Where we are:
The Wicking Dementia Research and Education Centre
Medical Science Precinct, 17 Liverpool Street, Hobart
Located in picturesque Hobart the Wicking Centre is in a central location, close to the Waterfront, Salamanca and various coffee shops.

The Organising Committee will be wearing red striped badges. The Committee includes the following people:
Dr Jenna Ziebell, Dr Sharn Perry, Dr Nicole Bye, A/Prof Anna King, Prof David Howells, and Prof James Vickers.
Internet - UTAS eduroam internet connection available for all Australian University Students and Employees. Please use your host institution to log in.

#neurotrauma2017
Neurotrauma Symposium Program
Hobart - October 16-17
Room: MS2 - LT1

Monday October 16
12.00 - 13:00 - Registration          13:00 - Welcome

Session 1: Neurodegeneration and disease
Chair: Dr Nicole Bye

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Affiliation</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:10</td>
<td>Denes Agoston</td>
<td>Uniformed Services University, USA</td>
<td>Understanding the complexities of traumatic brain injury: Big Data approach to tackle a Big Disease</td>
</tr>
<tr>
<td>14:00</td>
<td>Roger Byard</td>
<td>The University of Adelaide</td>
<td>&quot;Shaken Infant&quot; - Forensic fact or fiction</td>
</tr>
</tbody>
</table>

15:00 - 15:30 Afternoon Tea

Session 2: Inflammation after injury
Chair: Dr Jenna Ziebell

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>15:30</td>
<td>Jonathan Godbout</td>
<td>The Ohio State University</td>
<td>Priming the inflammatory pump of the CNS after TBI</td>
</tr>
<tr>
<td>16:30</td>
<td>Jana Vukovic</td>
<td>University of Queensland</td>
<td>Microglia depletion improves spatial learning and promotes hippocampal neurogenesis following traumatic brain injury</td>
</tr>
<tr>
<td>16:40</td>
<td>Kyria Webster</td>
<td>The University of Melbourne</td>
<td>Glycyrrhizin reduces neuroinflammation acutely after pediatric traumatic brain injury</td>
</tr>
<tr>
<td>17:00</td>
<td>Bridgette Semple</td>
<td>The University of Melbourne</td>
<td>Mild traumatic brain injury during adolescence protects against subsequent skull fracture but does not worsen neurobehavioural outcomes after a second brain injury at adulthood.</td>
</tr>
</tbody>
</table>

17:20 – Session close

6 pm for a 6.30 pm dinner at Frank (1 Franklin Wharf, Hobart).
Neurotrauma Symposium Program  
Hobart - October 16 - 17  
Room: MS2 - LT1

Tuesday October 17  
Coffee served from 8:15

**Session 3: Stroke**  
Chair: Prof. David Howells

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Affiliation</th>
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<tbody>
<tr>
<td>9:00</td>
<td>Robert Medcalf</td>
<td>Monash University</td>
<td>The influence of plasmin on the innate immune response after trauma</td>
</tr>
<tr>
<td>9:30</td>
<td>Leon Teo</td>
<td>Monash University</td>
<td>Linking development and regeneration: Attenuating astrogliosis to improve outcomes after CNS injuries</td>
</tr>
<tr>
<td>10:00</td>
<td>Annabel Sorby-Adams</td>
<td>The University of Adelaide</td>
<td>Take the pressure down: A novel agent for the treatment of cerebral oedema and elevated intracranial pressure following stroke</td>
</tr>
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</table>

10:20 One minute posters

10:40 - 11:10 Morning tea and even numbered posters

**Session 4: Sharper tools for superior science**  
Chair: Dr Matthew Kirkcaldie

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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Affiliation</th>
<th>Title</th>
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<tbody>
<tr>
<td>11:10</td>
<td>Rohan Walker</td>
<td>University of Newcastle</td>
<td>Microglial paralysis: a hidden risk in post-stroke neurodegeneration</td>
</tr>
<tr>
<td>11:40</td>
<td>Lindsay Parker</td>
<td>Macquarie University</td>
<td>From nanoscience to neuroscience: Novel probes for background-free imaging</td>
</tr>
<tr>
<td>12:10</td>
<td>Aiden O’Mara</td>
<td>University of Tasmania</td>
<td>Addressing the challenges of high-throughput image analysis</td>
</tr>
<tr>
<td>12:30</td>
<td>Stephanie Plummer</td>
<td>University of Adelaide</td>
<td>Is a Sprague really a Sprague?</td>
</tr>
</tbody>
</table>

12:50 - 13:30 Lunch  
13:00 - Odd numbered poster session

**Session 5: Plasticity and axonal pathology**  
Chair: A/Prof Anna King

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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Affiliation</th>
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<tbody>
<tr>
<td>13:30</td>
<td>Kelsey Hanson</td>
<td>University of Tasmania</td>
<td>The role of microtubules in excitotoxin-induced axon degeneration</td>
</tr>
<tr>
<td>13:50</td>
<td>James Bender</td>
<td>University of Tasmania</td>
<td>Excitotoxicity and the resulting degeneration in the visual system</td>
</tr>
<tr>
<td>14:10</td>
<td>Joel Ernest</td>
<td>University of Melbourne</td>
<td>Using telomere length as a biomarker for sports related concussion in Australian rules football</td>
</tr>
<tr>
<td>14:30</td>
<td>Stuart Portbury</td>
<td>The Florey</td>
<td>Trehalose improves traumatic brain injury-induced cognitive impairment</td>
</tr>
</tbody>
</table>
14:50-15:20 Afternoon tea

Session 6: Spinal Cord Injury

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
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<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:20</td>
<td>Sharn Perry</td>
<td>University of Tasmania</td>
<td>Dmrt3 derived neurons modulate the alternation-synchrony locomotor switch</td>
</tr>
<tr>
<td>15:50</td>
<td>Cathy Gorrie</td>
<td>University of Technology Sydney</td>
<td>A neonatal model of rat spinal cord injury: Age-related differences in cellular and inflammatory responses</td>
</tr>
<tr>
<td>16:20</td>
<td>Mitra Amiri</td>
<td>Monash University</td>
<td>The role of roof and floor plate cells in zebrafish spinal cord regeneration</td>
</tr>
<tr>
<td>16:40</td>
<td>Ellen Gillespie</td>
<td>University of Queensland</td>
<td>Understanding the splenic response to spinal cord injury</td>
</tr>
</tbody>
</table>

17:00 – Announcement of awards, hand over to Adelaide, meeting close.
17:30 – Light refreshments ahead of public forum, student hub
Neurotrauma Symposium Program  
Hobart - October 16 - 17  
Speaker Biographies

Prof. Denes V. Agoston  
Department of Anatomy, Physiology and Genetics,  
Uniformed Services University  

Denes V. Agoston, M.D., Ph.D. is tenured Professor at the Department of Anatomy, Physiology and Genetics, USU, Bethesda Maryland, U.S.A and Guest Scientist at the Karolinska Institutet, Stockholm, Sweden. Professor Agoston spent most of his early scientific career at the Max-Planck-Institute in Germany and at the National Institutes of Health (NIH), USA. After obtaining his M.D. degree at the University Medical School, Szeged, Hungary he won a Max-Planck-Fellowship and made his Ph.D. in neuroscience in Gottingen, Germany. He won a DGF Fellowship and he worked as Visiting Scientist before becoming the Head of Neurodifferentiation Unit at the NICHD, NIH.  
Current research in the Agoston Laboratory focuses on the relationship between early pathobiology and long-term consequences in TBI using proteomics approaches. The Agoston Laboratory has been collaborating with research groups and hospitals worldwide on various aspects of TBI including identification of predictive biochemical markers for post-TBI seizures.

Prof. Roger Byard  
Chair of Pathology  
The University of Adelaide  

Professor Roger Byard AO PSM holds the George Richard Marks Chair of Pathology at The University of Adelaide and is a Senior Specialist Forensic Pathologist at Forensic Science SA in Adelaide, Australia. He has published, or has in press, over 700 papers in peer-reviewed journals, over 100 chapters and a number of texts. He is the Editor-in-Chief/Managing Editor of Forensic Science Medicine and Pathology (Springer NYC). He is a Professorial Fellow at The Florey Institute of Neuroscience and Mental Health in Melbourne, Australia, and received Distinguished Alumni Awards from The University of Adelaide in 2013 and the University of Tasmania in 2016. In 2016 he was also the recipient of the Distinguished Researcher Award from the International Society for the Study and Prevention of Perinatal and Infant Death (ISPID) and was elected a fellow of the Australian Academy of Health and Medical Sciences.

Dr. Catherine Gorrie  
School of Life Sciences  
University of Technology, Sydney  

Dr. Catherine Gorrie completed her PhD in 2006 at UNSW while undertaking studies of the brains of people who died in motor vehicle crashes. Her research expertise is in the neuropathology of traumatic injury and she has extensively investigated brain and spinal cord injury in both human and animal models. In particular, she has conducted pre-clinical experiments showing the suitability of olfactory ensheathing cell transplants for spinal cord repair, and successfully shown that the modulation of connexin43 hemichannels by a mimetic peptide improves outcomes following spinal cord injury. Her most recent research examines age related changes and the temporal and spacial responses of spinal cord neural progenitor cells to spinal cord injury.  
Dr. Gorrie joined the University of Technology Sydney in 2011 and is now Program Director for the B. Biomedical Science degree and Deputy Chair of the UTS Animal Care and Ethics committee. She has published 29 papers, 2 government reports and 60 conference abstracts on findings from these studies.
Dr. Sharn Perry
Wicking Dementia Research and Education Centre
University of Tasmania

Dr. Sharn Perry began her scientific career at the University of Adelaide under the mentorship of Dr Karin Nordstrom, where she worked as a research assistant in the Vision Laboratory in the Department of Physiology. After graduating with Bachelor of Biomedical Science, she completed her Honours project in motion vision processing working in conjunction with the University of Adelaide and the Motion Physiology Laboratory, Uppsala University, Sweden. Dr. Perry continued working at Uppsala University as a research assistant before commencing her PhD studies in the Developmental Genetics Laboratory at the Department of Neuroscience (also within Uppsala University, Sweden). Her PhD research focused on characterising the functional role of defined spinal cord interneuron populations and their individual contributions to the locomotor central pattern generator. Following her PhD, Dr. Perry continued her research work in spinal cord interneuron populations working as a postdoctoral researcher and part time laboratory manager in the Developmental Genetics Laboratory, before accepting a postdoctoral position at the Wicking Dementia Research and Education Centre, University of Tasmania.

Prof. Jonathan Godbout
Wexner Medical Center,
The Ohio State University

Dr. Jonathan Godbout is a Professor of Neuroscience at the Ohio State University Wexner Medical Center. He is also appointed in the Institute for Behavioral Medicine Research and Center for Brain and Spinal Cord Repair. In addition, Dr. Godbout is the Co-Director of the Neuroscience Graduate Program. Dr. Godbout has a B.S. (1996) and a Ph.D. (2001) from the University of Illinois-Urbana and was a NRSA-supported postdoctoral fellow (2001-2005). As a Principal Investigator, Dr. Godbout’s research has been concentrated in neuroimmunology and neurotrauma. Overall, his research aim is to determine the degree to which the bi-directional communication between the brain and immune system is affected by age, psychological stress, and traumatic brain injury.

Dr. Lindsay Parker
ARC Centre of Excellence for Nanoscale BioPhotonics
Macquarie University

Dr. Lindsay Parker obtained a BSc in Psychology from Michigan State University in 2006, focusing on behavioural neuroscience. She then worked in the field of molecular neurochemistry at Michigan State University and Macquarie University for 9 years, primarily researching central autonomic neuron pathways activated following severe physiological stressors. Dr. Parker completed a PhD in Advanced Medicine in 2014 at Macquarie University. Since 2015 she has been a Research Fellow at the ARC Centre of Excellence for Nanoscale BioPhotonics at Macquarie University. Her multidisciplinary research is focused on using nanobiotechnology and advanced microscopy techniques to target and image cellular mRNA, protein and glycans. Dr. Parker has extensive expertise in widefield/confocal microscopy for biomedical applications and cell/tissue sample preparation.
Prof. Robert Medcalf
Australian Centre for Blood Diseases
Monash University
Prof Robert Medcalf is a NHMRC Principal Research Fellow working at the Australian Centre for Blood Diseases at Monash University. His major research focus has been on the role of the fibrinolytic system in the brain, including the influence of this system on the blood-brain barrier and the innate immune response. His laboratory is also interested in devising novel approaches to treat patients with ischaemic stroke and traumatic brain injury. Prof Medcalf was the recipient of the 2016 Prize of the International Society on Fibrinolysis and Proteolysis (ISFP) and is currently Chairman of the Brain Foundation of Victoria.

Dr. Jana Vukovic
School of Biomedical Sciences,
QBI, University of Queensland
Jana Vukovic graduated from The University of Western Australia in 2004 with a Bachelor of Science (Honours), majoring in both neuroscience and genetics. She was awarded her PhD from the same institution in 2008. She then relocated to the University of Queensland to join Professor Perry Bartlett’s laboratory at the Queensland Brain Institute as a Postdoctoral Research Fellow. She was awarded a Queensland Government Smart Futures Fellowship in 2010. In 2015, Jana established her independent laboratory in a joint appointment between the School of Biomedical Sciences and the Queensland Brain Institute. Her laboratory investigates how microglia, the brain’s resident immune cells, influence the process of learning and memory in ageing and disease. Jana has been the recipient of an Australian Research Council (ARC) Discovery Early Career Research Award, and her work on microglia is further supported by a Project Grant from the National Health and Medical Research Council.

Dr. Leon Teo
Australian Regenerative Medicine Institute
Monash University
Leon is an early-career researcher who joined A/prof James Bourne’s Lab at the Australian Regenerative Medicine Institute as a PhD student in 2011 and has since continued on as a post-doc in the group. Leon’s current work focuses on using the nonhuman primate model to better understand the cellular and molecular consequences of stroke and other CNS injuries. In particular, how the infant brain retain a greater capacity for functional recovery, compared to adults and the involvment of reactive astocytes and glial scarring in this process. Leon’s work with James Bourne has resulted in the development of strategies for improving outcomes by re-activating endogenous processes, present during early-life, in order to tip the balance in favour of functional recovery after CNS injuries during adult-life.
Glycyrrhizin reduces neuroinflammation acutely after paediatric traumatic brain injury

Webster, KM, Sun, M, Shultz, SR, O'Brien, TJ, Semple, BD

Department of Medicine (Royal Melbourne Hospital), The University of Melbourne, Parkville

Traumatic brain injury (TBI) is a leading cause of mortality and morbidity for children. Recent research suggests that children may be more vulnerable to poor outcomes after paediatric TBI (pTBI) compared to adults. One of the major initiators and recruiters of the inflammatory cascade, high mobility group box protein 1 (HMGB1) is associated with worsened outcomes after TBI in young patients. Glycyrrhizin (Gly) is a natural extract from liquorice root shown to inhibit HMGB1 after adult TBI but has never been investigated after pTBI, after which the inflammatory response is heightened. This study therefore aims to investigate the acute effects of Gly on the inflammatory cascade after pTBI. Male and female C57Bl/6 mice at postnatal day 21 were subjected to an experimental model of moderate-severe controlled cortical impact injury and randomly assigned to three treatment groups: pre-treated Gly (1 h prior to injury then 1, 6, 24, 48 and 72 h post-injury, 50mg/kg i.p.), post-treated Gly (post-injury treatment only) or vehicle. Focal brain tissue was collected at day 3 for western blot and oedema analysis, and perfused brains were taken for immunofluorescence analysis of inflammatory factors. Gly treatment was found to only reduce HMGB1 expression and oedema when administered prior to injury. This suggests that the mechanism by which HMGB1 can affect the brain after pTBI occurs earlier than 1 h post injury. This is in contrast to the anti-inflammatory effect of Gly afforded by treatment starting post-injury in adult experimental TBI models. These findings suggest that the expression, time course or role of HMGB1 may differ after TBI in the paediatric compared to adult brain.
MILD TRAUMATIC BRAIN INJURY DURING ADOLESCENCE PROTECTS AGAINST SUBSEQUENT SKULL FRACTURE BUT DOES NOT WORSEN NEUROBEHAVIOURAL OUTCOMES AFTER A SECOND BRAIN INJURY AT ADULTHOOD.

McColl TJ1, Lovick L1, Webster KM1, Brady RD1,2, McDonald SJ2, O'Brien TJ1, Shultz SR1, Semple BD1

1. Department of Medicine (Royal Melbourne Hospital), The University of Melbourne, Parkville, VIC, Australia. 2. Department of Physiology, Anatomy and Microbiology, La Trobe University, Bundoora, VIC, Australia.

While mild traumatic brain injuries (mTBI) are common in adolescence, the long-term consequences of such injuries are unclear. Limited evidence from patient cohorts suggests that exposure to mTBI at a younger age may result in poorer long-term outcomes. Here, we used a closed-skull, weight-drop model of mTBI in mice at adolescence (postnatal day 35; P35) and/or at adulthood (P70), to test the hypothesis that an adolescent mTBI would predispose towards poorer behavioural and pathological outcomes after a subsequent injury at adulthood. Mice were randomised to 1 of 6 groups: sham surgery at P35 only; mTBI at P35 only; mTBI at P35 + sham at P70; sham at P35 + mTBI at P70; mTBI at both P35 + P70; or sham surgery at both P35 + P70 (n=15-19/group). Behavioural tests investigating cognitive (Morris Water Maze), psychosocial (elevated plus maze, social interactions), and sensorimotor function (rotarod, ledged beam test) were conducted over one week after the P35 or P70 surgery, then brain tissue from a subset of mice was collected for immunohistochemical analysis. Acute measures of righting reflex, length of apnoea, and latency to exhibit a hind-limb pain reflex, demonstrated that an injury had indeed been induced at P35 and/or P70. None of the injury groups showed neurobehavioural deficits compared to sham controls. Mice injured at P70 only developed a robust increase in GFAP+ astrocytes and Iba1+ microglial reactivity in the ipsilateral cortex and hippocampus. Contrary to our hypothesis, a single mTBI to the adolescence mouse brain did not exacerbate the effect of a subsequent mTBI in adulthood. This may be attributed to the sub-concussive nature of the insult - below the threshold to induce neurobehavioural deficits - or the extended period of time between repeated injuries. Surprisingly, 63% of mice injured at P70 only exhibited a skull fracture at impact, compared to only 13% of P35 + P70 injured mice. Subsequent examination of the parietal bone by micro-computed tomography found that mTBI at P35 resulted in an increase in bone volume and rigidity compared to sham, indicative of bone remodelling that likely accounts for the difference in fracture likelihood and associated neuroinflammatory response. Together, these findings have implications for youth exposed to mTBI, and support future investigation into the consequences of mTBI on bone structure and integrity.
TAKE THE PRESSURE DOWN: A NOVEL AGENT FOR THE TREATMENT OF CEREBRAL OEDEMA AND ELEVATED INTRACRANIAL PRESSURE FOLLOWING STROKE

Sorby-Adams AJ¹, Leonard AV¹, Thornton E¹, Vink R², Turner RJ¹.

1. Adelaide Medical School and Adelaide Centre for Neuroscience Research, The University of Adelaide, Adelaide, SA, Australia 2. Sansom Institute for Health Research, University of South Australia, Adelaide, SA, Australia.

Cerebral oedema and elevated intracranial pressure (ICP) are the leading cause of death in the first week following stroke. Despite this, current treatments are limited and fail to address underlying mechanisms, highlighting the need for development of targeted treatments. Recently, neurogenic inflammation and associated release of substance P (SP) following stroke has been linked to the development of profound cerebral oedema. SP elicits its effects by binding the NK1 tachykinin receptor (NK1R), with administration of an NK1R-antagonist ameliorating cerebral oedema following stroke in rodent models. When screening novel agents, it is also essential to use clinically relevant large animal models to improve the likelihood of successful clinical translation. The current study thus examined the efficacy of NK1R-antagonist treatment in reducing cerebral oedema and ICP in an ovine stroke model. Merino-sheep (9M;13F) were anaesthetised-and-subject to 2hrs transient MCAo, then allocated into the following treatment regimes: early treatment (1mg/kg NK1R-antagonist at 28, 33, 52, 57, 76, 81hrs post-stroke; n=6), delayed treatment (1mg/kg NK1R-antagonist at 124 and 129hrs post-stroke; n=6) saline vehicle (n=6) or sham surgery (n=4). At 6d post stroke ICP was measured for 4hrs, followed by FLAIR MRI to assess cerebral oedema. Following stroke, ICP was significantly decreased following NK1R-antagonist administration in both the early (p<0.01) and late (p<0.0001) treatment regimes compared to vehicle. Profound cerebral oedema was observed in vehicle treated animals at 6d, in keeping with the elevated ICP. These findings provide substantial evidence that NK1R-antagonist treatment is efficacious for the treatment cerebral oedema and elevated ICP following stroke.
IS A SPRAGUE REALLY A SPRAGUE?

Plummer SL\textsuperscript{1}, Corrigan F\textsuperscript{1}, Thornton E\textsuperscript{1}, Cappai R\textsuperscript{2} and Van Den Heuvel C\textsuperscript{1}

\textsuperscript{1}Translational Neuropathology Laboratory, School of Medicine, The University of Adelaide, Australia; \textsuperscript{2}Department of Pathology, The University of Melbourne, Australia

Traumatic brain injury (TBI) is a life-threatening condition, for which there are currently no accepted pharmacological treatments. Current medications only target the complications as they arise, so efforts should focus on identifying novel therapeutic compounds through experimental research. Our research team utilises the Marmarou impact-acceleration model which is a widely accepted and well-characterized rodent model of diffuse axonal injury. It also produces noticeable changes in functional outcome and a fairly consistent injury level. However, over the previous 5 years, post-traumatic injury severity has appeared to steadily decrease, with a noticeable lack of functional impairment. Over time it became clear that the issue was not the injury device or experimental procedures, but the rats themselves. Prior to our current research utilising Harlan strain male Sprague-Dawley rats, Charles River strain Sprague-Dawley rats had been used. The aim of this abstract is to explore the differences in outcome and histology between Sprague-Dawley rats from the Harlan versus the Charles River strains following moderate-severe diffuse TBI. An initial pilot study was carried out using Charles River Sprague-Dawley rats purchased from Animal Resource Centre in Perth, to determine the optimal age and weight range to produce a sufficient injury with noticeable deficits. Post-TBI, considerable differences were observed between the two strains. Charles River Spragues recorded considerably higher scores on their clinical record sheets in the initial days than those from the Harlan strain, who also took longer to recover after injury. These animals also demonstrated substantially worse functional outcome in the initial 4-5 days post-TBI, as well as associated histological outcome. The success of the pilot study saw the establishment of a breeding colony for Charles River strain Spragues at the University of Adelaide animal housing facility, with rats bred through established breeding protocols. Over the course of the following year, however, these animals appeared to revert to the phenotype demonstrated by the Harlan strain rats, and showed a clear decrease in injury severity, functional outcome and histological analysis. Despite similar physical appearances, it appears that the strain of rat used in TBI research plays a critical role in the success of experimental research. This knowledge is critical, particularly when research aims to examine the efficacy of therapeutic options, and could ultimately impact the success of translatable therapies to treat conditions like TBI.
Microtubule breakdown has been implicated in axon degeneration in several neurodegenerative diseases. We investigated the early changes to axonal microtubules following an excitotoxic insult and the potential of the HDAC6 inhibitor, trichostatin A, which prevents microtubule deacetylation, to prevent microtubule alterations and subsequent axonal degeneration. Primary mouse cortical cultures were grown to 10 DIV in microfluidic chambers and were treated with kainic acid or trichostatin A for 6 or 18 hours. Microtubule post-translational modifications and associated proteins were assessed at 6 hours using ELISA to determine any changes. To assess the potential protective effect of trichostatin A, neurons were grown in microfluidic chambers which allows separation of axons from the somatodendritic compartment. Kainic acid was added to the cell soma, and axonal protection of trichostatin A was assessed through addition of the drug to the axonal compartment 2 hours prior to treatment. Live axon imaging was performed prior to and 18 hours following treatments. Microtubule acetylation was significantly (p<0.05) decreased after 25µM kainic acid exposure, however, treatment with trichostatin A significantly (p<0.05) increased microtubule acetylation relative to untreated neurons. Tau was also significantly (p<0.05) increased after 25µM kainic acid treatment. Furthermore, kainic acid-induced axonal fragmentation was significantly (p<0.05) reduced when cells were pre-treated with trichostatin A. This data suggests that loss of microtubule acetylation may be an early modification involved in kainic acid-induced axon degeneration and is a potential therapeutic target.
Using Telomere Length as a Biomarker for Sports Related Concussion in Australian Rules Footballers

Ernest, J, Mychasiuk, R, Shultz, S

Melbourne Brain Centre, University of Melbourne

Australian Rules football is one of Australia’s most popular sports and frequently involves collisions, some of which result in sport-related concussions (SRCs). There is increasing concern that a history of SRC, or even participating in collisions sports, may be associated with cumulative and long-term neurological consequences. As such, there is a need to better understand the effects of SRC and repetitive head impacts (RHI) and discover objective biomarkers that can help guide medical decisions related to participation. Telomeres are repetitive non-coding sequences of DNA found at the end of linear eukaryotic chromosomes. Telomere erosion has been implicated in neurodegenerative diseases such as Alzheimer’s, and we have previously found that telomere length (TL) is shortened in preclinical models of concussion. Therefore, this study aimed to assess TL as a biomarker for a history of SRC and participation in collision sport in humans. Obtained through saliva sampling, baseline TLs of amateur Australian Rules footballers (n=61) were compared to matched controls (age, sex and years of education) without a history of brain trauma or participation in collision sport (n=14). Background demographic information was collected for both groups and cognition compared through the administration of standardised concussion assessment tools and neuropsychological tests. TL was significantly shorter at baseline in footballers compared to controls. These findings suggest that TL may be affected by a history of collision sport involvement, though further studies are required.
Axon degeneration is a key pathological process in neurodegenerative diseases and may result in neuronal disconnection. However, little is known about the mechanisms of axon degeneration that occur under the pathogenic mechanisms of disease. Excitotoxicity is a pathological process known to occur in a variety of these neurodegenerative diseases and has been shown to be capable of inducing axonal degeneration. Cell culture studies indicated that excitotoxin induced axon degeneration involves axonal caspase activation and disruption to microtubules, however, mechanisms have not been confirmed in vivo. This study aimed to develop and characterise a CNS model of excitotoxic axon degeneration. The visual system is a part of the CNS that is amenable to analysis of axon degeneration. Thus, kainic acid was injected into the vitreous humour of the eye in mice to expose the retinal ganglion cells to the excitotoxin. Intravitreal injection of kainic acid resulted in a significant loss of visual acuity by 1-day post-treatment (p<0.001). Histologically there was a significantly (p=0.007) increased immunoreactivity of the astrocyte marker GFAP after 3 days, indicating an astrogial response which was exacerbated after 7 days (p<0.001). Additionally, analysis of retinal ganglion cell axons suggested increased expression of the intermediate filament protein alpha-internexin as well prominent changes to neurofilament proteins including the formation of neurofilamentous swellings within the axon. These data increase our understanding of axon degeneration in neurological disease and injury and provide an in vivo model to assess future therapeutic interventions to protect axons, such as the microtubule stabilising agent, epothilone D.
Trehalose Improves Traumatic Brain Injury-Induced Cognitive Impairment.

Portbury, SD, Hare, DJ, Finkelstein, DI, Adlard, PI.

Florey Institute of Neuroscience and Mental Health

In this study, we utilized a mouse model of TBI to assess the therapeutic potential of the stable disaccharide trehalose, which is known to protect against oxidative stress, increase levels of chaperone molecules and enhance autophagy. Furthermore, trehalose has demonstrated neuroprotective properties in numerous animal models and has been proposed as a potential treatment for neurodegeneration. As TBI (and associated neurodegenerative disorders) is complicated by a sudden and dramatic change in brain metal concentrations, including iron (Fe) and zinc (Zn), the collective accumulation and translocation of which has been hypothesized to contribute to the pathogenesis of TBI, then we also sought to determine whether trehalose modulated the metal dyshomeostasis associated with TBI. Three-month-old C57Bl/6 wildtype mice received a controlled cortical impact TBI, and were subsequently treated for one month with trehalose. During this time animals were assessed on multiple behavioural tasks prior to tissue collection. Results showed an overall significant improvement in the Morris water maze, Y-maze and open field behavioural tests in trehalose-treated mice. These functional benefits occurred in the absence of any significant modulation of biometals, as assessed by laser ablation inductively coupled plasma mass spectrometry. Western blot analysis, however, revealed an upregulation of synaptophysin, doublecortin and brain derived neurotrophic factor protein in trehalose treated mice in the contralateral cortex. These results indicate that trehalose may be efficacious in improving functional outcomes following TBI by a previously undescribed mechanism of action that has relevance to multiple disorders of the central nervous system.
Zebras have a robust ability to regenerate CNS tissue including the spinal cord following an injury. However, the spinal cord contains different types of cells and axon tracts which are highly organized. Therefore, how regenerating axons find their correct targets within the injured spinal cord and how diverse cell types are produced after injury are critical issues that need to be resolved. During development, cells in the floor and roof plates secrete competing signals that influence cell differentiation and the targeting of fibre tracts within the spinal cord. By using in vivo imaging and reporter lines we identified a small population of quiet radial glia-like cells in the dorsal and ventral parts of the ependymal layer around the central canal of zebrafish spinal cord which emerge from the roof and floor plate cell populations, respectively. These most dorsal and ventral ependymal cells become quiet early in development and are maintained until adulthood. Next, we investigated the behaviour of these cells in response to the injury using an established larval spinal cord injury model. Our results suggested that these cells may act as signalling centres to differentiate new born cells after spinal cord injury in zebrafish. A lack of these signals may be a significant factor that hinders spinal cord regeneration in mammals. Identification of the cellular process and signalling pathways which lead to successful spinal cord regeneration in zebrafish may offer bases for future therapies since the key cell types enabling neural and axonal regeneration in zebrafish have direct counterparts in mammals.
Spinal cord injury (SCI) can induce a systemic impairment of the immune system that is thought to render patients highly susceptible to infections. Aberrant release of glucocorticoids (GCs) and norepinephrine (NE) after high-level SCI is thought to increase infection risk by driving systemic immune depression (lymphocyte apoptosis, leukopenia and splenic atrophy). The impact of lower-level SCIs on immune function has, however, been less well studied, particularly during the very acute phase of injury. Here we explored the impact of a lower thoracic (vertebral level T9) SCI on the spleen during the first few hours and days post-operation (dpo). Significant splenic atrophy and loss of splenocytes was observed at 1dpo compared to naïve controls (p<0.005), which then resolved itself during the first week after SCI. Inhibition of GC and NE signalling with the pharmacological antagonists RU486 and butoxamine, respectively, was able to prevent this acute SCI-induced loss of select splenocyte populations and the associated splenic atrophy (p<0.05). As we previously identified a key role for the spleen in directing monocytes to the injured spinal cord, we lastly explored whether preventing splenic atrophy altered recruitment of these cells to the lesion. We found that SCI mice treated with RU486 and butoxamine had a significantly greater number of monocytes at the lesion site by 1 dpo compared to vehicle controls (p<0.05). Together, this data suggests that lower thoracic SCI also induces splenic atrophy, albeit transient, and that this stress-induced response may confer neuroprotection by limiting recruitment of myeloid cells to the lesion site.
Poster presentation Abstracts

1) THE EFFECTS OF SKELETAL MUSCLE INJURY ON TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) often involves multitrauma in which concurrent extracranial injury occurs. However, preclinical TBI research commonly employs independent injury models that fail to incorporate the pathophysiological interactions that may occur in multitrauma. We previously demonstrated that long-bone fracture exacerbates TBI outcomes, and this mitigated by modulating IL-1β mediated neuroinflammation. Therefore, it stands to reason that other forms of peripheral trauma that produce a robust inflammatory response, such as skeletal muscle injury, may have similar effects on TBI. As such, here we developed a novel mouse model of multitrauma involving a closed-skull TBI and a carditoxin-induced muscle injury, to investigate whether muscle injury worsens TBI outcomes. Adult male C57BL/6 mice were assigned into four groups: sham-TBI + saline (SHAM); sham-TBI + carditoxin (CTX); TBI + saline (TBI); TBI + carditoxin (MULTI). A portion of mice were euthanized at 24 hours post-injury to assess cerebral oedema and neuroinflammation. Other mice underwent behavioural testing after a 30-day recovery period. Analyses are ongoing.
The need for improved understanding of the effects of concussions has led to an increasing number of studies featuring rodent models that attempt to mimic concussion. Nonetheless, the relevance of many studies to clinical concussion is questionable, particularly regarding the use of surgery and anaesthesia, and the mechanism and severity of injury. To address these limitations, we have co-developed an awake closed-head injury (ACHI) rat model of concussion that completely omits surgery and anaesthesia, features clinically relevant head acceleration, and importantly allows for behavioural observations immediately post-injury. In this pilot study, we aimed to characterize the behavioural effects of a single ACHI. Rats were placed in a restraint bag and a 3D printed steel helmet positioned over the head such that the impact target was centred over the left parietal cortex. Once carefully positioned on a foam platform, a cortical impactor was used to strike the helmet target. Sham animals underwent the same procedure without impact. Rats performed beam walk, open field, Morris water maze and rotarod testing at baseline, as well as at 30 minutes and 24 hours post-injury. Preliminary findings with this model indicate that rats given a single ACHI display fine motor deficits and hyperactivity/impulsivity within the first 30 minutes post-injury, however these effects were largely resolved at 24 hours post-injury. Although analysis of the neurobehavioral and neuropathophysiological effects are ongoing, these preliminary findings indicate that ACHI may closely mimic a concussive impact in humans, and may be a valuable tool for pre-clinical concussion research.
3) EARLY INFLAMMATORY SIGNALS DRIVE NEURAL STEM CELL ACTIVATION DURING ZEBRAFISH SPINAL CORD REGENERATION

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Unlike mammals, the zebrafish can functionally recover from spinal cord injury (SCI). Neural regeneration in the zebrafish spinal cord is driven by the activation of quiescent neural stem cells called ependymal cells. Ependymal cells in mammals also act as stem cells after injury but fail to give rise to neurons. We have shown that ependymal cells in the zebrafish give rise to a lineage of transit amplifier progenitors (TAP) that rapidly migrate to the lesion site and contribute to neurogenesis. The signals that activate ependymal cells are largely unknown. We have shown that suppressing the immune response following SCI blocks spinal cord regeneration while stimulating the immune response enhances regeneration. To investigate the role of inflammation on ependymal cell activation we treated zebrafish with immunosuppressants and immunostimulants and quantified ependymal cell proliferation using Edu (5-Ethynyl-2'-deoxyuridine) labelling experiments. We found that temporal treatment using the glucocorticoid dexamethasone, an immunosuppressant, directly reduced ependymal layer proliferation, suggesting that early inflammation provides cues for ependymal cell activation. Furthermore, dexamethasone treatment at a later time point directly reduced TAP activation following injury. RNA-sequencing analysis of lesioned zebrafish identified prostaglandin (PGE) signalling as a candidate inflammatory pathway involved during neural regeneration. Interestingly, inhibition of prostaglandin signalling, using a PGE inhibitor and EP2 receptor antagonist independently reduced ependymal layer proliferation, demonstrating that prostaglandin signalling is required for ependymal cell activation. Taken together, these results suggest that early inflammation plays a significant role in orchestrating the activation of ependymal cells and TAP’s that are required for neural regeneration.
4) **ACUTE CHANGES IN CIRCULATING WHITE BLOOD CELLS AND CONCOMITANT INJURY FACTORS AS PREDICTORS FOR NEUROLOGICAL RECOVERY FOLLOWING TRAUMATIC SPINAL CORD INJURY: A RETROSPECTIVE COHORT STUDY**

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Being able to better predict the long-term prospects and likelihood of functional recovery in patients with traumatic spinal cord injury (SCI) is important for clinical studies that aim to assess the efficacy of experimental neuroprotective treatments. Here we performed a retrospective analysis of existing data in the Princess Alexandria Hospital Trauma Registry (2012-2016; n=140; 86% male, 14% female), with the aim to identify variables influencing SCI outcomes. We found that circulating neutrophil counts in trauma patients with SCI were already elevated upon hospital admission, and remained above the normal reference range for at least 24 hours (p<0.05). Patients with multi-trauma and/or more severe injuries had again significantly higher circulating neutrophil counts, and were less likely to show a neurological improvement (conversion in AIS grade), compared to those with less severe injuries (i.e. lower NISS scores). Interestingly, a small (<20%) ‘non-responder’ group of patients was also identified, where neutrophil levels remained within the normal range, and these individuals had better prospects in terms of their long-term recovery. In contrast to neutrophils, lymphocyte numbers were significantly reduced after SCI at 1-3 days post-admission (p<0.01). Patients with significant SCI-induced immune depression (SCI-ID), i.e. lymphocyte counts below the normal reference range, were more likely to have spontaneous recovery of neurological function (AIS grade improvement) compared to those without SCI-ID. Collectively, our findings suggest that changes in the circulating white blood cell count during the first week post-injury, particularly neutrophils and lymphocytes, may have some prognostic value for predicting the longer-term neurological outcome from SCI.
5) GENERATING PROPRIOSPINAL INTERNEURONS FROM INDUCED PLURIPOTENT STEM CELLS (iPSCs)

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Traumatic spinal cord injury (SCI) is a devastating condition that causes irreversible damage to neural circuits and pathways. Therapeutic strategies involving neural stem cell transplants hold significant promise to replace lost tissue, restore continuity across the lesion and, in doing so, promote functional recovery from SCI. Propriospinal neurons may be ideal for transplantation purposes as these cells naturally connect distant segment of the spinal cord through both ascending and descending projections, and they are thought to have crucial roles in motor control. In the present study, we explored the possibility of generating excitatory V2a propriospinal neurons from mouse iPSCs, with the longer-term aim to transplant these cells into SCI mice. To achieve this, we developed a 6-day differentiation protocol that includes timely addition of the specific morphogens retinoic acid, sonic hedgehog and also an inhibitor of notch signaling to steer iPSCs towards a caudal and ventral interneuron fate. Using this protocol, a significant downregulation (> 2.5-fold) of the pluripotency genes Nanog and Oct4 was observed by day 4, along with induction (> 4-fold) of the neural stem cell marker Nestin. Furthermore, using the transcription factor Chx10 and Tuj1 as neuronal lineage markers, our findings indicate that V2a interneurons can indeed be generated from mouse iPSCs (>20% efficiency). We are currently optimizing our protocol to further increase the yield of Chx-10⁺ cells, after which we will test their ability to form neuronal relays and restore neurological function after SCI.
Traumatic spinal cord injury (SCI) leads to the sequential recruitment of various leukocyte populations to the lesion site. Recently, we showed that the spleen plays a key role in regulating the influx of monocyte-derived macrophages following SCI in mice. The mechanism via which the spleen controls monocyte recruitment remains, however, poorly understood. In the present study, we investigated whether SCI induces mobilization of haematopoietic stem/progenitor cells (HSPCs) from the bone marrow (BM) to the spleen for so-called ‘emergency monocytopoiesis’. Colony-forming unit (CFU) assays were used as a readout for HSPC content across relevant body compartments, i.e. BM, blood and spleen. We found that low-thoracic (T9) SCI induced splenic atrophy (p<0.01) at 1 day post-injury (dpi), while both SCI and sham-operated mice showed an acute reduction (~2-fold; p<0.05) in splenic HSPC numbers compared to naïve controls. Administration of RU486 and Butoxamine (a glucocorticoid receptor and β2-adrenoceptor antagonist, respectively) fully counteracted the SCI-induced splenic atrophy and also restored HSPC content in this organ. These findings suggest that stress signals mediate splenocyte loss and splenic HSPC mobilisation during the acute phase of SCI (≤1dpi). By 7dpi, SCI-induced splenic atrophy had resolved itself, and the number of ‘macrophage and granulocyte/macrophage’ (M/GM) CFUs had significantly increased (~3-fold; p<0.001) over naïve controls (albeit lower than shams). We are currently exploring whether this seeding of the spleen with monocyte precursors is indeed a critical step as to how infiltration of monocyte-derived macrophages into the injured spinal cord is regulated.
Few studies have investigated the long-term effects of sport-related concussion (SRC) in current amateur athletes. Therefore, this study used ocular motor, cognitive, and multimodal magnetic resonance imaging (MRI) measures to assess for neurological abnormalities in current asymptomatic amateur Australian rules footballers (i.e., Australia’s most participated collision sport) with a history of SRC. Participants were 15 male amateur Australian rules football players with a history of SRC greater than 6 months previously, and 15 sex-, age- and education-matched athlete control subjects that had no history of neurotrauma or participation in collision sports. Participants completed a clinical interview, as well as cognitive and ocular motor testing. MRI investigation involved structural imaging, as well as diffusion tensor imaging and resting state functional MRI sequences. Despite no group differences on standard cognitive tests and multimodal MRI measures, Australian rules football players with a history of SRC performed significantly worse on an ocular motor switch task. Specifically, for the switch task, Australian footballers performed significantly shorter latency prosaccades and had a significantly larger switch cost than control subjects. Australian footballers also demonstrated a susceptibility to increased cognitive load, whereas the control group was not affected by increasing load. Poorer switch cost was significantly associated with poorer performance on a number of cognitive tasks. These initial results suggest that some current asymptomatic amateur Australian rules football players with a history of SRC may have persisting ocular motor abnormalities. Future studies are required in order to further elucidate the full nature and clinical relevance of these findings.
Currently there is no clear consensus on the method of diagnosis or management of sports-related concussion. With increasing concern about the safety of collision sports and the potential for long-term neurological impairments caused by concussions, there is a pressing need to develop an objective biomarker than can be used to diagnose and manage concussion in the acute and chronic phases of the injury. There is increasing evidence to suggest that concussion can disrupt multiple neural networks, including those involved with oculomotor function. This study aimed to identify differences in pre- (i.e., preseason baseline) and post-concussion oculomotor performance in amateur male Australian rules football players (n=8). Prior to the onset of the season, 61 players underwent a suite of baseline oculomotor tests that consisted of (in order): visually-guided saccades, antisaccades, memory-guided saccades, and self-paced saccades. These tests were chosen based on their promising results from previous studies of similar design. During the season, 8 of these players suffered a concussion and underwent the same oculomotor testing at 2 days, 6 days, and 13 days post-injury. Our preliminary findings indicated that there were no significant differences between the pre- and post-injury oculomotor outcomes. These findings suggest that the oculomotor measures examined are not reliable markers for concussion diagnosis and return to play decisions, although further research is still required.
9) **ACUTE NEUROLOGIC IMPAIRMENT WITHOUT OVERT STRUCTURAL DAMAGE IN A NEW MODEL OF CLOSED HEAD INJURY IN NON-ANESTHETISED JUVENILE RATS.**

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The potential for repeat concussion to alter the structure and function of the developing brain is recognized as a serious concern. To better study this issue, we developed a model for reliably producing mild closed head injuries in awake juvenile rats that can be used repeatedly. An advantage of this awake closed head injury (ACHI) model is that it allows for immediate assessment of neurological function following an impact. The neurological assessment severity score (NASS) is composed of a series of simple tasks that assess an animal’s level of consciousness and basic motor and reflexive capacity. Our results indicate that we can reliably produce a mild closed head injury in both male and female juvenile rats without significant mortality. Single and repeat injuries produced by the ACHI model cause acute neurological deficits resembling clinical concussion signs that can be measured using the NASS protocol, as well as with common behavioural tests. Repeat injured animals spent more time in the periphery of an open field arena, indicative of anxiety. They also had a shorter latency to fall from the Rotarod after injury, suggesting they developed vestibular or motor impairments. Structural magnetic resonance imaging (MRI) indicated that this model did not produce significant structural damage, or volumetric loss in the cortex, hippocampus, or corpus callosum of animals at 1 or 7 days post-ACHI. Together these data indicate that the ACHI model can provide a reliable means to study the effects of mild closed head injuries in juvenile rats.
Neurological heterotopic ossification (NHO) is characterised by the formation of bone in soft tissue following a neurological condition. NHO frequently occurs following a traumatic brain injury (TBI) and concomitant peripheral injury and is associated with significant morbidity and reduced quality of life. The mechanisms through which a TBI facilitates ectopic bone formation are incompletely understood, and as such pharmaceutical interventions to prevent the development of NHO have shown limited efficacy. This is in large part due to the challenges and limitations involved in studying this condition in humans. Animal models allow for the control of these confounds. Therefore, here we aimed to develop a novel mouse model of TBI-induced NHO. Male mice were assigned into four groups: muscle injury + TBI, sham muscle injury + TBI, muscle injury + sham TBI or sham muscle injury + sham TBI. The injury methods included a closed skull weight drop TBI and a muscle injury induced via injection of cardiotoxin into the right hamstring. Mice were killed at 24 hours and 35 days post-injury and the right hamstring was analysed for mRNA expression of markers of bone and cartilage formation, at 35 days post-injury bone formation was analysed via micro computed tomography. Analysis is ongoing.
TROPOMYOSIN RELATED KINASE B (TrkB) REGULATES NEURITE OUTGROWTH VIA A NOVEL INTERACTION WITH SUPPRESSOR OF CYTOKINE SIGNALLING 2 (SOCS2)

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One of the components of neuroregeneration following injury is neuron growth. Suppressor of cytokine signalling-2 (SOCS2), has an important role in the regulation of newborn adult hippocampal neuron survival and it has been shown that SOCS2 expression increases after forebrain ischemia in the hippocampus. It was identified in our lab that SOCS2 enhances neurite outgrowth in neural cell culture. One of the receptors involved in neurite outgrowth in the hippocampus is TrkB. In this study, we hypothesised that SOCS2 may also have a regulatory role in neurite outgrowth by regulating TrkB. SOCS2 contains a central Src homology domain (SH2) which binds to phosphotyrosine residues, a SOCS box domain, which targets proteins for ubiquitination and degradation. Full length (FL) and mutated forms of both TrkB and SOCS2 were constructed to determine the regions of each protein required for interaction via immunoprecipitation. The involvement of the SOCS2 SH2 domain and the Kinase domain of TrkB in forming their interaction was displayed. Both SOCS2 and TrkB are abundant in the hippocampal region of the brain. Once an endogenous interaction of SOCS2 and TrkB was confirmed in hippocampal lysates via immunoprecipitation, the role of this interaction in neurite outgrowth was studied in SOCS2KO and SOCS2TG hippocampal neurons (+/-BDNF). Also, wildtype rat hippocampal neurons were transfected with SOCS2 FL and mutant constructs (+/-BDNF). Both these experiments showed a co-regulatory role for BDNF and SOCS2 in increasing neurite growth in hippocampal neurons. Finally, TrkB intracellular events regulated by SOCS2 was studied using bimolecular florescence complementation assay. Results indicate that TrkB phosphorylation, ubiquitination and endosomal recycling is increased in the presence of SOCS2. Collectively, this data presents a novel role for SOCS2 in increasing TrkB activation providing an explanation for the increase in neurite outgrowth, opening therapeutic avenues for neuron growth following injury.
Misfolding proteins may contribute to neurodegeneration after traumatic brain injury (TBI). The unfolded protein response (UPR) is triggered by the aggregation of misfolded proteins. As part of the UPR, activation (i.e., phosphorylation) of protein kinase RNA-like ER kinase (PERK) can be neurotoxic. How the PERK branch of the UPR response is affected after TBI is not well understood, however PERK activation is implicated in neurodegenerative conditions with similar proteopathies to TBI. Therefore, here we first investigated whether the PERK-UPR pathway is activated after moderate-severe TBI in mice. Mice were administered either a fluid percussion injury (FPI) or sham-injury and received a 2hr, 24hr, or 1wk recovery period. We found a significant increase in phosphorylated-PERK at 2hr post-injury, followed by a significant increase in the downstream mediator, phosphorylated-eukaryotic translation initiation factor-α, at 24hr post-injury. Next, we investigated the potential therapeutic effect of a potent PERK inhibitor, GSK2606414 that has been shown to improve outcomes in other proteopathies. Mice were administered an FPI or sham-injury and treated with three doses of either GSK2606414 (50mg/kg) or vehicle treatment over 36hrs. Treatment with GSK2606414 did not have any significant effect on behavioural or pathophysiological outcomes assessed at four weeks post-injury. Together, these findings suggest that a transient activation of the PERK arm of the UPR occurs following moderate-severe TBI. However, acute treatment with GSK2606414 did not improve long-term outcomes. Further research is required to determine the role of the PERK-UPR pathway in TBI, and whether alternative treatment strategies targeting this pathway would be beneficial.
Alzheimer’s disease (AD) has a number of key pathological hallmarks, including the accumulation of beta-amyloid, a peptide generated by the cleavage of amyloid-precursor protein, forming subsequent senile plaques. There are currently increased evidences suggesting that apart from neurons, oligodendrocytes found in the central nervous system, may also be affected by the presence of the plaques and progression of AD. Oligodendrocytes are responsible for metabolic support and the formation of myelin, which is now known to continuous throughout adulthood as part of the neuroplasticity process (the continual “fine-tuning” of neuronal networks). Research has shown focal demyelination to occur at sites of senile plaques, suggesting oligodendrocytes may also be affected in AD as the disease progresses. Our hypothesis is amyloid-beta (Aβ) affects the myelination process and the maturation of oligodendrocytes. Oligodendrocytes collected from primary Sprague Dawley mixed glial cells were exposed to Aβ 1-40 and Aβ 1-42 peptides in vitro. Our study is currently investigating oligodendrocyte process outgrowth alterations following Aβ exposure. Our current work is demonstrating that Aβ reduces the number of primary, secondary and tertiary branches during oligodendrocyte maturation. This evidence suggests that Aβ does alter oligodendrocyte differentiation and potentially myelination, in the progression of AD. Our current and future research will focus on understanding the role of Aβ on the continue development of oligodendrocytes and myelination in response to plasticity changes in vivo.
Axonal projections have a unique purpose of propagating the neural signal while branching and targeting a diverse set of postsynaptic cells. Reorganisation of axonal boutons can therefore have a profound effect on neural circuits following neural trauma, or in neurodegeneration. Synaptic loss is one of the hallmarks of Alzheimer type neural degeneration within the nervous system. The reduction in both pre- and postsynaptic structures was identified in both human post mortem tissue as well as in animal models of AD. Environmental enrichment (EE) paradigm in wild-type animals was previously associated with increased synaptic connectivity and increase in both pre- and postsynaptic proteins. Here we have investigated the effect of EE on density of axonal boutons in the APP/PS1 transgenic model of neurodegeneration. APP/PS1 male transgenic and wild-type littermates were randomly allocated to either standard housing (APP/PS1 n=4, wild-type controls n=4), or environmentally enriched (EE) housing (APP/PS1 n=4, wild-type controls n=8). All mice carried the Thy1-YFP-H reporter transgene, which labels excitatory layer V pyramidal neurons. After 6 months, the animals were perfused, coronal sections were obtained, and the presence of beta amyloid depositions confirmed with a Thio-S stain. Axonal density was measured across 4 sections of the frontal region for each animal between bregma +3.10 and +1.5mm.