a sex effect ($p=0.003$), and an interaction effect ($p=0.041$).

Interpretation: Females may have greater regulation of photic information, and thereby, the circadian system, whereas males may be more susceptible to circadian desynchronisation following RmTBI. Deficits were not seen following photic stimulation, and are therefore likely to not contribute to sleeping difficulties following RmTBI.

Exposure to Perinatal Trauma Modifies Nociception and Gene Expression in the Prefrontal Cortex and Hypothalamus of Adolescent Rats

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Background: Intimate partner violence (IPV) and early life stress/neglect, during the perinatal period can negatively affect neurodevelopmental processes and mental health outcomes, which subsequently can increase an individual's risk chronic pain. Although epigenetic programming likely contributes, the mechanisms driving the relationship between neurotrauma in the perinatal period and adverse health outcomes, are not fully understood. Therefore, this study explored the relationship between perinatal neurotrauma and socio-emotional functioning, nociceptive sensitivity, and transcriptomic changes within the prefrontal cortex (PFC) and hypothalamus in dams and their adolescent offspring.

Methods: Rat dams were randomly assigned to IPV (i.e., combined mild traumatic brain injury and non-fatal strangulation) or sham injury during pregnancy. Offspring were assigned to the early life neglect or control paradigm (P2-P12). In adolescence (P30), offspring received a plantar incision or sham injury. Adolescent rats went through a behavioural battery (EPM, open field, hot/cold plate, von Frey, novel context, forced swim). RNA-sequencing was run on dam and offspring PFC and hypothalamus tissue. Four-way ANOVAs with post-hoc analyses were run.

Findings: Perinatal trauma increased nociceptive sensitivity and impaired socio-emotional functioning in a cumulative manner. Transcriptomic changes related to DNA transcription and within the PFC and hypothalamus were identified in dams. The offspring transcriptome highlighted impairment in immune regulation, dysfunction in stress-reactivity, as well as microglia activation, and altered expression of genes associated with chronic pain.

Interpretation: Results demonstrate that neurotrauma in the perinatal period modifies offspring behaviour. Changes in gene expression within the PFC and hypothalamus of offspring highlight the persistent neurological changes that result from traumatic experiences early in life, while transcriptomic changes in the brain's of dams demonstrate that epigenetic processes may be involved in the intergenerational transmission of trauma.

Funding: We would like to thank NHMRC for their financial contribution through the Investigator Grant funding scheme to RM – Grant number 1173565.

DAY 2 – SESSION 5

Biomarkers of Injury

Next-Day Serum Glial Fibrillary Acidic Protein Levels to Aid Diagnosis of Sport-Related Concussion

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Background: Previous studies on sport-related concussion (SRC) may have measured brain injury blood-based biomarker, glial fibrillary acidic protein (GFAP), either before or after its peak, potentially underestimating diagnostic value. The primary aim of this study was to evaluate the diagnostic performance of serum GFAP at 24 hours post-SRC. Secondary objectives included assessing whether the timing of sample collection affected GFAP levels, and evaluating if combining GFAP with symptoms improved discrimination of SRC compared to symptoms alone.

Methods: In a prospective cohort study, adult male and female Australian football players with and without SRC had blood sampled around 24 hours post-injury/match. GFAP levels were quantified using Simoa assays, and area under the curve (AUC) values were calculated for time-bins of 16-24 hours, 24-32 hours and 36-52 hours. Symptom severity at blood collection was assessed using the Sport Concussion Assessment Tool 5 (SCAT).

Findings: One hundred and fifty-one athletes with SRC and 97 controls were sampled at a median of 24.5 hours (interquartile range [IQR], 21.7-28.0; min-max, 16-52). Time to sample post-match did not affect GFAP levels in controls; however, higher GFAP levels correlated with shorter time post-SRC (Spearman's r=-0.25 [95% confidence interval (95% CI), -0.40--0.09]). Median GFAP concentrations were 65.9 pg/mL (IQR, 49.1-81.3) in controls, and for SRC, 124.6 pg/mL (IQR, 86.7-190.7) at 16-24 hours, 94.5 pg/mL (IQR, 61.6-163.9) at 24-32 hours, and 59.9 pg/mL (IQR, 49.1-94.7) at 36-52 hours. AUC values at 16-24 and 24-32 hours were 0.83 (95% CI, 0.76-0.90) and 0.72 (95% CI, 0.64-0.80), respectively**.** Furthermore, combining GFAP with SCAT symptoms at 16-24h enhanced discriminatory capability compared with SCAT symptoms alone (AUC increased from 0.91 to 0.97; z=2.48, p=0.01).

Interpretation: Serum GFAP measured at 16-24 hours following potential or suspected SRC appears to be a useful objective aid to SRC diagnosis.

Instrumented Mouthguard Head Kinematics as Predictors of Concussion and Elevated Biomarkers of Astroglial and Axonal Injury in Amateur Australian Football Players

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Context: Sport-related concussion (SRC) poses detection challenges, with missed and delayed diagnoses linked to negative outcomes. Instrumented mouthguards (iMGs) may enhance detection by accurately measuring head kinematics, such as peak linear (PLA) and peak rotational (PRA) acceleration, though their relationship to clinical and neurobiological outcomes remains unclear. This study compared head kinematic metrics in amateur Australian footballers during head acceleration events, distinguishing between concussive and non-concussive impacts, and examined associations between PLA/PRA, SRC symptom severity, and biomarkers of astroglial and axonal injury.

Methods: A three-year prospective cohort study followed 277 amateur Australian football players wearing HitIQ Nexus iMGs. For players with suspected SRC, iMG data were located through time-stamped video analysis, and venous blood was collected along with symptom questionnaires at 24-hours and 6-days post-injury. Non-concussive (control) data were randomly selected from age- and sex-matched players, choosing the head impact with the highest magnitude based on percentiles for PLA or PRA for analysis. Differences in PLA/PRA between groups were analysed using Mann-Whitney U tests, while Spearman correlations explored associations with symptom severity and plasma GFAP and NfL levels, measured using a Simoa HD-X analyser.

Findings: Thirty-one SRC cases were reported during the study period, with 21 having verified iMG and paired blood data. While analysis is ongoing, preliminary findings revealed that compared to the 21 matched controls, the SRC group had higher median [IQR] values for PLA (64g [42-104g] vs 26g [18-36g]; $U=37$, $p<0.001$) and PRA (6626rad/s^2 [3714-8288rad/s^2] vs 3148rad/s^2 [1889-3819rad/s^2]); $U=75$, $p<0.001$). Preliminary analysis indicates no significant associations between PLA/PRA and symptom severity within SRC cases. Biomarker quantification and analysis is ongoing.

Interpretation: Head impacts leading to SRC had greater PLA/PRA magnitudes compared to controls. We hypothesise that kinematic measures will align more closely with brain injury biomarkers than clinical symptoms.

Funding:
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Biological Resilience in Stress Environments: The impact of Mild Traumatic Brain Injuries on Saliva Biomarkers

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3. Dr Sarah C Hellewell; BSc, PhD; Curtin Health Innovation Research Institute, Australia; Perron Institute for Neurological and Translational Science Perth, Australia.

Background: Modern warfare has resulted in a high percentage of military personnel experiencing mild traumatic brain injury (mTBI) and blast exposure due to training accidents and other occupational risks. These 'mild' injuries are thought to decrease mental resilience and increase the risk of developing maladaptive physiological processes.

Methods: This study compared saliva neuroendocrine biomarkers in Canadian Armed Forces Personnel (n=51; 39 male) over three unique stress environments: pre-deployment, deployment in Afghanistan and post-deployment reintegration. At each timepoint, participants provided saliva samples which were assessed for amylase, Chromogranin A (CgA) C-reactive protein (CRP), cortisol and testosterone. Participants were grouped based on their baseline TBI history (i.e. mTBI vs none), with further subgrouping for (a) both blast+mTBI: (b) blast only: (c) mTBI only: (d) no history of blast or mTBI. Two-way repeated measures ANOVAs were used to compare groups over time.

Findings: Significant differences were found in amylase, CgA, CRP and testosterone concentrations (all $p<0.05$), with significant interactions between group, timepoint and sex ($p<0.05$). Notably, these differences were driven by the blast and blast+concussion subgroups for amylase and CgA, while CRP and testosterone levels were elevated over time only in the mTBI subgroup. No differences were found in cortisol concentrations at any timepoint.

Interpretation: These findings suggest that blast and mTBI may cause differential responses to stress and influence biological resilience or susceptibility. Our findings provide unique insight into the mechanistic changes which occur during and following high stress military environments in at-risk populations, suggesting that blast and mTBI should be considered and treated as separate entities.

Funding: This study was funded by Royal Canadian Legion.

DAY 2 – SESSION 6

Neuroimaging

White matter microstructure in women who have experienced intimate partner violence related mild traumatic brain injury

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Background: Intimate partner violence (IPV) is a significant public health concern affecting one in four Australian women. Physical attacks commonly cause injury to the brain, such as concussion or non-fatal strangulation; however, intimate partner violence brain injuries (IPV-BI) have been overlooked and are under research. This study aimed to investigate white matter microstructure in victim-survivors of IPV-BI. It was hypothesised that IPV-BI will have greater white matter damage compared to control groups.

Methods: A case-control study of 66 females aged between 18-75 recruited into four groups. 25 IPV-BI participants who have experienced a probable IPV-related mTBI were compared to 15 IPV controls (history of IPV but not mTBI), 10 mTBI controls (with history of mTBI but not IPV), and 16 healthy controls (with no history of either mTBI or IPV). Diffusion tensor imaging data were acquired using a 3 T MRI scanner and analysed using tract-based spatial statistics (i.e. fractional anisotropy; FA, axial diffusivity; AD, radial diffusivity; RD, mean diffusivity; MD) to investigate white matter abnormalities between the experimental groups.

Findings: IPV-BI ($p = 0.03$) and IPV controls ($p < 0.0001$) had significantly reduced FA indicative of poorer white matter compared to mTBI controls. Similarly IPV-BI had significantly greater RD ($p = 0.02$) and IPV controls had significantly greater MD ($p = 0.03$), and RD ($p = 0.001$) compared to mTBI controls. There were no significant differences in DTI metrics between any other group comparisons.

Interpretation: Preliminary findings suggest that IPV victim-survivors, both with and without BI, have significantly poorer white matter microstructure compared to controls with a previous history of mTBI. While the analysis is ongoing, the inclusion of comorbidities (i.e. mental health diagnosis, substance use and premorbid IQ) and a measure of mTBI exposure may help to explain these findings further.

Funding: NHMRC

Quantitative electroencephalography reveals regional brain dysfunction in mild traumatic brain injury

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Background: Individuals with mild traumatic brain injury (mTBI) experience symptoms in domains like physical, psychological, cognitive and sleep-related , though it is unclear whether these symptoms reflect underlying brain dysfunction. The aim of this study was to analyse quantitative electroencephalography (qEEG) to detect regional brain dysfunction and determine correlation with symptoms following mTBI.

Methods: 24 participants (36.56 years ±12.87; 10F) with diagnosed mTBI and 30 matched controls (33.88 years ±12.15; 14F) were recruited as part of the CREST study. Five days post-injury participants completed the Post-Concussion Symptom Scale (PCSS) and Depression Anxiety Stress Scale (DASS-21). qEEG scans (resting-state, eyes-open, 5 mins) were acquired using NeuroGuide with a 19-channel Electro-cap (standardised 10-20 placement) and MITSAR-EEG-BT amplifier. Artifact-free data was imported into NeuroNavigator to generate current source density (CSD) for Brodmann areas (BAs). T-tests were used for each BA to determine the effects of mTBI on CSD. Pearson correlations were performed to assess the relationship to PCSS and DASS-21 scores.

Findings: Substantial bilateral increases in CSD were detected within the cingulate and retrosplenial cortices across multiple bands: delta, theta, beta and high beta. In the mTBI group, increased CSD in the delta band within the left cingulate was associated with PCSS total score ($r = -0.48$, $p<0.05$) and symptom severity ($r = -0.53$, $p<0.05$). In the beta band, bilateral increases in CSD in the cingulate (BAs 23, 31) and retrosplenial cortex (BAs 26, 29) positively correlated with DASS-21 anxiety and stress subscale scores (all $r>0.44$; $p<0.05$), while unilateral CSD increases correlated with depression scores: right-BA 23, $r=0.47$, $p<0.05$; left-BA 26, $r=0.52$, $p<0.05$; right-BA 29, $r=0.63$, $p<0.001$.

Interpretation: These findings suggest that the cingulate and retrosplenial cortices are specifically vulnerable to mTBI. Early CSD alterations may drive emotional symptom development post-injury, as they correlate positively with various emotional states and are linked to brain regions involved in anxiety, depression, and stress-related memory.

Parsing Cortical Thickness Heterogeneity in TBI: A Normative Modelling Approach

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Background: Traumatic brain injury (TBI) represents a major global health challenge, where research has been hindered by the complexities of heterogeneity. To parse heterogeneity, we propose a novel analysis technique in TBI, Normative Modelling. This offers a flexible framework for assessing individuals, comparing them to a reference cohort. We aim to examine the utility of normative modelling in characterising heterogeneity of neuroanatomical pathology, measuring Cortical Thickness (CT) following TBI. We hypothesise the majority of TBI participants will have significant deviations, but a minority will have shared neuroanatomical pathology.

Methods: We analysed 170 T1w MRI scans (71 TBI and 99 controls). We conducted two approaches, first, following a case-control structure, analysing statistically significant differences between TBI and controls via a mass univariate two-sample independent t-test. Second, we used the Hierarchical Bayesian Regression model to derive individual deviation scores for each participant in each brain region, with an extreme deviation defined as a z-score <=-2 or >=2.

Findings: The case-control approach resulted in 61 of a possible 150 brain regions being significantly different between groups (p-value<0.05). For the normative model, analysis is ongoing but preliminary results suggest TBI participants have at least one extreme deviation, however, there is minimal overlap of neuroanatomical pathology, with a maximum 28% of TBI participants sharing an extreme deviation in the same region.

Interpretation: By conducting parallel analyses of the same dataset, we were able to better understand the limitations of a case-control approach to measuring CT in TBI, and the utility of normative modelling as a possible technique to parse neuropathological heterogeneity. As expected, CT in the TBI group showed significant differences across vast brain regions, however, widespread heterogeneity in extreme deviations were observed between individuals. Thus, we conclude that normative modelling presents as a promising analysis technique to encapsulate the nuanced differences between TBI participants.

DAY 2 – SESSION 7

Preclinical models and behaviour

Acute and chronic brain and behavioural pathology produced in a neonatal mouse model of repetitive abusive head trauma

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Background: Traumatic brain injuries are the leading cause of death and disability in infants, with 1/3 of cases being inflicted by a trusted caregiver, referred to as abusive head trauma (AHT; previously known as shaken baby syndrome). Unfortunately, there are few diagnostic characteristics unique to AHT, and many children initially present asymptomatic or with non-specific symptoms. This results in children being released back into abusive environments where they may be subjected to repetitive injuries; it has been reported that a single child may sustain ~30 shaking injuries before diagnosis or death. Despite this, there are few preclinical models examining AHT. Therefore, we developed and characterised a mouse model of AHT to examine the progression of acute brain pathology and chronic behavioural deficits that manifest from single or repetitive AHTs.

Methods: Unanaesthetised mice were restrained on postnatal days (P) 8-12 and placed on a 400rpm shaker for 60s. Mice received 1, 3, or 5 shaking injuries and were euthanised on P14, P21, or P45. Prior to euthanasia mice underwent a behavioural battery to examine social interactions, anxiety-like behaviour, and nociception. Brain tissue was collected for analysis of gene expression and immunohistochemistry.

Findings: Mice that received AHTs had alterations in social interactions and increased thermal sensitivity to heat. There were changes at P14 in the hippocampus and prefrontal cortex in genes related to growth, development, cell excitability and cell damage, that were largely normalised by P21. There was an increase in blood vessel leakage, brain oedema, and alterations to water channel expression in the brain.

Interpretation: This mouse model is the first step in examining the short- and long-term consequences of AHT to the developing brain and the resulting behavioural manifestations. This will allow for the future exploration of diagnostic biomarkers and prevention of repetitive injuries.

Funding: NHMRC to BS, RM, HC.

Does pre-existing brainstem tau pathology exacerbate Alzheimer's-related behavioural deficits following a mild traumatic brain injury?

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Background: Traumatic brain injury (TBI) is an environmental risk factor for the later development of neurodegenerative diseases, including Alzheimer's disease (AD). However, TBI does not always lead to persistent neurodegeneration, instead TBI may accelerate disease progression in those with pre-existing pathology. The locus coeruleus (LC) is identified as the first site of tau pathology in AD and may be particularly susceptible to effects of TBI due to its high metabolic demand and anatomical location. This study aimed to examine the effect of pre-existing inflammatory-induced tau pathology within the LC on the development of AD-related behavioural deficits following a mild TBI.

Methods: 10-week-old male Sprague-Dawley rats (n=15-16 per group) were randomly allocated to sham or stereotaxic LC injection of artificial CSF. One week following, animals received sham surgery or diffuse TBI via the Marmarou weight-drop model. Three months following TBI, rats underwent a behavioural battery to assess anxiety-like behaviour on the Elevated Plus Maze (EPM), cognition on the Barnes Maze and affective state via burrowing.

Findings: No synergistic effect of pre-existing LC pathology and TBI was shown on the development of cognitive deficits ($p=0.85$), anxiety-like behaviour ($p=0.98$) or affective state ($p=0.67$) at 3-months. Injury alone was associated with a significant reduction to cognitive flexibility observed on the Barnes maze ($p=0.04$), with no effect of injury on anxiety ($p=0.76$) or affective state ($p=0.36$). Conversely, LC pathology was associated with increased anxiety-like behaviour ($p=0.03$) and depressive-like behaviour ($p=0.04$).

Interpretation: LC pathology was associated with dysfunction in neuropsychiatric but not cognitive domains, suggesting distinct LC neuronal sub-populations respond differently to similar insult. The lack of synergistic effect between LC pathology and TBI on cognitive and neuropsychiatric outcomes may indicate a 3-month timepoint is too acute for interaction between both insults. Future work will utilise immunohistochemistry to assess synergistic impact of LC pathology and TBI within the LC.

Funding: This project was funded by the Neurosurgical Research Foundation and approved by the University of Adelaide Animal Ethics Committee under ethics number, M-2023-020.

Changes to nociception and inhibitory neurotransmission in the cerebellum following a traumatic peripheral nerve injury in adolescent female rats

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Background: Peripheral nerve injuries resulting from the traumatic compression or transection of somatosensory nerves can lead to chronic changes in the brain and subsequently, neuropathic pain. Emerging evidence suggests a role for the cerebellum in neuropathic pain, yet its specific contributions to pain remain unknown, and much of the existing research neglects adolescent female populations. Therefore, this study aimed to characterise functional changes associated with inhibitory neurotransmission in the cerebellum that may be associated with altered nociception, using a sciatic nerve chronic constriction injury (CCI) model, in adolescent female rats.

Methods: Female Sprague Dawley rats were randomly allocated to receive a sham injury or sciatic CCI at 6-weeks-old. The elevated plus maze (EPM) quantified anxiety-like behaviour, and the von Frey test and hot/cold plate respectively assessed mechanical and thermal nociception. At 11-weeks-old, brains were collected and processed for immunofluorescence analysis of calbindin, GAD-65/67, and GABAAα1 in the cerebellum.

Findings: All rats spent less time in the open arms of the EPM, relative to pre-injury assessments, irrespective of injury group. The uninjured hind paw of CCI rats responded to larger filaments in the von Frey when compared to sham rats from post-injury day (PID) 14. The injured hind paw responded to smaller filaments, between PID 5–14. On the cold plate, CCI rats displayed faster latencies to react than sham rats. In the simplex and crus I of the cerebellum, CCI rats exhibited a higher density of calbindin-positive cell bodies than sham rats, and reduced intensity of GAD-65/67- and GABAAα1-positive signal.

Interpretation: In adolescent female rats, CCI is associated with the reduced density of Purkinje cells and altered inhibitory signalling in the cerebellum which may be related to their heightened sensitivity to mechanical and cold nociception. Future studies should clarify the precise mechanistic relationships between cerebellar function and neuropathic pain.

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Machine learning-based segmentation and classification of axons following optic nerve injury.

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Background: Changes to axonal ultrastructure provide important pathological insight into secondary degeneration following neurotrauma and other neurodegenerative conditions. Manual and semi-automated traditional methods for quantifying axonal alterations require significant user input for axon segmentation, making them subjective and labour intensive. AxonDeepSeg is an open-source convolutional neural network software for automatic analysis of micrographs. We hypothesised that AxonDeepSeg could be used to derive traditional and new axon and myelin metrics, with high fidelity to manual measurements.

Methods: We trained an AxonDeepSeg model to segment axons in transmission electron micrographs of optic nerves from female Piebald Virol-Glaxo rats at 2 weeks following partial transection injury (n=5) or sham surgery (n=5). Our model classified 84.7% of axons and myelin accurately and was comparable to manual measurement of axon diameter.

Results: Using AxonDeepSeg measurements, we found that injury increased g-ratio ($p<0.03$), solidity ($p<0.02$), and axon area/fibre area ratio ($p<0.02$). Unsupervised spectral clustering revealed six clusters of axons with unique defining metrics. We discovered that injury significantly altered these cluster metrics, resulting in a larger g-ratio ($p=0.02$), solidity ($p=0.03$) and axon area/fibre area ratio (0.03) in cluster 1 and larger g-ratio ($p=0.02$), axon area ($p<0.001$), axon diameter ($p=0.03$), solidity ($p=0.02$), and axon area/fibre area ratio ($p=0.02$) in cluster 2.

Interpretation: We conclude that AxonDeepSeg reproduced manual measurements of axon diameter, and enabled discovery of novel morphometrics that distinguished injured axons from uninjured axons, allowing assessment of injury-related changes. AxonDeepSeg will be a valuable tool for objective and high-throughput analysis of axonal morphology, facilitating future ultrastructural investigations in neurodegeneration.

DAY 2 – SESSION 8

Mental Health Consequences of Injury

Mental health, personality and quality of life factors affecting mTBI recovery in an Australian cohort.

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Background: 17,700 Australians present to hospital annually with mild traumatic brain injury (TBI). 10-50% of people with mTBI experience poor recovery and deal with the sequelae of brain injury for months or years. Our objective was to gain insight into psychosocial factors of Australians with mTBI and identify those experiencing persistent post-concussion symptoms (PPCS), so that strategies can be employed to improve their recovery.

Methods: An online retrospective survey was conducted, inviting Australian residents aged 18-65 who experienced mTBI within the preceding 18 months. All surveys were completed in an anonymised format. Results were analysed using Chi-squared tests or ANOVA using PPCS as the outcome variable. Logistic regression was used to determine the relationship between mental health (MH), personality traits (using the Big Five Inventory-10) and quality of life (QoL) and the presence of PPCS at 18m. This study received ethics approval by the Curtin University Human Research Ethics Committee (Approval Number HRE2020-0536).

Findings: Of 201 participants (47.6%F), 27(13.4%) had PPCS at 18m, with headache and nausea (physical disturbances), the most common complaints. 81.5% of those experiencing PPCS had a MH disorder, vs. 40.8% of those without symptoms ($p<0.002$). Participants were 3x more likely to experience PPCS if they had a MH diagnosis pre-injury ($p=0.048$), and 5x more likely to remain symptomatic with a MH diagnosis post-injury ($p=0.018$). Of the five personality traits, neuroticism and extraversion were associated with anxiety, depression and/or panic attacks ($p<0.025$) and QoL was lower in the group with PPCS ($p=0.002$).

Interpretation: These findings suggest the presence of a MH disorder and scoring high in the neuroticism or low in the extraversion personality domains, may predispose people to poorer recovery. Incorporating these measures into clinical practice may allow early identification and personalised intervention to aid recovery.

Funding: Funded by the Perron Institute for Neurological and Translational Science through the award of a Perron Internal Grant.

The relationship between early-life trauma and mental health outcomes among women IPV victim-survivors

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Background: Intimate partner violence (IPV) is a common health and welfare issue worldwide that predominantly affects women, and a substantial proportion of victim-survivors develop psychiatric problems. Identifying those who are most susceptible to developing these conditioning is important to facilitate early intervention. Exposure to adverse childhood experiences (ACE) is a risk factor for psychiatric problems in other contexts but has been specifically investigated in IPV. Therefore, this study aims to investigate the impact of ACEs on mental health outcomes in IPV victim-survivors. We hypothesize that IPV victim-survivors with a history of ACEs will have significantly worse mental health outcomes compared to those without a history of ACEs.

Method: Seventy-two female IPV victim-survivors aged 18-75 were recruited as part of an Australian study investigating brain injury in intimate partner violence. IPV victim-survivors completed questionnaires to categorise as ACE+ or ACE-, as well as self-reported questionnaires related to PTSD, depression, and anxiety symptoms. Regression analyses were run to determine the relationship between ACEs and IPV on mental health outcomes.

Findings: Of the 72 participants, 37 have probable PTSD, 43 have probable depression, 41 have probable anxiety. Although analysis is ongoing, our preliminary findings suggest that exposure to ACE can predict more significant depression among IPV victim-survivors.

Interpretation: ACEs may compound the mental health outcomes of IPV, and screening accordingly may be important for timely intervention. Ongoing analysis is also investigating the roles of IPV exposure and resilience on mental health.

Moderation Effects of Resilience and Coping Style on Relationships Between Psychological Health and Symptom Severity after Mild Traumatic Brain Injury.

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Background: Poor psychological health is associated with increased symptom severity following mild traumatic brain injury (mTBI). Highly resilient people who adopt adaptive coping mechanisms may be better equipped to manage and limit the negative influence of psychological well being on symptom severity compared with low resilient individuals or those who rely on maladaptive coping strategies. We investigated how acute measurements of resilience and coping style moderate relationships between psychological health and 3-month symptom severity.

Methods: 30 participants (13F, 36.6±13.5 years) recruited ≤7 days post-mTBI as part of the Concussion REcovery STudy completed self-reports: Depression Anxiety and Stress Scale-21 (DASS-21; Sub-scores: depression, anxiety, stress), Brief Resilience Scale (low resilience:≥mean-1SD, high resilience:≥mean+1SD) and Utrecht Coping List (coping styles: active, passive, avoidant, palliative, emotion, social, reassuring thoughts). At 3-months post-injury Post-Concussion Symptom Scale scores (PCSS) determined symptom severity; higher scores indicating increased severity. Moderation analysis using Hayes PROCESS model 4 was conducted.

Findings: Elevated DASS-21 sub-scores predicted increased PCSS (depression: $\beta=0.425$, $p=0.025$; anxiety: $\beta=0.580$, $p=0.002$; stress: $\beta=0.817$, $p<0.001$). Resilience moderated

relationships between PCSS, depression (p=0.002), anxiety (p=0.002) but not stress; low resilience increased PCSS (depression: β=0.670, p=0.031; anxiety: β=0.833, p=0.001) while high resilience mitigated these effects. Emotional (p=0.006), social (p=0.010), passive (p=0.031) and avoidant (p=0.021) coping moderated depression and symptom severity relationships. Use of emotional (β=1.444, p<0.001), social (β=1.146, p=0.001) and avoidant coping (β=0.858, p=0.005) increased effects of depression, elevating PCSS scores.

Interpretation: Elevated depression, anxiety or stress at the time of injury increases vulnerability to greater symptom severity experienced 3-months post-injury. High resilience may buffer the effects of depression and anxiety while low resilience may exacerbate symptoms. Preference for maladaptive coping styles uniquely exacerbates effects of depression on symptom severity. Implementing early interventions focused on fostering adaptive coping strategies and building resilience may attenuate symptom severity and improve long-term outcomes.

Funding: None

Characterizing the neurological consequences of intimate partner violence within a community-based sample of women victim-survivors.

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Background: Intimate partner violence (IPV) is a pervasive form of violence, affecting 1 in Australian 4 women over the age of 15. It has been reported that victim-survivors often experience persistent post-concussion symptoms (PPCS) and psychiatric conditions, such as post-traumatic stress disorder (PTSD), depression, and anxiety, as a results of their abuse. The prevalence of these conditions within a community sample of IPV victim-survivors is not well understood, as current research conducted from mental health clinics, women's shelters, and other crisis settings may not accurately characterize the mental health landscape of this population. Thus, community-based research is required to provide a clearer picture.

Methods: Women aged 18-75 were recruited through the placement of flyers in the general community including hospitals, libraries, sports centres, newsletters, and rehabilitation clinics. 36 participants were categorized as healthy controls, 35 as a history of IPV with no brain injury (IPV), 37 as a history of IPV with brain injury IPV-BI)), and 21 as a history of brain injury but not IPV (BI). Questionnaires were used to assess PPCS, PTSD, depression and anxiety symptoms, frequency of substance use, and other lifestyle factors.

Findings: IPV victim-survivors are at risk for a multitude of neurological consequences including PTSD, depression, anxiety, stress, and a worsened perception of their overall health compared to healthy controls and are more likely to experience PPCS compared to mTBI controls. Ongoing analyses is investigating the role of factors such as the number and duration of IPV relationships, substance use, and number of head impacts.

Interpretation: The results of this research underscore the mental and physical burdens that IPV places on victim-survivors within the community. Thus, it is imperative that support and treatment options that are accessible to all women within the community are developed.

DAY 2 – SESSION 9

Poster Blitz 2

Evaluating Cognitive and Motor Behavioural Changes within a Gyrencephalic Ferret Model of Mild Traumatic Brain Injury

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Introduction: Mild traumatic brain injury (mTBI) can lead to chronic cognitive and balance deficits in some patients, though the mechanisms underlying these symptoms are not fully understood. Preclinical models, particularly gyrencephalic ones, are valuable as they closely replicate the mechanical stress effects on the brain. This pilot study explored the outcomes of mTBI in ferrets up to six months post-injury.

Methodology: Ferrets (6-9months; 1-1.6kg) were randomly allocated to sham or TBI (n=5/group), with injury induced via the Closed-Head Injury Model for Engineered Rotational Acceleration (CHIMERA). Behavioural assessments included Open field (OF) for general locomotion and Puzzle Box (PB), and Quadrant maze (QM) to assess hippocampal memory and pre-frontal cortex based executive function. OF was performed at 14d and 6m post-injury, with PB and QM at 3 and 6-months post-injury

Results: No significant differences in distance travelled on the OF were seen at 14d (15.74±3.70 vs 15.21±2.79) or 6m (18.55±3.61 vs 16.85±2.66). In the QM all ferrets regardless of injury learnt the location of a milk reward over four trials (p=0.97), confirmed with a no-reward trial to rule out use of olfactory cues. When the reward location was changed injured ferrets took longer on the second new location trial at 3 (43.40±23.99 vs 26.40±14.26s) and 6m post-injury (45.80±36.94 vs 18.5±11.96s), although this was not significant (p=0.07). In the PB ferrets navigated a tunnel blocked with increasingly difficult obstructions (straw, foam, wood block), with 3 trials/obstruction. While injured ferrets showed similar latencies on straw and foam trials, they took significantly longer on the last wood block trial, conducted 24h after the previous trial, suggesting an impairment in long-term memory (p=0.029).

Conclusion: Subtle effects of injury of cognitive function may be present up to 6m in ferret mTBI. Future work will investigate the histopathological correlates of these behavioural changes.

All research was funded by the Neurosurgical Research Foundation and was approved by the South Australian health and Medical Research Institute (SAM 22-116)

Exploring the long-term blood-brain-barrier alterations associated with secondary neurodegeneration in Ischaemic stroke.

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Background: More than 70% of stroke survivors experience long-term cognitive impairments, which has been linked to secondary neurodegeneration (SND). SND involves the progressive death of neurons in regions not initially affected by the stroke i.e., thalamus and hippocampus. Within these regions blood-brain-barrier (BBB) dysfunction has been observed out to 3-months with links to cognitive decline, however long-term investigations remain scarce.

Methodology: 88 Male Sprague-Dawley rats (12 weeks) underwent photothrombotic stroke (n=30) or sham surgery (n=14/) and brain tissue was collected at 12- or 15-months. To assess SND-induced BBB leakage, immunofluorescence was conducted using albumin and immunoglobulin G, with analysis being conducted on Qupath (v0.5.1). BBB leakage was also assessed in 30 Merino sheep (2-3 years) that underwent 2h middle cerebral artery occlusion. Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) (3T Siemens) [TR/TE: 5.06/1.98] was conducted at baseline, 1, 3 and 6-months post-stroke (n=10/timepoint; 5F, 5M). Data was registered with the FMRIB Software Library (v6.0.7.9) and Ktrans maps were created using Quantiphyse (v0.9.9).

Findings: Immunofluorescence staining has been optimised for BBB antibodies in rodent brain tissue, with data analysis currently underway. Qualitative assessment of the Ktrans maps did not highlight broad regions of permeability at the delayed timepoints, but quantitative analysis is currently pending.

Interpretations: We anticipate that once analysis is complete these findings will help characterise the spatio-temporal profile of subtle BBB permeability changes in post-stroke SND.

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Tracking the temporal development of cellular hallmarks of neurodegenerative disease following repeated mild traumatic brain injuries in a rat model

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Background: Repeated mild traumatic brain injury (rmTBI) is prevalent in contact sports and increases risk of developing neurodegenerative conditions like Alzheimer's and Parkinson's diseases. While neuroinflammation and accumulation of alpha-synuclein (α-syn) and tau proteins are known pathological hallmarks of secondary neurodegeneration following rmTBI, the onset and progression patterns of these pathological markers from acute to chronic timepoints are unclear. It is unclear whether neuroinflammation precedes pathological protein accumulation or vice versa. Also, we do not know when brain-infiltrating immune cells, such as CD8+ T cells, become activated, or if brain-resident microglia interact with CD8+ T cells, thereby contributing to activation. Such research may inform early therapeutic interventions to mitigate secondary pathology progression.

Methods: A closed-head rmTBI rat model, where sham (no injury) or two injuries were delivered 24 hours apart, was used to investigate phosphorylated α-syn and tau accumulation in dopaminergic neurons (Tyrosine Hydroxylase+) of the substantia nigra, and activated CD8+ T cells (CD8+ GranzymeB+) and Iba1+ microglia densities in the brainstem and substantia nigra. Sagittal whole-brain sections collected at 4 days, 2 weeks, and 3- and 7-months post-injury were assessed by multiplexed fluorescence immunohistochemistry, imaged on a Zeiss AxioScan Z.1 Slide Scanner, and analysed using the Zen Blue 3.8 software. Experiment groups were compared by Two-way ANOVA and multiple comparisons tests.

Findings: Cross-sectional comparisons of brainstems from rmTBI versus sham show that CD8+ T cell density increased at 3-months ($p < 0.0001$) and 7-months ($p = 0.0028$) post-injury, suggesting increased brain infiltration. Also, CD8+ GranzymeB+ cell density increased at 3- ($p < 0.0001$) and 7- ($p = 0.0011$) months post-injury. No change was seen in CD8+ Granzyme B- cell density, indicating CD8+ GranzymeB+ cells accounted for the rise in CD8+ T cell density. The density of CD8+ GranzymeB+ cells that co-localised with Iba1+ cells increased at 7-months post-injury ($p = 0.0010$), indicating that activated CD8+ T cells have prolonged interactions with microglia, which can activate T cells.

Interpretation: These data suggest rmTBI induces peripheral CD8+ T cell infiltration, activation and microglia interaction in the brain, months after the initial injury. Data from this study will provide valuable insight into the relationship between neuroinflammation and proteinopathies associated with neurodegeneration post-rmTBI.

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Connecting the spots: Adapting the void spot assay as a non-invasive bladder assessment for rats with spinal cord injury

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Introduction: Regaining bladder function is one of the highest priorities for individuals with SCI, yet only 3.1% of preclinical SCI research assess urodynamics. Typical urodynamic assessments for rats with SCI are invasive, necessitate animal sacrifice, and require specialised equipment. Such barriers prevent researchers from evaluating bladder function in SCI studies. The void spot assay (VSA) involves placing animals in a cage lined with filter paper to evaluate voiding volume and pattern. While the VSA is an accessible, non-invasive option, it has not been used to evaluate bladder function in rats with SCI. As such, we evaluated whether the VSA can distinguish SCI animals from uninjured rats based on their voiding behaviour.

Methods: We randomised male Sprague Dawley rats into groups: naïve (n=4), sham (n=9), SCI-only (n=8), SCI+Intervention 1 [I1] (n=10), and SCI+Intervention 2 [I1] (n=9). SCI, I1 and I2 animals received a T10 SCI induction (200kdyne, Infinite Horizon), while sham animals received a T10 laminectomy. VSAs were performed at baseline and every two days post-SCI for two weeks. Animals received enrichment and food but had no water. Following the VSA, residual urine volume was measured. VSA papers were imaged under UV light and void size, number, bladder capacity and voiding efficiency were calculated using ImageJ. Any overlapping void spots were manually segmented.

Results: Despite rats with SCI exhibiting bladder dysfunction, the volume of urine voided was similar between non-injured (naïve, sham) and injured rats (SCI, US, BS) at all timepoints. However, bladder capacity in rats with SCI increased up to 6 times, and voiding efficiency significantly decreased at all time points post-SCI ($p<0.01$). Neither intervention affected bladder function.

Conclusion: We successfully distinguished rats with SCI from non-injured rats using the VSA, establishing this test as an effective and accessible method for evaluating bladder function in preclinical SCI studies.

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Alteration of Brain White Matter Tracts and Plasma Free Fatty Acid Concentrations following Mild Traumatic Brain Injury

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Introduction:: White matter (WM) tracts in the brain are susceptible to subtle alterations resulting from mild traumatic brain injury (mTBI), although these are not readily detectable using conventional MRI or fluid biomarkers. Given that WM is enriched with lipids which can cross the blood-brain barrier, lipids may be promising biomarker candidates and adjuncts to more sophisticated research MRI techniques to assess WM. This study aimed to determine

whether there are significant differences in WM alteration and plasma lipid concentration in participants with mTBI compared to healthy control participants.

Methods: The Concussion REcovery STudy (CREST) recruited participants with mTBI and healthy controls from the Western Australian community. 48 participants (23 mTBI, 25 control; 40% female) were included with a mean age of 35y. Plasma samples collected within 7d of injury were analysed for free fatty acid (FFA) concentrations using a colorimetric assay. Diffusion MRI scans were acquired within 9d, and fractional anisotropy (FA) values for mTBI participants were compared to controls using tract-based spatial statistics for voxel-based analysis.

Results: Participants with mTBI had significantly elevated FFA concentrations compared to controls, with mean concentrations of 0.035 and 0.027 nmol/μL respectively. ($p<0.001$). Significant clusters of reduced WM FA were found in the corpus callosum, corticospinal tract, optic radiations and internal capsule.

Conclusion: mTBI results in concomitant increases in plasma FFA and WM alterations in major commissural and projection fibres of the brain. The essential role of FFAs in membrane integrity suggests this may be a promising complementary biomarker to WM diffusion MRI.

Intrathecal administration of a neurotrophin-3-delivering hydrogel in rat spinal contusion injury model

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Background: Spinal cord injury (SCI) is a debilitating condition that can cause permanent neurological impairment, highlighting the need for effective regenerative treatments. Neurotrophic growth factor-loaded hydrogels have shown potential, but a reliable method to deliver and retain the hydrogel within the intrathecal space surrounding the injury site is needed.

Methods: We developed a technique to inject a hydrogel into the intrathecal space immediately following contusion SCI, placing it around and above the injury site. The hydrogel, composed of hyaluronic acid-modified heparin-poloxamer, was designed to be injected as a liquid and gel in situ to maintain its position. We optimized this delivery method using non-injured and SCI pilot rats with a fluorescently labeled hydrogel. Four treatment groups of 2–3 month-old female Sprague Dawley rats (n = 8–11 per group) were then assessed for motor and sensory recovery over 6 weeks: NT-3 in solution, unloaded hydrogel, NT-3-loaded hydrogel, and saline injections (sham). Tissue processing and immunohistochemical staining were performed on spinal cord sections.

Findings: Pilot studies confirmed that the fluorescently labeled hydrogel could be safely injected and retained within the spinal cord for 7 days without causing hind limb deficits or welfare issues. However, neither NT-3-loaded hydrogel nor unloaded hydrogel significantly improved motor or sensory outcomes over 6 weeks, nor did they affect histological markers (analyzed using two-tailed unpaired t-tests or one-way ANOVA).

Interpretation: The intrathecal injection and in situ gelling hydrogel provide a promising platform for delivering therapeutic agents in SCI models. However, NT-3 infusion did not yield measurable improvements in this study.

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Changes in radiological biomarkers of distal femur following concomitant spinal cord injury and traumatic brain injury

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Introduction: Individuals who have sustained a concomitant traumatic brain injury (TBI) at the time of spinal cord injury (SCI) risks physical and cognitive impairment. Unfortunately, clinical strategies are limited in identifying concomitant injuries, which presents challenges to appropriately identify and rehabilitate patients. Current literature supports the hypothesis that both SCI and TBI alone have peripheral effects, including long-term consequences in bone remodelling. However, it is unknown whether unique bone remodelling in a concomitant injury occurs, compared to a single neurotrauma. Therefore, in a newly developed rodent model of mild TBI+SCI (mTBI+SCI), we explored whether specific cortical and trabecular bone tissue biomarkers could diagnose concomitant trauma.

Methods: Femurs harvested from male Sprague-Dawley rats (N= 38), 6-weeks post-injury (Naive, Sham, SCI [C5 hemi-contusion, Infinite Horizon;100kdyne or 200kdyne], mild TBI [Marmarou weight drop, 1m], TBI+SCI [mild/moderate]) underwent micro-computed tomography (35µm, 85kV, 235mA), reconstruction (NRecon software) and analysis (Dragonfly software). Within each distal femur, cortical and trabecular bone were measured in three regions: subchondral bone; primary spongiosa; and secondary spongiosa. Bone volume fraction (BV/TV), Trabecular number (Tb.N), Trabecular thickness (Tb.Th), Trabecular separation (Tb.Sp), and Cortical thickness (Ct.Th) were analysed.

Results: mTBI and SCI alone induced bone remodelling evidenced by significant decreases in BV/TV (5.4-5.10%), Tb.Th (1.5-2.7%) and Ct.Th (7.7-9.4%). Additive effects of TBI+SCI were evident in primary spongiosa, with an observed increased Tb.Th (6.8 ± 3µm3) and Ct.Th (24.7 ± 11.2µm3). Contrastingly, mTBI+SCI demonstrated significant decline in BV/TV (-0.061 ± 0.027µm3) and Tb.N (-599.2 ± 148µm3) of primary spongiosa, in comparison to SCI.

Conclusion: Currently clinical strategies in detecting concomitant mTBI and SCI are limited. For the first time, we demonstrated unique bone remodelling outcomes post-injury. Therefore, non-invasive medical imaging and quantification of biomarkers in the distal femur may serve as a tool for detecting concomitant neurotrauma. Further histological and proteomic characterisation is currently underway.

Perceived and measured chronic cognitive function after traumatic spinal cord injury: insights from a clinical survey and testing approach.

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Background: Chronic cognitive dysfunction (CCD) is 13 times more prevalent in individuals with spinal cord injury (SCI) than in the general aging population, impacting memory, learning, and attention. Despite research evidence, awareness of CCD remains limited among SCI individuals, leading to its frequent oversight. This study aims to explore whether individuals' self-perceptions of their cognitive function align with objective cognitive assessments.

Study Design: This cross-sectional study involved 44 English-speaking adults (age ≥18) from Australia and New Zealand, all at least one-year post-traumatic SCI and free of severe brain, visual, or motor impairments. Participants completed an online survey on demographics and self-perceived cognitive function, followed by a web-based cognitive assessment measuring attentional shift, pattern recognition, working memory, visual memory and new learning.

Analysis: Cognitive scores were reported as normative standard scores, with ≤-1.5 indicating dysfunction. Descriptive statistics were generated using Structured Query Language. Ethics approval was granted by the University of Adelaide's Human Research Ethics Committee (H-2022-020), and all participants provided informed consent.

Findings: Preliminary data revealed that despite 46% of participants perceiving no cognitive changes after their SCI, nearly half scored ≤-1.5 on at least one cognitive test, indicating possible unrecognized dysfunction. Cognitive test results revealed a mean standard score of 0.41 (SD=0.77) in attention shift, -0.08 (SD=1.1) in pattern recognition memory, and -0.14 (SD=0.96) in spatial working memory. The most pronounced difference was observed in visual memory and new learning, with a mean score of -0.58 (SD=1).

Interpretation: Initial findings indicate limited awareness regarding CCD among SCI individuals. The discrepancy between perceived and actual cognitive function emphasizes the importance of utilising neuropsychological assessment to identify unrecognized CCD. Additionally, our results suggest that visual memory and new learning may be particularly vulnerable post-SCI and warrant close monitoring to address CCD in this population.

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