Dr. Daune MacGregor

The Hospital for Sick Children

Dr. Daune MacGregor is a Paediatric Neurologist at the Hospital for Sick Children. Her current position is as a staff neurologist and Director of the Headache Program. She has a cross appointment at the Centre for Headache, Women's College Hospital. She recently completed two terms as Associate Pediatrician-in Chief, and Associate Chair, Clinical Services, in the Department of Pediatrics at the Hospital for Sick Children, University of Toronto. She has been the Associate Medical Director, SickKids International.

Dr. MacGregor completed her medical training at the University of Saskatchewan graduating cum laude in 1971. She then trained in Paediatrics and Neurology in Toronto at the Hospital for Sick Children and did postgraduate studies in Developmental Neurology at the Hospital for Sick Children, Great Ormond Street, London, England and the Children's Hospital Medical Center at Harvard University in Boston, Massachusetts. She was appointed a full Professor of Paediatrics and Neurology at the University of Toronto in 1995. Her research interests are in the study of cerebral vascular disorders including stroke and headache, and neurodevelopmental disorders including acquired brain injury in children. Dr. MacGregor is a Past President of the Canadian Association of Child Neurologists. She has completed MBA studies at Athabasca University, Edmonton, Alberta completing a thesis in project management.

Dr. MacGregor is the owner of MacGregor Equestrian Farms, a Hunter Jumper facility in Chatsworth, Ontario. She is involved in the breeding of warmblood horses and has been recognized by awards at the Royal Winter Fair in Toronto.

Back to School

Acquired Brain Injury Across the Ages

Daune L MacGregor, MD MBA

September 28, 2017

SickKids

Back to Pre-School or Grade School

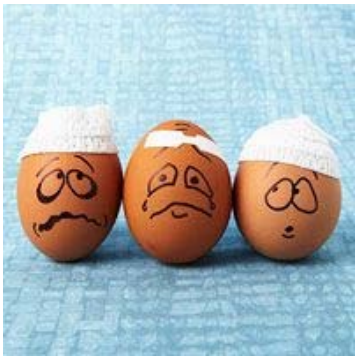
Pediatric Brain Injury
Planning for Milestones

SickKids

Pediatric Brain Injury

Daune L. MacGregor:

Nothing to Declare and No Conflicts of Interest



Pediatric Brain Injury

GOALS and OBJECTIVES:

1.Definitions of Acquired Brain Injury

2. Classification of Head Trauma Severity

3. Markers of Outcome and Recovery
   - Imaging
   - Biomarkers
   - Functional Connectivity : the Connectome

4.Comments about Concussion

5. Stages: Acute Hospital Care and Rehabilitation

6. Unique Aspects of Pediatric Rehabilitation –
   Focus on Developmental Milestones

Pediatric Brain Injury

Ella suffered a terrifying accident when she was thrown off a horse in July 2015. The horse rolled on top of her, causing multiple skull fractures and brain swelling. Ella was rushed to SickKids and had plastic and neuro surgery treatment. She was discharged after only eight days at SickKids and is still monitored by her doctors. Today, she is continuing with her recovery and rehabilitation , and has made it her mission to fundraise for SickKids.

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Pediatric Brain Injury: Definitions

CanChild (2017)

Acquired brain injury is damage to the brain occurring after birth and not related to developmental disability, degenerative disease or congenital disorder

Traumatic Brain injury is a subtype of acquired brain injury occurring when a sudden trauma causes damage to the brain

American Congress of Rehabilitation Medicine (2010)

Traumatic brain injury is defined as an alteration in brain function, or other evidence of brain pathology, caused by external force

Pediatric Brain Injury: Definitions

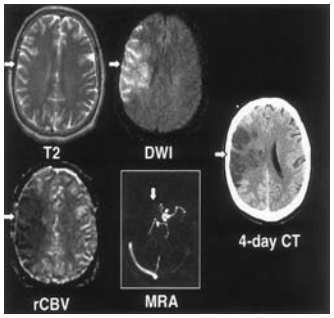
Canadian Pediatric Society Position Statement (2016)

Non-traumatic brain injury

- ❑ infection – meningitis or encephalitis
- ❑ stroke
- ❑ ruptured blood vessels – aneurysm or arteriovenous malformation
- ❑ anoxic (lack of oxygen) – example: near drowning
- ❑ brain tumor

Traumatic brain injury

- ❑ falls
- ❑ bicycle or motor vehicle accidents
- ❑ sports related injuries
- ❑ assault (NAI) – violence
- ❑ penetrating injuries



Pediatric Brain Injury

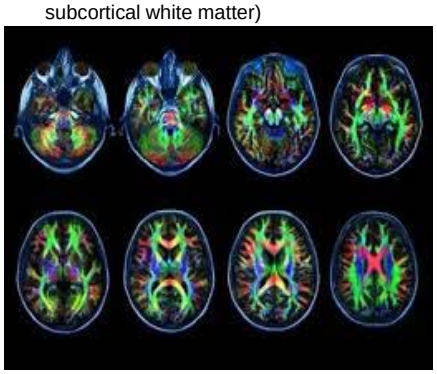
Classification of Severity of Head Trauma

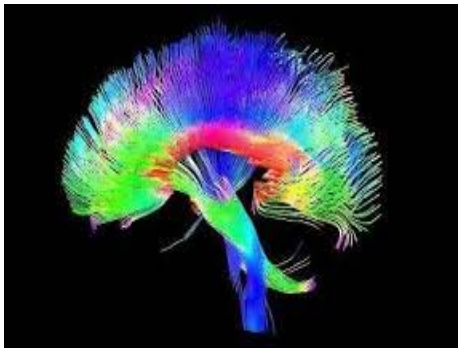
- Mild: Glasgow Coma Scale 14 – 15 (75 – 80%)
- Moderate: GCS 9 –13
- Severe: GCS ≤ 8

Pediatric Brain Injury: Markers of Outcome and Recovery

Diffusion Tensor Imaging (DTI)

- detects changes in diffusion and assesses direction of water diffusion
- can identify microscopic tissue damage and examine white matter tracts
- even one mild TBI can show damage to white matter tracts (internal capsule, corpus callosum and subcortical white matter)

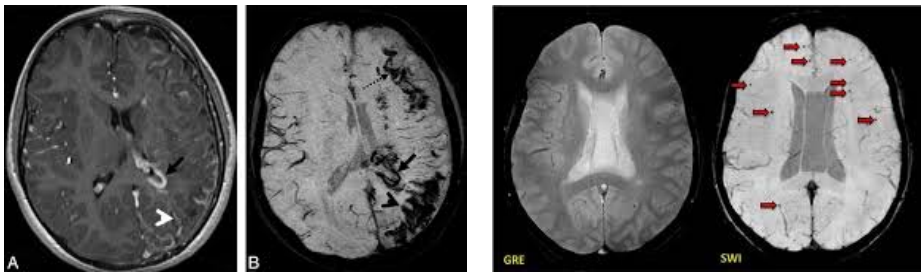




Pediatric Brain Injury: Markers of Outcome and Recovery

Susceptibility Weighted Imaging (SWI)

- detection of micro-hemorrhages not seen on conventional MRI
- location of micro-hemorrhaging can be related to patient symptomatology
- significant inverse relationship between GCS and the number and size of hemorrhagic diffuse axonal injury lesions



Pediatric Brain Injury: Markers of Outcome and Recovery

Biomarkers

- S100B
- Cleaved-Tau Protein (CTP)
- Neuron Specific Enolase (NSE)
- Glial Fibrillary Acidic Protein (GFAP)
- Myelin Basic Protein
- Ubiquitin C – terminal hydrolase – L1

Pediatric Brain Injury: the Connectome

The connectome: traumatic brain injury as a disorder of brain conductivity

JP Hayes: J Int Neuropsychol Soc : 22 (2) 120 – 137, 2016

Studies examining connectivity (structural and functional MRI methods) in TBI have shown altered structural and functional connectivity with decreased integrity of white matter pathways and imbalance and efficiency of functional networks associated with neurocognitive dysfunction and poor outcome. Traumatic brain injury has a negative impact on distributed brain networks.

Use of resting state functional connectivity MRI methodology to examine neural networks disrupted by axonal injury

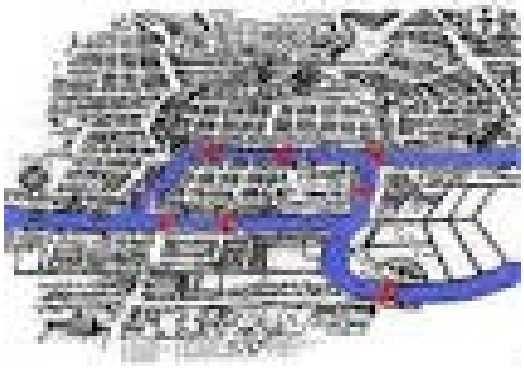
Leonhard Euler 1736:

The problem, which I understand is quite well known, is stated as follows: In the town of Königsberg in Prussia there is an island called Kneiphhof, with the two branches of the river Pregel flowing around it.

There are 7 bridges--a, b, c, d, e, f, and g—crossing the two branches.

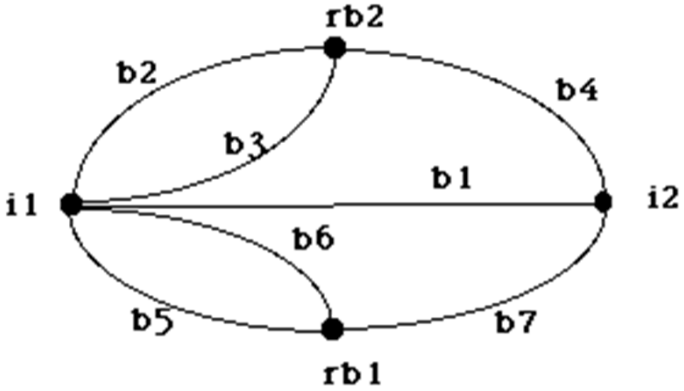
The question is whether a person can plan a walk in such a way that he will cross each of these bridges once but not more than once."

Euler, the 7 Bridges of Konigsberg: Graph Analysis

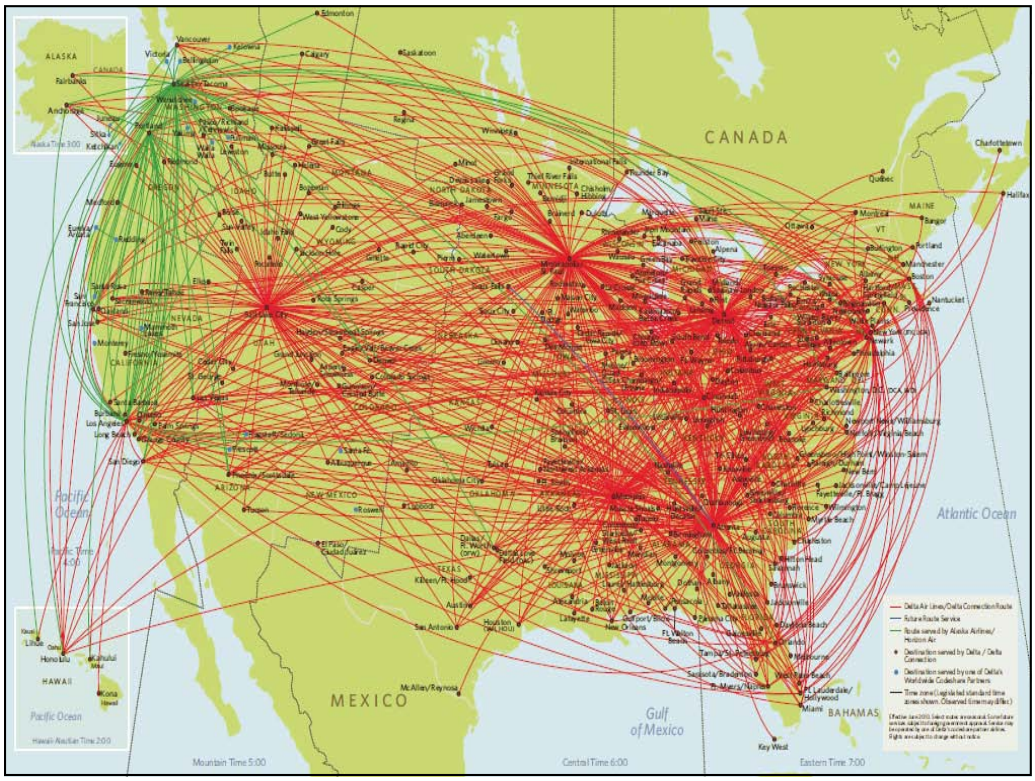


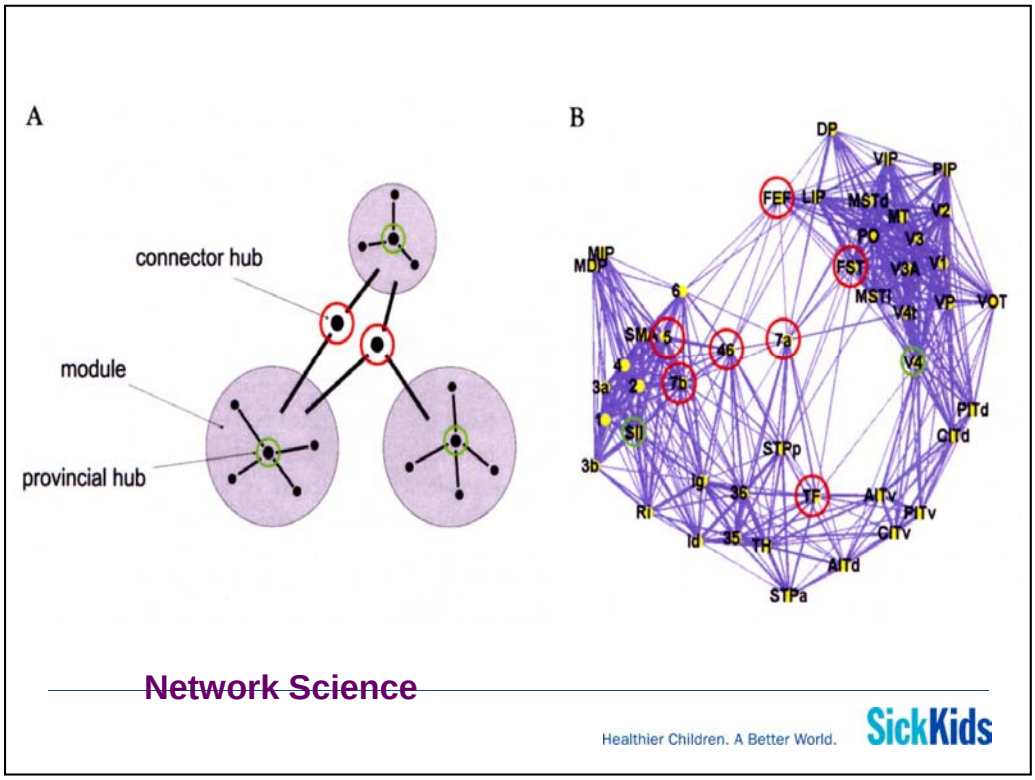
EULER'S APPROACH

Graph of the Konigsberg Bridge Problem



GRAPH THEORY





Network Science

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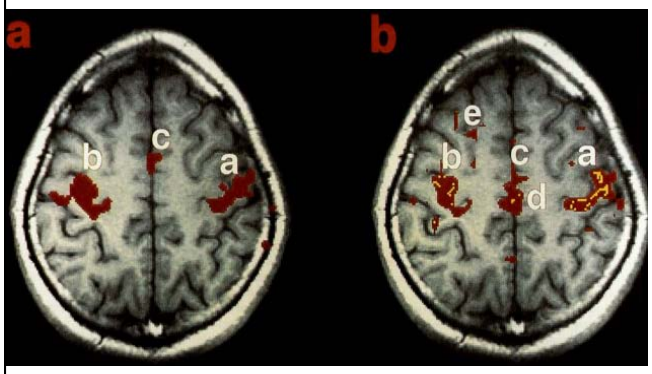
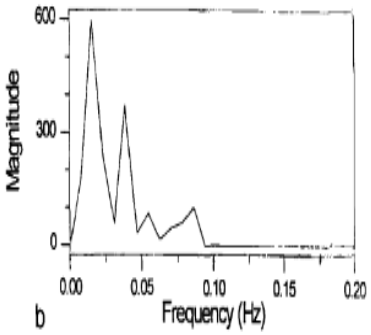
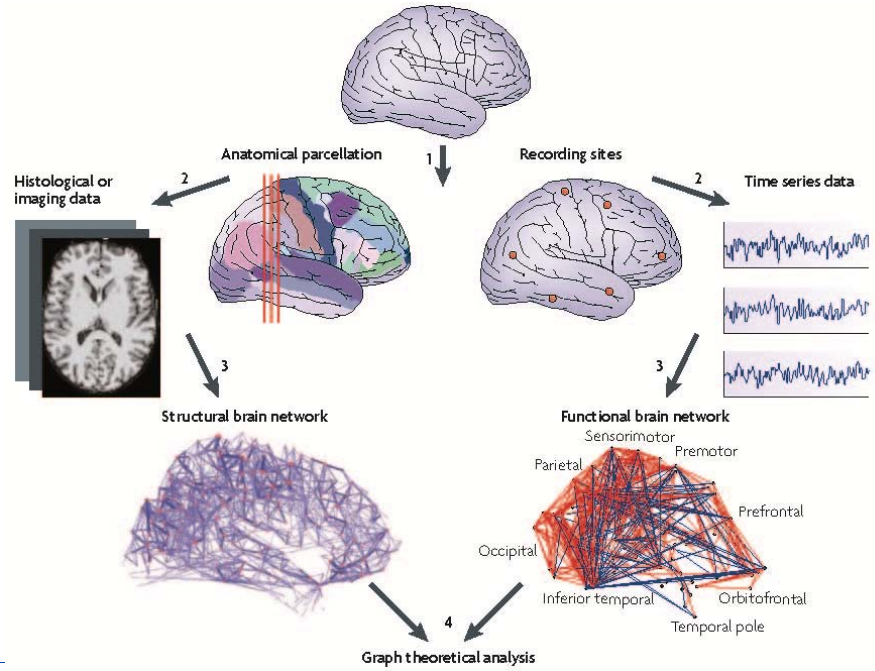
Intrinsic connectivity (“resting-state”) networks

Landmark paper by Biswal in 1995



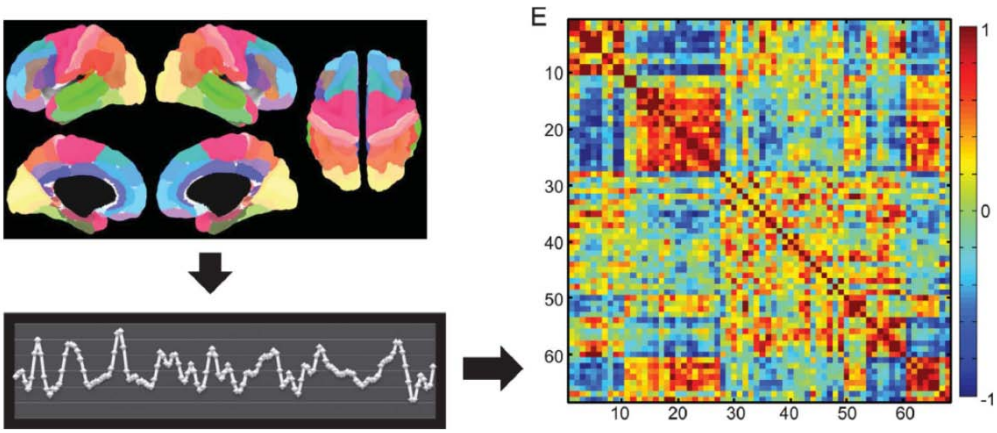


Biswal et al., MRM, 1995



Bullmore E, Sporns O. Nature Rev Neurosci 2009;186

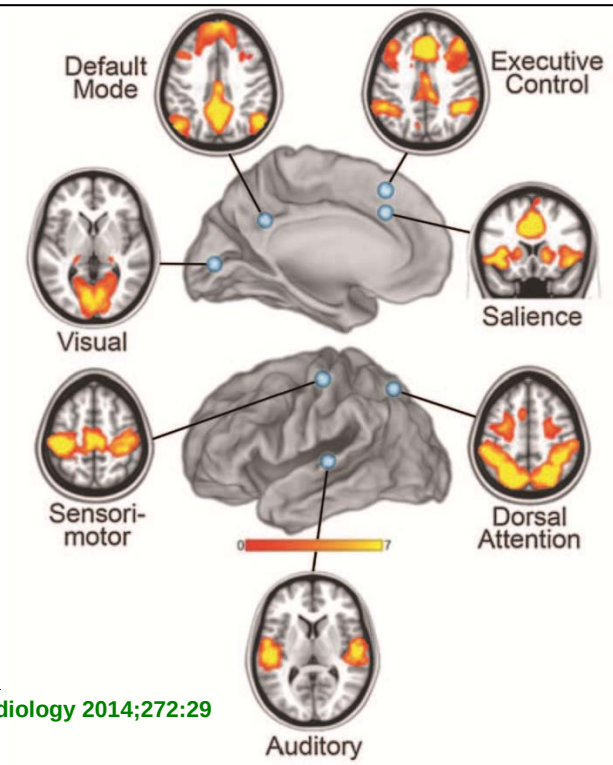
Intrinsic connectivity ("resting-state") networks



Jones et al., Neurology 2013

Functional Connectivity

Describes the relationship between different brain regions that network together to perform a common function



Barkhof et al. Radiology 2014;272:29

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Pediatric Brain Injury: the Connectome

K. Caeyenberghs: Neuro image 2016 December 3 DOI: 10. 1016/J. Neuro image. 2006. 12. 003

TBI is thought to affect cognition and behaviour by changes in functional connectivity. Graph theory is a powerful framework for quantifying topological features of neuroimaging derived functional networks.

TBI is associated with hyperconnectivity and suboptimal global integration with increased connectivity degree and strength. There is reduced efficiency of functional networks (related to diffuse white matter pathology and reductions in grey and white matter volume)

Pediatric Brain Injury: the Connectome

The connectome is derived from conductivity maps reflecting distributed brain networks. Micro-structural changes can be detected through regional and global properties of these neuronal networks.

With healthy neural dynamics, brain regions interact simultaneously maximizing integration and segregation. TBI represents structural disconnection with axonal injury damaging large-scale connectivity with the production of impaired cognition, slowed information processing and reduced cognitive flexibility.

Pediatric Brain Injury - Concussions

Concussion

The mildest form of the mild traumatic brain injury usually with temporary symptoms although there is variation in individuals by duration, onset and type of symptomatology which can be very mild or subtle. Onset can be severe and immediate or delayed. The commonest symptoms are headache, loss of memory surrounding the event and confusion or disorientation. Concussion can occur without loss of consciousness.

Pediatric Brain Injury - Concussions

Signs and symptoms of a Concussion:

- headache
- nausea
- problems with balance
- dizziness
- drowsiness
- problems with sleep
- sensitivity to light
- sensitivity to noise
- increased irritability
- sadness
- anxiousness
- becomes “more emotional”

Pediatric Brain Injury - Concussions

Concerns:

- ❑ guidelines for return to play (RTP)
- ❑ persistent postconcussive symptoms (PPCS)
- ❑ recurrent concussions and risk of Chronic Traumatic Encephalopathy (CTE)

Consensus Guidelines 2001 - 2016

- ❑ rest until asymptomatic with graduated return to play approximately five days
- ❑ concern for risk of second impact syndrome
- ❑ increased recommendations regarding physical rest and cognitive rest with limited social interaction

JAMA: December 20, 2016:316 (23) 2491 – 2492

- prospective cohort study: **Predicting and Preventing Postconcussive Problems in Pediatrics**
- enrolled 2413 participants 5 to 17-years old with acute concussion
- 30.4% developed PPCS – 24% in the early physical activity group versus 43.5% in the group that reported no early physical activity
- concluded earlier physical activity after concussion may be associated with beneficial outcomes
- resolution requires a randomized clinical trial

Pediatric Brain Injury - Concussions

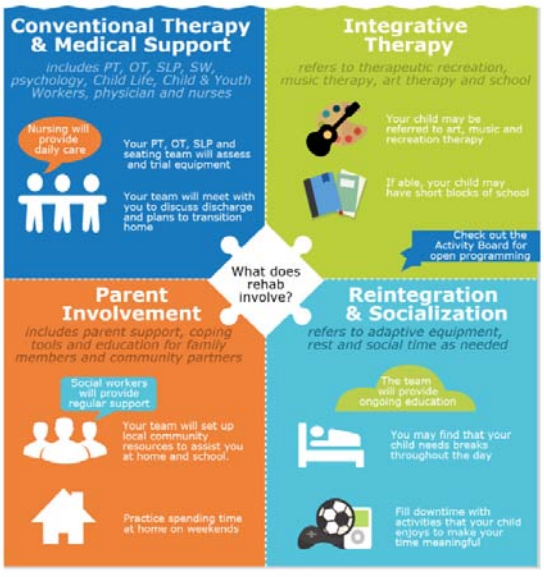
Biomarkers evaluating sports related concussions

Neurology: February 7, 2017: 88:512 – 513 and 595 – 602

- collegiate athletes with preseason plasma tau sampling and cognitive testing
- 46 athletes had sports related concussions with sampling done six hours – seven days with controls and non-athlete controls compared at baseline
- both SRC and athlete controls had significantly higher mean tau at baseline
- SRC athletes with long RTP had higher tau concentrations over all
- concluded elevated plasma tau concentration within six hours following a sports -related concussion was related to having a prolonged RTP – may be able to identify athletes most at risk for poor recovery needing additional monitoring and clinical care
- why do athletes have higher plasma tau? Physical exertion or sub- concussive hits

More to rehab than therapy

We can help the transition from hospital to home



Holland Bloorview | Kids Rehabilitation Hospital

Pediatric Brain Injury
Outcomes and Rehabilitation

TBI is a risk for negative impact on brain maturation and development – can be thought of as a developing disability over time (R. C. Savage IBIA)

Critical Factors:

- The brain in childhood and adolescence is not static but develops with changes in growth, maturation and functioning over time
- There are different milestones reached at various ages and stages of childhood and adolescence
- Need to evaluate TBI deficits in relationship to the child's age and developmental stage time of the injury and determine functional outcome as well as relationship to affected regions of the brain (brain regions have their own particular stages of growth and maturation).
- Example – infants and toddlers with fronto-temporal injury appear functionally normal weeks to months after the injury but with brain maturation there are cognitive, behavioural and motor deficits which emerge.

Pediatric Brain Injury
Outcomes and Rehabilitation

Ewing Cobbs (2003):

- Recovery from severe brain injury may be limited to skills already established
- Recovery of previously acquired skills may not ensure continued development of new and later emerging skills – or skills that were in a rapid rate of development at time of injury i.e. deficits following early injury associated with disruption to skills in the process of development at the time of injury.
- Children have limited cognitive reserve (cognitive ability) – little or no prior knowledge or life experiences to use to support recovery including cognitive behavioural functioning and the development of compensatory strategies

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Pediatric Brain Injury
Outcomes and Rehabilitation

Neurocognitive Stall

Recognized as part of a second phase of brain recovery – halting or slowing occurring more than one year after brain injury affecting later developing stages

Initial recovery curves can be followed by plateaus in functioning and then equivalent declines in comparison to typically developing peers

Pediatric Brain Injury
Outcomes and Rehabilitation

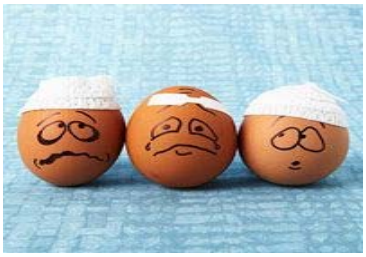
Neuro-plasticity

- Fake news: the brain of the child is resistant to trauma as it is more plastic – that is able to take over function for damaged brain regions
- Fact: neuro-plasticity may help with recovery from focal injuries but the concept does not apply to complicated injuries – diffuse or shearing injuries or those involving multiple brain regions
- Opposing view: following very early injury, rapid developmental changes typical in the preschool period, can result in unlimited neuro- plasticity
- Fact: Multiple processes can be disrupted (concept of the connectome) by multiple types of injury and may not be protective but rather result in greater deficits that in comparison to older children

Pediatric Brain Injury
Outcomes and Rehabilitation

What is the extent to which normal development is possible and spite of an early brain insult (A. McKinley):

- capacity for recovery is not universal to all developmental functions
- neuro- plasticity is not the ability to return to pre-injury function
- there will be influences by the type and severity of injury and the child's environment
- early injury may lead to greater deficits



Pediatric Brain Injury
Outcomes and Rehabilitation

Differences in Normal Development for Preschool Children

- There may be no objective information about the child's functioning prior to injury and evaluation is of deficits in potential – not decline in existing function
- Skills that are assessed represent a reduction in potential – not a reduction in existing skills
- Absence of deficits does not mean no requirement for rehabilitation support – deficits may become apparent over time (skills fail to emerge)
- Long-term approach and follow-up is needed particularly for times of transition i.e. preschool to school

Pediatric Brain Injury
Outcomes and Rehabilitation

Recognized Deficits: Infants and Preschoolers

- ❑ with more severe injury – poor adaptive skills and behavioural difficulties (psychosocial functioning and psychiatric problems in later life), long-term compromise of arithmetic skills
- ❑ with mild TBI requiring hospitalization – ADHD, conduct disorder and substance abuse

- assessment based on the developmental stage from parent report of preinjury function – need for multiple time point assessments post injury
- greatest deficits may be seen in skills at the time of injury which were in development
- lack of communication skills (i.e., preverbal infants) and lack of cognitive and language capacity affecting child's understanding of postinjury changes with limited coping skills

Pediatric Brain Injury
Outcomes and Rehabilitation

Parental Reaction

Importance of the quality of parent – child interaction disrupted by an early injury – parental reaction under stress i.e. protective or punitive responses

Children are reliant on the family system and parental coping for aspects of recovery

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Pediatric Brain Injury

Conclusions and New Approaches:

1. Acquired Brain Injury – a developing disability over time
2. Traumatic Brain Injury – a disruption of the connectome and of functional connectivity

Pediatric Brain Injury

Conde V, Andreasen SH, Petersen TH, Larsen KB, Madsen K, Andersen KW, Akopian I, Madsen KH, Hansen CP, Poulsen I, Kammersgaard LP, Siebner HR. Alterations in the brain's connectome during recovery from severe traumatic brain injury: protocol for a longitudinal prospective study. British Medical Journal 2017: 7 (6): pp 1-9.

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