





Working Towards Predicting Post-Concussion Syndrome in the ED

Melinda Fitzgerald lindy.fitzgerald@curtin.edu.au

22.11.2018



for neurological and translational science

Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J

Neurotrauma Research















Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J

Mild Traumatic Brain Injury / Concussion



80-90% of TBIs are concussion

Multiple causes of concussion: falls, vehicle accidents etc.

Data on incidence limited:

1 in 4 - 10 people seek medical attention i.e. under-reported Recent NZ study 790/ 100,000 Indicates 180,000pa in Australia



Concussion and Post-Concussion Syndrome: Symptoms



Adapted from Halstead et al., (2010) Pediatrics, 126(3), 597-615.

PCS: prolonged concussion symptoms, 1 - 3 months or longer, up to 20%

Who will go on to develop PCS?

Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J



Current Procedures in the ED

	Search "QT interval" or "QT" or "EKG"	Log in	SIGN UP (/SIGNUP)
P Cł	aging all new residents!	Challed Declara Making The State of the State of the State of the State State of the State of the State of the State of the State State of the State of the State of the State of the State State of the State of the State of the State of the State State of the State of the S	Go!

Canadian CT Head Injury/Trauma Rule 🗠

Clears head injury without imaging.

INSTRUCTIONS

Only apply to:

- Glasgow Coma Scale (GCS) (https://www.mdcalc.com/glasgow-coma-scale-score-gcs) 13-15 with LOC
- Amnesia to the head injury event
- Confusion

Exclusion Criteria:

- Age <16
- Blood thinners
- Seizure after injury

When to Use 🗸	Pearls/Pitfalls 🗸	Why Use 🗸
---------------	-------------------	-----------

High Risk Criteria: Rules out need for neurosurgical intervention

	GCS <15 at 2 hours post-injury	No 0	
		Yes +1	
Curtin University is a trade	Suspected open or depressed skull fracture	No 0	
CRICOS Provider Code 0		Yes +1	

Neurosurgical problem?

CT scan?



Follow-up...

Mild brain injury discharge advice (for adults)

You have had a mild brain injury, often called a concussion.

Most people will make a full recovery. You should start to feel better in a few days and be back to normal in a few weeks. In a very small number of cases, serious complications can develop in the first 24 hours after the injury. Make sure you go home in the care of an adult.

∧ Warning signs: the first 24 hours after injury

If you or your carer notices any of these symptoms, see your local doctor immediately, go to the hospital's emergency department or call triple zero (000):

- feeling faint or drowsy
- cannot be woken up
- acting strangely, saying things that do not make sense
- have a constant severe headache or a headache that gets worse
- cannot remember new events, recognise people or places

- pass out or have a blackout or a seizure
- cannot move parts of your body
- clumsiness
- · have blurred vision or slurred speech
- · have fluid or bleeding from the ear or nose
- have loss of hearing
- vomiting more than twice

When should I return to the hospital emergency department?

Sometimes serious problems develop after a head injury. Return immediately to the emergency department if you experience any of the following symptoms:

- → Repeated vomiting
- → Headache that gets worse and does not go away
- → Loss of consciousness or unable to stay awake during times you would normally be awake
- → Getting more confused, restless, or agitated
- → Convulsions or seizures
- → Difficulty walking or difficulty with balance
- → Weakness or numbness
- → Difficulty with your vision

Most of all, if you have any symptom that concerns you, your family members, or friends, **don't delay, see a doctor right away**.





Prediction of Outcome

Prediction of PCS in the ED would be helpful:

reduce redundant imaging

enable individualised patient prognosis

focus on neurorehabilitation strategies to enhance outcomes

indicate need for more intensive monitoring



Pilot Study to Predict PCS



Prof Daniel Fatovich, A/ Prof Carmela Pestell, A/Prof Mike Bynevelt, Dr Melissa Licari, PhD candidate Ola Gozt

Recruited 62 patients from RPH ED, and age/gender matched controls for baseline

No one outcome likely to be predictive

- demographic information, symptom assessment
- neuropsychological tests, blood biomarkers, MRI at T0

Follow-up one month later: assess for PCS (T1); final N = 36

Inclusion criteria:

- Patients between 18 and 50 years of age
- Presenting to ED within 48 hours of head injury with symptoms that may be attributable to that injury
- Cranial CT scan shows no intracranial injury, or CT was not performed
- GCS score >13

Pilot Study to Predict PCS



mTBI Injury by Type





Diagnosis of PCS

PCS was diagnosed at T_1 (28 days) according to the following criteria:

Patient scores in the moderate-to-severe range (25+) on the Rivermead Post-Concussion Symptoms Questionnaire

OR

Scores \geq 1.5 SD than mTBI group mean on two or more total neuropsychological test scores

5 participants developed PCS



Neuropsychological Test Outcomes

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Cognition – analysis compared mTBI to PCS, hypothesis driven



translational science

Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J

Neuropsychological Test Outcomes





Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J



translational science

Blood Biomarkers: High Sensitivity

Requires release of markers from the injured brain: breach of blood brain barrier range of possibilities: proteins, miRNA, cell free DNA



Ultrasensitive analyses Quanterix Simoa HD-1 Analyser™ system



Blood Biomarker: GFAP



Also assessed neuron specific enolase (NSE) and neurofilament light chain (NFL) No significant differences



Subset of participants: N=15 mTBI (3 with PCS), N=8 controls Tract based spatial statistics: mTBI compared to control, no significant differences



Red - areas of the brain in which mTBI patients had lower FA values than healthy, uninjured age and gender-matched controls within the mean FA skeleton (green).



Region of interest analyses: multiple regions assessed



Left Inferior Fronto-Occipital Fasciculus

Probabilistic Map Johns Hopkins University White Matter Tractography Atlas FSL Eyes



Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J



Left Inferior Fronto-Occipital Fasciculus Threshold 30





Mean FA for the whole Left Inferior Fronto-Occipital Fasciculus tract, threshold of 30 on FSL Eyes





Correlation Between Function and MRI



Pearson r = 0.552, p = 0.033

No one measure predictive



Predictive Analyses

Univariate logistic regression analysis for all outcomes: normal recovery and PCS

- Low numbers therefore multi-variate analysis not appropriate

Provides a measure of the extent of predictive power

- odds ratio: how likely an event is to occur
- assessed all outcomes: here show those with significant differences at ANOVA level between mTBI and PCS

Measures	Odds Ratio (e ^β)	P value
Total RBANS	0.873	0.024
TMT-B	1.043	0.058
RBANS- IM	0.838	0.027
RBANS-DM	0.910	0.056
RBANS-Attention	0.924	0.043



Other Potential Predictors

Demographic Features:

OR 4.86: The odds of PCS increase by almost five-fold for individuals with a history of concussion

OR 4.36: The odds of PCS increase by over four-fold for individuals who reported a history of a psychological disorder

Anxiety:

OR 1.37: Higher scores on the DASS-21 Anxiety Subscale generate greater odds of developing PCS

For each 1-point increase on the DASS-21 Anxiety subscale, the odds of developing PCS increase by 37.2%



Validation study to follow





Impact-TBI

A national approach to improving lives following traumatic brain injury of all severity in all ages, including concussion



Paramedics, Intensivists, Trauma specialists, Neuroscientists, Psychiatrists, Psychologists, Rehabilitation experts, Community







Some patients recover quickly and completely and others do not.

What are the predictors of poor outcome following TBI?

What interventions can improve the chances of recovery?



Many Thanks...

Team Members

Present **Carole Bartlett** Terry McGonigle Wissam Chiha Priya Naidu Lily Toomey Ola Gozt Eleanor Denham **Jacinta** Thorne Libby Thomas

Recent Past Michael Archer Ryan O'Hare Doig Nathanael Yates **Brooke Fehily** Chloe Gray Nik Gavriel Hannah Milbourn Alex Gough Sushmitha Raja Gopana Gopalasingam Anna Black Tom Clarke Marcus Giacci Yilin Mao

Veurotrauma Research Program Australian Government National Health and TOWARDS ZERO Medical Research Council SPEED AND RED LIGHT **CAMERA FUNDED PROJECT** getting there together HARRY PERKING INST OF MEDICAL RESEARCH

Curtin University is a trademark of Curtin University of Technology CRICOS Provider Code 00301J

100

Collaborators

Experimental and Regenerative Neurosciences, UWA Prof Sarah Dunlop, Assoc. Prof Jenny Rodger BioNano and School of Molecular Sciences, UWA Prof K. Iver Swaminathan, Dr Nicole Smith, Dr Nic Taylor School of Human Sciences. UWA Prof Alan Harvey, A/Prof Stuart Hodgetts, Assoc. Prof Livia Hool. Prof Miranda Grounds School of Psychology, UWA A/Prof Carmela Pestell

AMMRF/ CMCA, UWA Prof Matt Kilburn

Perkins Institute/UWA, Royal Perth Hospital, SCGH Prof Daniel Fatovich, A/Prof Mike Bynevelt School of Human Sciences, UWA Dr Melissa Licari

Curtin University Dr Mark Hackett, A/Prof Ryu Takechi, Suzanne Robinson

University of Tasmania/ Menzies Institute Dr Kaylene Young

University of Sydney, AMMRF Dr Minh Huynh

Hong Kong University of Science and Technology Prof Karl Herrup, Dr Franki Tse



