SPINAL CORD INJURY
Research Forum
2015
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WELCOME

to the SCI Research Forum 2015, presented by The Spinal Research Institute.
# SCI RESEARCH FORUM PROGRAM

**12 JUN 2015**

**REGISTRATION:** 08:30

<table>
<thead>
<tr>
<th>SESSION 1</th>
<th>SESSION 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chair: Prof John Furness</td>
<td>Chair: Dr David Berlowitz</td>
</tr>
<tr>
<td>09:00</td>
<td>Welcome, Assoc Prof Doug Brown</td>
</tr>
<tr>
<td>09:10</td>
<td>Dr Stephen Davies: Intrathecal infusion of Decorin for treatment of SCI</td>
</tr>
<tr>
<td>09:40</td>
<td>Dr Peter Bragge: Development of a Bi-national SCI research strategy</td>
</tr>
<tr>
<td>10:00</td>
<td>Dr Mark Habgood: Neuroprotective treatments to limit secondary tissue damage after SCI</td>
</tr>
<tr>
<td>12:10</td>
<td>Assoc. Prof James Brock: Improving Bladder Health After Spinal Cord Injury</td>
</tr>
</tbody>
</table>

**10:20 | MORNING TEA | 12:30 | LUNCH + MAGIC MOBILITY PRESENTATION**
# SCI Research Forum Program

### 12 JUN 2015

**Tea breaks 30 min**

**Lunch 1hr**

<table>
<thead>
<tr>
<th>Session 3</th>
<th>Session 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chair:</strong> Prof Mary Galea</td>
<td><strong>Chair:</strong> Assoc Prof Doug Brown</td>
</tr>
<tr>
<td>13:30</td>
<td><strong>Dr Peter Batchelor:</strong> Cooling and early decompression for SCI: ICED trial progress</td>
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<tr>
<td>Magnetic resonance imaging of the upper airway in patients with quadriplegia and obstructive sleep apnoea</td>
<td><strong>15:40</strong></td>
</tr>
<tr>
<td>13:50</td>
<td><strong>Rachel Schembri:</strong> The relationship between neuropsychological function and sleep apnoea in acute tetraplegia</td>
</tr>
<tr>
<td><strong>14:10</strong></td>
<td><strong>Dr David Berlowitz:</strong> The Sleep Health in Quadriplegia (SHiQ) Program</td>
</tr>
<tr>
<td><strong>14:30</strong></td>
<td><strong>Dr Brid Callaghan:</strong> Improving Health after Spinal Injury: Bowel Management</td>
</tr>
<tr>
<td>15:20</td>
<td><strong>Dr Maryam Zoghi:</strong> The Brain Motor Control Assessment</td>
</tr>
<tr>
<td><strong>16.00</strong></td>
<td><strong>Dr Christine Migliorini:</strong> Trialling an online intervention treating mood disturbance in adults with chronic SCI</td>
</tr>
<tr>
<td><strong>16:20</strong></td>
<td><strong>Gillean Hilton:</strong> The experience of seeking, gaining and maintaining employment following traumatic spinal cord injury</td>
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<tr>
<td><strong>16:40</strong></td>
<td><strong>Dr Min Goh:</strong> Diurnal blood pressure patterns in SCI</td>
</tr>
</tbody>
</table>

### Timetable

- **14:50 | Afternoon Tea**
- **17:00 | Refreshments & Meeting Close**
Intrathecal Infusion of Decorin for treatment of SCI

Regulating scar formation and promoting axonal / synaptic plasticity of surviving circuits are now recognized as rational treatment strategies for traumatic spinal cord injury. Pre-clinical studies from our laboratory have shown that direct infusion of the small leucine rich proteoglycan decorin into acute spinal cord or brain injuries can suppress manifold aspects of scar formation, including levels of several axon growth inhibitory chondroitin sulfate proteoglycans (CSPGs) and Semaphorin 3A respectively, rendering the injury site more permissive for axon growth. Additionally, treatment with human recombinant decorin core protein (hr-decorin) also upregulated the plasticity-supportive, serine protease plasmin after SCI, and suppressed the sensitivity of adult sensory neurons to multiple axon growth inhibitory CSPGs and myelin associated molecules in vitro. These studies provided the rationale for testing the ability of intrathecal infusion of hr-decorin to promote neuro-plasticity and functional recovery in a rodent cervical spinal cord contusion injury model, when administered at clinically relevant time points of either 12 days (sub-acute) or 6 months (long term chronic) after injury. Horizontal ladder and Catwalk behavior testing showed robust recovery of multiple locomotor parameters in both sub-acute and chronic SCI rats treated with hr-decorin compared to untreated controls. Histological analysis revealed similarly robust increases in axonal and synaptic plasticity within spinal graymatter below sites of injury in hr-decorin treated SCI rats. Our results provide further support for the development of hr-decorin based therapies for treatment of SCI, and also other neurological disorders where suppression of scar formation and promotion of neuro-plasticity could be of benefit.
Development of a Bi-national SCI research strategy

The NTRI Forum is a 3-year, TAC funded research program that addresses pressing issues in neurotrauma practice, research and policy through an established process of evidence review and stakeholder consultation. One of the topics covered in this program was the development of a regional spinal cord injury (SCI) research strategy that can optimise SCI research and impact and therefore, improve the lives of people with SCI. This Forum was undertaken in collaboration with the Spinal Cord Injury Network and the Spinal Research Institute.

The SCI research strategy development involved:

- Identification and synthesis of research evidence, including grey literature reports, pertaining to SCI research priorities and research strategy development;

- Consultation with key local and international SCI research stakeholders representing basic scientists, clinical researchers, administrators, consumer advocates, policy makers and funders;

- A day-long structured stakeholder dialogue of research, clinical and other leaders with a stake in optimising SCI research, during which the key aims, objectives and principles that could underpin an SCI research strategy were discussed and debated.

This presentation will outline key findings of this work and measures undertaken to date to advance the SCI research strategy.
Neuroprotective treatments to limit secondary tissue damage after SCI

Spinal cord injuries remain an intractable clinical problem for which there are no effective therapies to restore lost functions. Animal and human studies have shown the extent of functional losses correlates with the extent of tissue loss. Thus limiting tissue loss after SCI offers the prospect of improving the quality of life of spinally injured patients by preserving greater residual spinal cord function. Traumatic damage to the spinal cord occurs in two phases; primary impact damage concentrated in the central grey matter and characterised by extensive necrotic cell death, followed by secondary expansion into surrounding undamaged tissue in which apoptotic cell death predominates. There is little that can be done “after the fact” to limit primary damage, but secondary damage is amenable to therapeutic intervention because this is tissue that survived the initial impact. We have promising evidence of neuroprotection after SCI for two compounds: psalmotoxin (PcTx1) a selective blocker of acid-sensing ion channels (ASIC) and capromorelin which is an agonist of ghrelin receptors. ASICs are voltage insensitive H+-gated cation channels found on nearly all CNS neurons and oligodendrocytes. Ghrelin receptors (also known as growth hormone secretagogue receptors) are present on many CNS neurons including in the spinal cord. Systemic administration of PcTx1 or capromorelin soon after SCI significantly reduced the secondary loss of grey matter neurons in the ischaemic penumbra regions around spinal contusion lesions, but not in the primary lesion site. We also have preliminary evidence that PcTx1 might also reduce loss of white matter.
Early decompression may improve neurological outcome after traumatic spinal cord injury (SCI), however, can be difficult to achieve because of the time occupied by transportation, investigation and organisation of surgery. We present the initial studies of the Immediate Cooling and Early Decompression (ICED) study aimed at determining 1) The current timing of early decompression across Australia and NZnd 2) Where delays to decompression occur and 3) whether early paramedic neurological assessment can determine the level and severity of SCI. A total of 192 patients were included from all states in Australia and NZ. The median time from accident to decompressive surgery was 22h. This was similar across all centres and substantially improved from 2010 to 2013. Two areas of patient management had the greatest influence on the time to surgical decompression. The first was pre-surgical hospital admission. When patients attended another hospital prior to the surgical hospital, the median time to decompression was 26h. However, in cases taken straight to a surgical hospital the median time to decompression decreased to 12h. The second area of delay resulted from the time taken to complete investigations and organise theatre at the surgical hospital.

Our data also indicate that the level and severity of cervical SCI can be accurately identified in the first few hours following injury using the Spinal Emergency Evaluation of Deficits (SPEED) assessment tool. Together, these studies demonstrate that patients with cervical SCI can be accurately identified in the field and that most patients undergo timely decompression in Australasia.
Mapping Traumatic Spinal Cord Injury Pathways across NSW Trauma Services: Preliminary Findings of a Prospective Study

**Objectives:**
To describe pathways of care for patients sustaining traumatic spinal cord injury in NSW and Victoria, examining timeliness of access to care, rate limiting steps and decision-making processes along the early care pathway from scene of injury to definitive treatment in a specialized Spinal Cord Injury Unit.

**Design:** Prospective observational study.

**Methods:**
A prospective cohort over two years, identified at participating sites across New South Wales and Victoria. Included participants will be aged 16 years and older and diagnosed with a traumatic spinal cord injury (TSCI). Detailed data is collected from the point of injury through acute care and subacute rehabilitation, discharge from hospital and community follow up regarding date, time, location and external cause of injury; ambulance response, assessments and management; all episodes of hospital care including assessments, vital signs, diagnoses and treatment, inter-hospital transfers, surgical interventions and their timing, lengths of stay and complications. Telephone follow-up of survivors will be conducted at 6, 12 and 24 months.

Transition paths for patients through the pre-hospital, emergency, trauma/hospital systems will be examined against existing Trauma Service policies and procedures for variation in triaging, transport times, bypass/inter-hospital transfer and patterns of care, as well as clinical outcomes, grouped by factors such as injury severity and rurality.
Results:

234 patients are currently enrolled and being followed in the study, with 26 of those patients having died within the acute period. A majority have undergone spinal decompression and stabilization, generally within the first 24 hours after injury, although surgery was delayed in over 20%. Data demonstrates inconsistency and delays in the transfer of some patients with TSCI to specialist care, whereby such delay has been shown to impact adversely on outcomes in terms of survival, potential for recovery, health complications and financial costs.

Conclusion:

Expeditious transfer (within 24 hours of injury) to a specialist Spinal Cord Injury Unit for comprehensive care following a traumatic spinal cord injury (TSCI) is recommended to achieve best patient outcomes to address the many complex issues associated with injury. Future work will be undertaken to understand barriers to best practice and the underlying clinician, health service, policy and other factors that drive unacceptable clinical variation, developing best practice guidelines, suitable process indicators, and measures for patient and system outcomes.
A Retrospective analysis of Traumatic Spinal Cord Injury Care Pathways through the Healthcare service in NSW: Analysis of linked health record data

Sharwood LN, Boufous S, Muecke S, Middleton J

Objectives
To describe pathways of care for patients sustaining traumatic spinal cord injury, investigating factors determining admission to a specialist spinal unit compared with admissions elsewhere, and factors predicting delayed admission to specialist care.

Design
Retrospective analysis of linked health record dataset (APOStLE) – July 2006-June 2009

Methods
A total of 311 patients, transferred by NSW Ambulance Service between July 2006-June 2009, following an event resulting in traumatic spinal cord injury, were analysed with respect to age, gender, geographic location of injury, mechanism of injury, level and presence of bony injury, neurological level of injury (complete, incomplete and intact), ambulance and hospital triage and prioritisations, transfers and admissions and length of hospitalisation prior to rehabilitation or discharge.

Results
311 patients were identified as having sustained a traumatic spinal cord injury during the study period, 75% male with a mean age of 48.8 years (21.7 SD). Falls (41%) and transport related incidents (42%) were the principal mechanisms of injury, with falls more likely in older ages, and transport incidents in younger ages. Mortality was 15% (n=48), 9% (n=28) died within seven days of injury; and 16% (n=51) of all cases sustained complete lesions of the
cervical/thoracic spinal cord. Most patients received diagnostic imaging (CT or MRI) within 24 hours (88%), however, only 56% (n=175) received any acute care in a specialist spinal cord injury unit (SSCIU). Thirty-eight % of these patients (n=66) were taken directly to the SSCIU from the scene of injury; a further 54% (n=95) transferred as their second admission and 6.2% (n=11) having two other transfers until SSCIU arrival. Fifty nine percent (n=103) of the 175 patients taken to SSCIU arrived there within 12 hours, a further 25 (14.2%) within 24 hours. Patients more likely to be admitted to SSCIU within 24 hours had a cervical cord injury only (OR 2.04, p=0.01), have aeromedical transport to the SSCIU (OR 2.5, p=0.003), have radiological investigation within 24 hours (OR 3.9, p=0.047) and have a surgical spinal procedure within 24 hours from the time of injury (OR 3.22, p<0.001). Patients over the age of 75 years were less likely to be transferred to SSCIU within 24 hours compared with their younger counterparts (OR 0.33, p=0.02). Patients aero-medically transferred to the SSCIU were 4.5 times more likely to have sustained their injury in an outer regional location, compared with metro locations (p<0.001).

Conclusion

Patients with traumatic spinal cord injury do not consistently experience standardised treatment pathways across the state of NSW. They do not all attend the specialist spinal cord services, and this may have implications for long term outcomes. While it appears that patients with more evident neurological deficit are appropriately triaged and transferred, those patients with distracting, multiple or less easily diagnosed injuries may have delays to their care that compromise long term outcomes. Retrieval patterns are consistent with previous research demonstrating delays for patients closest to metropolitan centres. Further study is required to determine health service and policy reasons that may contribute to this, as well as the influence of these factors on patient outcomes for this population.
Immobilisation is accompanied by bone loss due to a reduction in bone formation by osteoblasts and increased bone resorption by osteoclasts. However, the cell responsible for orchestration of these two executive cells of bone remodelling is the osteocyte, the most numerous and longest living cell in bone. Bone contains ~42 billion osteocytes, ~3.7 trillion dendritic projections forming 175,000 km, 23 trillion connections with each other and with bone surface cells providing a total surface area of the lacunocanalicular system of 215 m². This network provides a communicating network able to sense deformation and promote the gain or loss of bone as required to adapt mass and microstructure to prevailing loading circumstances.

The cell is a mechanosensor that communicates via numerous canaliculi with other osteocytes, with cells lining the intracortical canals traversing the cortex, the endocortical surface lining the medullary canal, and trabecular surfaces. All remodelling which ‘turns over’ mineralized bone matrix - removes a volume of bone then deposits the same, more or less bone depending the circumstance - is initiated upon these surfaces. If less bone is deposited, bone loss and structural decay occur. One means of modulating the gain or loss of bone is the regulation of sclerostin, a product of the SOST gene. Immobilisation increases levels of sclerostin and this results in reduced bone formation and bone loss. Inhibition of sclerostin stimulates bone formation.

This discovery has resulted in the production of a potentially useful treatment of osteoporosis that may play a role in prevention of bone loss in SCI. Antisclerostin antibody (Scl-Ab) administration increases bone formation and reduces bone resorption. Recent work in rats with induced SCI confirm that antisclerostin antibody administration prevents bone loss and
increases bone formation as determined using histomorphometry. Beggs et al (2015) report that 21 days post-injury, SCI animals has reduced cancellous bone volume at the proximal tibia and distal femur, characterized by reduced trabecular number, thickness and connectivity and deficits in femoral diaphysial strength. Scl-Ab prevented cancellous bone loss by increasing increased osteoblast surface and bone formation, prevented the reduction in cortical bone strength (1).

We studied 39 men with complete SCI (44.2 ± 14.5 years, duration of paralysis ranging from 3 weeks to 20 years) and 70 age-matched healthy men recruited from the controls at Austin Health, University of Melbourne. Images of the non-dominant distal tibia were obtained using high-resolution quantitative computed tomography (HR-pQCT, Scanco, 82 micron isotropic voxel size). The bone microarchitecture and matrix mineralisation density were quantified using StrAx1.0 (StraxCorp, Melbourne, Australia), a non-threshold based image processing software separating bone from background and bone into its cortical, transitional zone and trabecular compartments. Compared to controls, men with SCI had a 43.3% lower cortical area (p<0.05) and 51% lower cortical thickness (p<0.001). Total vBMD was reduced by 25% (p<0.001). Trabeculae were fewer by 45% with a 3.2 fold higher trabecular separation. Cortical porosity data are unavailable at the time of writing.

Profound and rapid loss of cortical and trabecular bone underlies the risk for fracture. Given the data from animal models, studies are needed to evaluate the effects of antisclerostin antibody in this illness.

Urinary tract infections are a significant issue for people with spinal cord injury (SCI). This project supported by the Institute of Safety, Compensatiom and Recovery Research focuses on understanding the mechanisms that contribute to the rapid disruption of the bladder lining (urothelium) that occurs within the first few days following SCI. The urothelium forms the barrier that resists invasion of the bladder wall by bacteria and its disruption is likely to contribute to increasing the risk of urinary tract infections in people with SCI. We are developing protocols using changes in urine composition to monitor SCI-induce damage to the bladder urothelium. In addition, we are testing drug treatments that potentially protect the bladder from injury in the period immediately follow SCI. Importantly, the drugs we are studying are already used clinically for other purposes and could be rapidly applied to patients with an SCI as a novel preventative treatment. The project has the potential to reduce incidence of urinary tract infections and the impact of other bladder-related complications following SCI by building knowledge and contribute to the development of methods for early identification of changes to the bladder and early preventative management approaches.
Obstructive sleep apnoea (OSA) is extremely prevalent among people with quadriplegia. The reasons for this increased prevalence rate remain unclear, but may be due to changes in upper airway anatomy that occur after acute quadriplegia. This study utilised 3-Tesla (3T) magnetic resonance imaging (MRI) to investigate the differences in upper airway anatomy between 3 groups: People with quadriplegia and OSA (SCI-OSA), able-bodied people with OSA (AB-OSA), and able-bodied people without OSA (AB-CTRL). Specifically it was hypothesised that SCI-OSA participants would have a smaller airway lumen than both able-bodied participant groups. Participants were recruited to this study from two sites; Austin Health in Melbourne and Royal North Shore Hospital in Sydney. Fifty participants across both sites were recruited to the study with 11 SCI-OSA, 19 AB-OSA, and 20 AB-CTRL participants and all underwent a 3T MRI scan of their upper airway. Utilising mixed model analysis, results indicated that there were no significant differences in total airway lumen volume observed between the three groups. However, SCI-OSA participants were found to have a larger volume of soft palate and retroglossal lateral pharyngeal wall tissue than able-bodied participants. The results suggest that the high rate of OSA in quadriplegia is not solely due to a structurally smaller upper airway lumen.
Obstructive sleep apnoea (OSA) is highly prevalent following spinal cord injury (SCI) and is likely caused by the injury. Beyond the devastating physical consequences of SCI, neuropsychological dysfunction is also common. OSA is known to impair many areas of neuropsychological function in both the able-bodied and chronic SCI patients. However, this has not been investigated in patients with acute SCI. The aim of this study was to investigate the relationship between OSA severity and neuropsychological function in patients with acute quadriplegia and OSA. 104 patients with acute quadriplegia and OSA participated across 11 international sites. Overnight sleep studies and neuropsychological testing were performed on average two months post-injury, with neuropsychological tests assessing attention, information processing, executive function, memory, learning, mood, and quality of life. OSA severity was significantly associated with attention, information processing, immediate recall, freedom from distractibility, and executive function, with more severe OSA being associated with poorer performance. Deficits largely did not extend to memory, which differs from previous literature investigating the able-bodied and patients with chronic OSA. Higher pre-injury intelligence and being younger appeared to lessen the effects of OSA on performance; however, these protective factors were insufficient to counter the damage done to attention, immediate recall, information processing, and freedom from distractibility by OSA. More widespread OSA-related deficits, including memory, may only be seen with longer exposure to OSA. These findings have important implications for neuropsychological functioning and skill acquisition during rehabilitation and, as such, highlight the importance of sleep health following SCI.
The Sleep Health in Quadriplegia (SHiQ) Program

As the Sleep Health in Quadriplegia (SHiQ) program of research nears completion this presentation will revisit the aims of the funders and the program to put the outcomes and achievements of the research in perspective. SHiQ was established with a program grant from the Victorian Neurotrauma Initiative (VNI), a joint venture of the Victorian state government (Department of Innovation and Industry Development) and the Transport Accident Commission. The VNI aimed to reduce the impact of neurotrauma and improve the quality of life of those affected, to expand the scope of innovative neurotrauma research through multidisciplinary, national and internationally-linked collaboration and to focus Victorian, Australian and international research and attention on the consequences of neurotrauma. Within SHiQ we aimed to address the unmet sleep needs of people with high spinal cord injuries (tetraplegia) by developing novel treatments in both acute and chronic tetraplegia, by investigating the causes of sleep apnoea and by translating the research findings to improve patient outcomes. With the VNI support we built local, national and international research collaborations and infrastructure that have successfully produced unique data and future research capacity. As the program draws to completion, we have now generated sufficient evidence in key areas such that effective translation can occur.

There are no shortcuts to improving the lives of the people we all got into this business to help. Real progress requires sustained, long-term support from people living with SCI, the research and general community and critically from all branches of government and the insurance agencies that stand to reap the economic benefit of scientific discovery.
Improving Health after Spinal Injury: Bowel Management

Background
Following injury to the spine, which severs ascending and descending nerve pathways, there is a loss of conscious control of the bowel. Therefore the bowel cannot be emptied voluntarily at a convenient time, which can lead to accidents (leakage from the overfull bowel) and cause great inconvenience and embarrassment. Between 42% and 95% of spinal cord injury patients report constipation and 75% report incontinence at least once a year (Emmanuel 2010). Bowel problems like this cause a lot of anxiety and distress and can reduce the quality of life of those who suffer them. In the longer term, impaction of bowel contents, with associated weakening of the bowel wall, can require surgery to remove the bowel and the creation of an ileostomy, further compromising quality of life.

In 2006, we published the first evidence that the defecation centres in the spinal cord could be specifically targeted by compounds that are bioavailable and likely to be safe for patient use. We showed that centrally acting ghrelin receptor agonists trigger defecation via activation of excitatory pathways in the spinal cord between L6-S1 (Shimizu, Chang et al. 2006). After successful proof of principle experiments with the lead compound (Capromorelin) in animal models of spinal cord injury (Ferens, Habgood et al. 2011) we have completed a single centre, open label, phase I single ascending dose study investigating the safety, tolerability and pharmacokinetics of oral Capromorelin in non spinal cord injured and spinal cord injury (SCI) people. This trial demonstrated that Capromorelin, given orally, was well tolerated in people with paraplegia and in non injured volunteers. There were no adverse side effects. (Ellis, Zeglinski et al. 2015).
Project Aims

The current project consists of three parts.

1. Animal proof of principle studies on newer generation compounds.

2. A double-blind, placebo controlled, phase I single randomised dose study to investigate the safety and effectiveness of oral Capromorelin in people living with a spinal cord injury (paraplegia and quadriplegia).


Benefits of project

This project aims to improve patient outcomes, by reducing inconvenience and embarrassment of bowel accidents and facilitating return to work. In the longer term, there is an anticipated reduction in hospitalisation and surgery for impacted bowel. There is a further anticipated gain in client health, mental state and welfare through improved social interactions of clients and improvements in rates of return to work.


The Brain Motor Control Assessment

Worldwide, the recovery of voluntary movement and sensation after spinal cord injury (SCI) is tracked clinically through the use of International Standard for Neurological Classification of Spinal Cord Injury (ISNCSCI). Using the ISNCSCI framework, clinicians determine the level of SCI injury and also the severity of the injury [A (complete) through B, C, D (incomplete) to E (normal)].

Although clinical assessment is important, it cannot fully describe the condition of long spinal cord tract function. Between the categories of ‘complete’ and ‘incomplete’ lies ‘discomplete’, a category that has been defined neurophysiologically. In this category, patients who are clinically paralyzed show sub-clinical evidence of translesional motor connections.

Electrophysiological methods can complement the clinical evaluation by providing quantitative, objective data about conduction across the SCI site; however, these techniques are not used routinely in clinical practice. The relationship between changes in multiple electrophysiological measures and recovery has not been fully investigated. Additionally, the mechanisms of recovery from incomplete and complete SCI require further investigation.

In our project we propose to use multiple recording techniques in combination, which can provide comprehensive information about nervous system function after SCI that cannot be determined using current clinical assessment techniques. These neurophysiological investigations have much potential in the assessment of SCI, the prediction of functional outcomes and for planning and measuring the results of therapeutic interventions.

The aims of our current project are to:

1. Conduct a longitudinal investigation of sensorimotor control in people with complete and incomplete SCI over the first 12 months of injury.
2. Quantify sensorimotor changes over time and after intervention, using a range of electrophysiological methods
3. Correlate electrophysiological changes with clinical assessments of functional recovery
Assessing Body Composition after Spinal Cord Injury

Maya G. Panisset1, Kate Desneves2, Jillian Rafferty2, Helena Rodi2, Leigh Ward4, Geoff Roff4, Andrew Nunn3, Douglas Brown6, Doa El-Ansary7, Mary P. Galea1,3

1Department of Medicine, Royal Melbourne Hospital, The University of Melbourne
2Department of Dietetics and Nutrition, Austin Health
3Victorian Spinal Cord Service, Austin Health
4School of Chemistry and Molecular Biosciences, University of Queensland
5Department of Endocrinology, Austin Health
6Spinal Research Institute, Austin Health
7Department of Physiotherapy, The University of Melbourne

Malnutrition in trauma patients is defined as weight loss of >10%. However, after spinal cord injury (SCI) the expected initial weight loss is 8-14%, despite nutritional supplementation. Malnutrition is associated with decreased immune function and delayed wound healing. This is particularly salient in this population, because their altered mobility, sensation and sympathetic regulation puts them at greatest risk for pressure ulcers, a common costly complication. Nutritional supplementation is vital for wound healing and recovery from acute trauma, yet over-feeding can prolong weaning from ventilation. In the longer term, weight gain should be avoided, as diabetes mellitus is three times more prevalent after SCI than in the general population.

It is important to differentiate between weight loss from malnutrition and weight loss from expected denervation atrophy. While dual x-ray absorptiometry (DEXA) is considered the gold standard measure of body composition, there can be accessibility issues with DEXA with acute SCI. A novel alternative, Bioelectrical impedance analysis (BIA) is an objective, non-invasive and cost-effective clinical tool that can be used at bedside. While BIA was shown to be accurate in SCI patients 4 months post injury, it hasn’t been validated for use in the acute phase.
The aim of this pilot study was to validate this novel tool to measure segmental body composition in acute SCI. Preliminary analysis shows that BIA correlates very highly with DEXA measures of body composition and may be a clinically viable metric. Further analysis is required to assess the reliability of BIA to monitor changes in body composition, and to explore the usefulness of these measures for informing dietetic practice.
Trialling an online intervention treating mood disturbance in adults with chronic SCI

A previous population-based study confirmed a significant unmet need for the provision of psychological help and suggested a need for a more relevant method of delivery than typical face-to-face appointments. The successful development and pilot of a flexible electronically delivered psychological treatment for depression and/or anxiety (ePACT) encouraged a larger scale randomised control trial that became the focus of the current study.

Adults with chronic SCI (N=573) were screened over a 15-month period. Those who presented with clinically significant symptoms (n=263, 46%) were offered a range of support options that included participating in the current study. In total, 71 adults consented to participate, 59 adults completed the intake process and were randomly assigned into either Group A Immediate Start or Group B Waitlist Control groups. Finally, 48 adults completed the Time 2 post-intervention or time equivalent interviews. A small sub-set of Immediate Start participants completed a further short interview 6-months post-intervention (Time 3).

Multilevel analyses revealed symptoms of depression significantly decreased over time for participants of both groups. Non-significant change was noted in stress while improvement in anxiety was borderline (p=.06). Satisfaction with life improved in the intervention group only and was directly attributable to the ePACT program. Time 3 interviews showed the improvement in mood was maintained but satisfaction with life was not.

Overall, the results were positive and encouraging. The implementation of the program provided valuable lessons regarding recruitment and trial participation as well as reinforced the need for long term mental health reviews. These will be shared.

This work was supported by an award from the beyondblue Victorian Centre of Excellence 2011 Research Grant Round: Randomised control trial of ePACT: a flexible treatment for depression and anxiety in adults living with chronic spinal cord injury.
Abridged Publication List


The experience of seeking, gaining and maintaining employment following traumatic spinal cord injury.

Gillean Hilton¹²³, Greg Murphy², Peter Trethewey¹, Carolyn Unsworth⁴, Rwth Stuckey²

¹AQA Victoria, Fairfield, Victoria; ²La Trobe University, Melbourne, Victoria; ⁴Central Queensland University, Melbourne, Victoria; ³Austin Health, Heidelberg, Victoria.

The experience of seeking, returning to and maintaining employment following a Spinal Cord Injury can be complex and lengthy, requiring navigation of various services, resources, legalities and entitlements; combined with the physical, environmental and psycho-social barriers that emerge along the way. Thus achieving successful and durable return to work (RTW) can be considered a significant achievement, but key in facilitating high post-injury quality of life, since employment status is the most influential factor of this for those post traumatic injury.

Community SCI organisations, vocational rehabilitation providers, clinicians and academics agree that the complicated and variable pathway of RTW in Australia post SCI contributes to lowered employment outcomes. To understand more about the processes and parties involved, and how these influence individual decisions and outcomes, we need to first gain improved understanding of the RTW process, inclusive of the influence exerted on the individual by major key players.

This research project aimed to identify influential factors associated with three main post injury trajectories of stable, unstable and without employment.

Retrospective cases of ‘exemplars’ across the three subgroups were recruited and interviewed.

The interviews were semi-structured and included collection of detail regarding demographics, pathways, timelines, health and vocational services utilised, entitlements and interventions received, stakeholders involved, barriers, facilitators and outcomes.

The project was funded under an Institute for Safety, Compensation and Recovery Research Small Development Grant.
Diurnal blood pressure patterns in SCI

Spinal cord injury (SCI) results in a disruption of transmission of autonomic nervous system signals that regulate blood pressure. As a result, people with SCI experience issues such as autonomic dysreflexia (very high blood pressures) or symptoms of low blood pressure when upright (eg fainting or dizziness), causing an impact on their participation in rehabilitation and daily life.

Blood pressure usually falls, or "dips" at night, so that night time pressures are lower than daytime pressures. This usual pattern is lost or reversed in cervical SCI, and also in diseases of the autonomic nervous system. It has been suggested that increased night time blood pressures in autonomic neuropathy causes increased nocturnal urine production, resulting in volume depletion and this exacerbates postural hypotension when getting up in the morning.

We noted a high rate of night time hypertension and reversed diurnal blood pressure pattern in patients with SCI who had been referred to our Blood Pressure Service.

We compared the diurnal blood pressure and urine patterns of patients admitted with acute SCI to that of immobilised and mobilising controls and found that the quadriplegics had the greatest reversal of diurnal blood pressure pattern compared to controls, but a loss of the usual dipping was also present in paraplegics and immobilised controls, suggesting that both activity limitation and neurological deficit had a role. There was a high rate of nocturnal hypertension compared to daytime hypertension in the quadriplegics. The diurnal blood pressure remained similar over a year in quadriplegics. Quadriplegics had a higher rate of nocturnal urine production than the other groups.

We found that while the majority of people with chronic SCI do have some symptoms of low blood pressure, most of these people had made adjustments to their daily life to manage these symptoms. Our findings suggest that significant postural hypotension is not a prevalent condition in the community, however there are small numbers who have troublesome symptoms, even if they appear to be coping generally, therefore they should be questioned about symptoms.
We recommend routine use ambulatory blood pressure monitoring in people with SCI to detect abnormalities that would otherwise be undiagnosed, and to aid management of symptoms. More widespread use of this technique in the SCI population will allow examination of how these blood pressure abnormalities affect longer term cardiovascular health, and thus help generate guidelines on optimal management.
BIO Dr Stephen Davies Ph.D.

Dr. Stephen Davies is a principal research fellow and heads the spinal research laboratory at the Florey. He is an internationally recognized research scientist who has devoted his scientific career to gaining a better understanding of why axon regeneration fails in the mammalian central nervous system (CNS) and the development of new technologies for repairing the injured or diseased brain and spinal cord.

Dr. Davies completed his doctoral thesis in neurobiology studying axon growth in the adult mammalian CNS at the National Institute for Medical Research, Mill Hill, London which was awarded by University College London in 1996. It was upon moving from London to Case Western Reserve University in Cleveland, Ohio as a postdoctoral fellow that Dr. Davies initiated a series of adult neuron to adult CNS transplantation experiments that fundamentally changed the scientific community’s understanding of the role of scar tissue in preventing axon regeneration in the traumatically injured adult brain and spinal cord.

He was recruited as an assistant professor to Baylor College of Medicine, Texas in 2000, and later in 2007 to the University of Colorado, Denver as an Associate Professor with appointments in Neurosurgery, Neurology and Neurosciences. It was during his tenures in Texas and Colorado that Dr. Davies focused on the development of two complementary approaches to repairing the injured adult CNS. The first was a novel stem cell-based technology for making specific subtypes of beneficial astrocytes suitable for repairing the injured adult central nervous system. The second was to investigate the use of a small leucine rich proteoglycan called Decorin as a means of promoting regeneration and plasticity of neural circuits within the axon growth inhibitory environment of the injured adult CNS. Dr. Davies was awarded the American Spinal Injury Association prize for breakthrough in spinal cord injury research for his studies with Decorin. In 2014, Dr. Davies was recruited to the Florey where he is continuing the development of Decorin and stem cell-derived human astrocytes for use in treating a variety of neurological disorders with a particular interest in chronic spinal cord injury.

His research has been highlighted in numerous international news media articles and programs ranging from Discover Magazine to The Hindu newspaper. More recently his studies of stem cell-derived astrocytes were featured in a book “Physics of the Future” by Michio Kaku as a technology that will have a significant impact on human civilization over the next century.
Dr Peter Bragge

Peter Bragge is a Senior Research Fellow in Knowledge Translation and Quality Improvement at the National Trauma Research Institute. Dr Bragge leads the NTRI Forum program, which aims to improve the care of spinal cord and brain injury by bringing together key stakeholders in priority areas of care for structured and facilitated stakeholder dialogues informed by review of relevant research. The NTRI Forum program underpins a range of knowledge translation activities including Clinical Practice Guideline development and implementation. Dr Bragge also has a clinical background in physiotherapy.

Dr Mark Habgood

Dr Mark Habgood has been a research fellow in the Department of Pharmacology & Therapeutics at The University of Melbourne since 2001. He received his PhD in Physiology from The University of Southampton in the UK and was a Post Doc in the labs of Prof Mike Bradbury and Prof Joan Abbott at King’s College London investigating blood-brain barrier function before taking up a teaching and research position at the University of Tasmania. The major focus of his current research is neurotrauma, particularly spinal cord injury, the timing and nature of tissue damage, neuroprotective treatments and trauma-induced changes in blood-brain barrier function. He and his colleagues are also investigating the potential of sailing to promote greater participation in physical activity by spinally injured patients and assessing the effects this has on physical and psychological health.

Dr Peter Batchelor

Dr Peter Batchelor is a clinical neurologist at RMH and Barwon Health. In addition to an active clinician, he is a Senior Lecturer in the Department of Medicine at The University of Melbourne. He is the Chief investigator in the ICED trial investigating the use of immediate hypothermia and early decompression to treat acute spinal cord injury.
Prof James Middleton

James is a Consultant in Rehabilitation Medicine, with extensive clinical experience and research expertise in the field of spinal cord injury medicine and rehabilitation, having worked in the acute hospital, sub-acute rehabilitation centre and community outreach services. He is Director of the NSW State Spinal Cord Injury Service, Agency for Clinical Innovation. Prior to taking up his current role, he was Medical Director of the Moorong Spinal Unit at the Royal Rehabilitation Centre Sydney, between 1996 and 2006, providing inpatient rehabilitation to a majority of spinal cord injured clients in NSW. He was also a Staff Specialist at the Royal North Shore Hospital, between 1994 and 2001, after which he became a VMO.

Combining a continuing clinical involvement (currently as the Senior Medical Specialist for the NSW Spinal Outreach Service) with service and academic roles affords Associate Professor Middleton a unique opportunity as a committed clinician-researcher to translate research evidence into practice, service development and quality health system improvements based on the life challenges he sees confronting people with spinal cord injury in clinical practice.

As a strongly committed clinician-researcher, he undertakes collaborative, interdisciplinary research aimed at improving health outcomes, function, independence and quality of life after spinal cord injury. Having received over $9M thus far in career funding, he will be presenting here some preliminary findings from an NHMRC Partnership Grant, for which he is Principal Investigator, awarded in 2012: “Right care, right time, right place: improving outcomes for people with spinal cord injury through early intervention and improved access to specialised care.”

Dr Lisa Sharwood

Dr Lisa Sharwood is an epidemiologist, working on a range of post-doctoral project in the area of traumatic spinal cord injury outcomes, health service cost and delivery and defining best practice care in trauma. Lisa completed her PhD at The George Institute for Global Health, an ARC Linkage funded study on the crash risk of commercial vehicle drivers related to medical conditions, in particular obstructive sleep apnoea, as well as issues such as remuneration and scheduling. During her time at The George Institute Lisa also worked on a child safety in cars project, as well as investigating government consultations sought for medical research. Prior to moving to Sydney, Lisa coordinated the Emergency Department research group for the Murdoch Children's Research Institute, managing a range of staff from medical science research students, research assistants and fellows undertaking research projects. She made a significant contribution to the development of research governance training both within this group and the wider institute. Prior to this at the Monash University Accident Research Centre Lisa worked on a variety of real world crash investigation projects.
while completing her Masters in Public Health. Her interest in injury prevention and health care outcomes research originally germinated from a clinical career as a Critical Care nurse; spent predominantly in the trauma services at The Alfred hospital, Melbourne, as well as several countries overseas, with some work additionally in developing countries. Lisa is also an adjunct Research Fellow at Monash University. Lisa is currently managing the NHMRC Partnership Project “Right care, right time, right place: improving outcomes for people with spinal cord injury through early intervention and improved access to specialised care”, and is presenting data from analysis of a large linked dataset from NSW Ambulance.

**BIO Dr Min Goh**

Dr Min Goh is a research fellow at the Austin Hospital. She has gained experience in the management of blood pressure disorders in autonomic dysfunction under the supervision of Dr Chris O’Callaghan, who has expertise in the field. They are working on TAC funded research examining the course and effects of blood pressure patterns in spinal cord injury, and investigating a potential treatment for symptoms arising from disordered blood pressure.

**BIO Prof James Brock**

James Brock is a Senior Research Fellow. He graduated in biological sciences and then spent 6 years in industry as a toxicologist before completing a DPhil in pharmacology. A major focus of his current work is the effects of nerve injury on tissues innervated by the autonomic nervous system. In particular, his work has focused on the effects of spinal cord injury and peripheral nerve injuries on blood vessel function. For example, he demonstrated for the first time that spinal cord injury produces a marked augmentation of neurovascular transmission; a change that almost certainly contributes to unusual high blood pressure episodes (autonomic dysreflexia) in spinal cord injured people. Currently he is leading an investigation of the effects of spinal cord injury on the epithelial lining (urothelium) of the urinary bladder. His work also focuses on sensory transduction in polymodal and cold-sensitive receptor nerve terminals of corneal sensory neurons, and he has developed electrophysiological techniques that, for the first time, have allowed direct investigation of action potential initiation in the naked nerve endings of C- and Ad-sensory neurones.

**BIO Hailey Meaklim**

Hailey coordinates the Imaging project for the Sleep Health in Quadriplegia program of research. The Imaging projects aim is to investigate upper airway anatomy in people with quadriplegia using Magnetic Resonance Imaging (MRI).
Her role involves recruiting participants, performing in home and in lab sleep studies, supporting participants through the 3T MRI scan, and analyzing MRI scans using volumetric segmentation techniques.

Hailey holds a Bachelor of Science (Honours) and has just completed a Master of Psychology whilst working for the Sleep Health in Quadriplegia program. She is now a registered psychologist with a keen interest in sleep psychology.

**BIO Rachel Schembri**

Rachel manages the Continuous Positive Airway Pressure for Obstructive Sleep Apnoea in Quadriplegia (COSAQ) study, for the Sleep Health in Quadriplegia research program. The COSAQ study aim is to investigate the effect of treating OSA acutely, on neuropsychological function, in people with acute quadriplegia. Her role involves overseeing the study locally and across 10 national and international sites.

Rachel holds a degree in Psychology and Psychophysiology with Honours and Masters in Psychology. Rachel has also just completed her PhD investigating the relationship between the severity of OSA and neuropsychological function in patients with acute quadriplegia.

**BIO Dr David Berlowitz**

David is a Research Physiotherapist and Chair of the Medical and Scientific Research Committee at the Institute for Breathing and Sleep (IBAS) at Austin Health. He was the founding Physiotherapist of the Victorian Respiratory Support Service and a recipient of an American Association of Respiratory Care International Fellowship. He recently completed a Clinical Post-Doctoral Fellowship from the Transport Accident Commission and was recognised in 2011 as a “Difference Maker” by the Rick Hansen Foundation for his leadership in Spinal Sleep Research.

David’s PhD thesis examined sleep and breathing in the first year following acute quadriplegia and found that acute cervical cord injury causes obstructive sleep apnoea. Building on this, David has played a key role in the development of a world-leading program of sleep research in spinal cord injury and he currently leads the five-year Sleep Health in Quadriplegia (SHiQ) research program.

**BIO Dr Brid Callaghan**

Dr. Brid Callaghan completed a bachelor degree in Biomedical Science at the University of Ulster, Coleraine, Northern Ireland in 2000, followed by a PhD in Cellular and Molecular Physiology and Pharmacology at the University of Nevada, Reno, USA in 2005. Her research
focused on the ionic mechanisms underlying the control of smooth muscle contraction. In 2006, Bríd took up a postdoctoral position at the Queensland Brain Institute, University of Queensland and at the Health Innovations Research Institute at RMIT University. Her postdoctoral research focused on the identification and characterisation of novel conotoxins and analogues selective for voltage gated calcium and sodium channels expressed in dissociated sensory neurons as potential drug leads for the treatment of neuropathic pain. Since joining the Digestive Physiology and Nutrition lab in the Department of Anatomy and Neuroscience in 2011 she has been studying the effects of novel compounds that act at ghrelin receptors, including their roles in the control of gastrointestinal function, as well as their potential as a treatment of bowel complications following spinal cord injury.

**BIO Dr Maryam Zoghi**

Dr Zoghi has a long-standing interest in brain functions, particularly aspects relevant to brain excitability, motor control, sensory-motor integration and neuroplasticity. During her career she managed to attract over $800,000 to support her research projects including NHMRC project grant and Strategic Grant Scheme. Currently, She is running 4 research projects in parallel at Royal Talbot Rehabilitation Centre and Royal Melbourne Hospital.

- Project 1: Neurophysiological evaluation after spinal cord injury.
- Project 2: The effect of hormonal fluctuations during the menstrual cycle on manual dexterity in healthy right-handed adult females.
- Project 3: The effects of cathodal transcranial direct current stimulation on epileptic patients (a pilot study).
- Project 4: The effect of transcranial direct current stimulation in decreasing pain level in patients with Multiple Sclerosis.

She is also co-supervising 2 PhD students and 3 honours students. Overall she has 70 publications in peer reviewed journal articles in high impact factor journals (e.g. Plos One, Brain Stimulation, Clinical neurophysiology, Journal of Physiology) and abstracts.

**BIO Maya Panisset**

Maya Panisset was an Orthopedic Clinical Specialist Physiotherapist in the USA before immigrating to Australia. She is currently a PhD candidate at the University of Melbourne, undertaking research which examines the changes in body composition in acute spinal cord injury, including muscle changes with early Functional Electrical Stimulation cycling (the SCIPA Switch-On trial), with supervisors Prof. Mary Galea and Dr. Doa El-Ansary. Maya has developed expertise in MRI image analysis of atrophy and muscle quality, and comparative
measures analysis methods. Maya’s broader research interests also include healthy ageing, falls prevention, and physical activity as a driver of neuro plasticity

**BIO Dr Christine Migliorini**

Christine Migliorini is a Project Manager, Mental Health Clinician, Social Worker and Research Fellow based at Monash University’s Department of Occupational Therapy and the Centre for Developmental Psychiatry & Psychology, and externally at the Summer Foundation. The focus of Christine’s research is the psychosocial context of living the significant neurological impairment.

**BIO Gillean Hilton**

As an occupational therapist Gillean has worked with the Victorian Spinal Cord Service (VSCS) at Austin Health for almost 15 years, holding numerous different roles as leisure specialist, senior occupational therapist and project manager. Gillean is currently completing her PhD with the Department of Occupational Therapy at Central Queensland University. Her PhD topic is Employment outcomes for people following traumatic spinal cord injury. She has long been interested in how best to support individuals with spinal cord injury to experience successful and sustained engagement in meaningful life roles such as in work and leisure. She is particularly interested in what interventions may be most effective in enhancing employment outcomes in this group having observed the complexity of the return to work process for people after injury. Gillean is currently balancing her studies with motherhood, whilst maintaining a strong affiliation with Austin Health and community organisation AQA Victoria.

**BIO Prof Ego Seeman**

Professor, Dept Medicine, Austin Health, University of Melbourne
Endocrinologist, Dept Endocrinology, Austin Hospital, University of Melbourne
Head, Metabolic Bone Disease, Austin Health, University of Melbourne
Editor of Progress in osteoporosis.
Associate Editor Osteoporosis International,
Member of the WHO committee defining osteoporosis.
Over 350 Publications. Citation index 66., cited >19,000 times.
Awards


2008  Distinguished Scientist Award. Austin Hospital Medical Research Foundation

2009  International Osteoporosis Foundation Medal of Achievement for Outstanding Investigation in Osteoporosis Research.

2013  John Haddad Jnr Award. International Bone Mineral Society for outstanding contributions to clinical research leading to understanding of physiology and disease and changes in disease management and prevention.

2014  Inaugural ANZBMS Career Achievement Award for outstanding and major scientific and clinical contributions, excellence in teaching and service to the bone and mineral field.