Concussion as a complex system: Building a system dynamics model of mild traumatic brain injury

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Innovations in Collaborative Modeling
June 2016
Concussion is common

- In the United States, an estimated 1.7 million people suffer a traumatic brain injury every year (Faul et al. 2010).
- 70-90% of these cases are mild TBI, or concussion (Cassidy et al. 2004).

- Concussion is vastly underreported; one study found that at least 88% of cases might go unrecognized (Delaney et al. 2005). In fact, a recent NPR poll found that 1 in 4 Americans report having suffered a concussion.

- Has become a known issue in athletic and military arenas; sufferers are also the elderly, motor vehicle accident victims, and domestic violence survivors, among others.
Concussion is poorly understood

- No single definition of concussion is accepted across disciplines, though several different definitions are available (Comper et al. 2005; Hawryluk & Manley 2015).
  - Complicates clinical trials

- Recovery trajectories are unpredictable: some people recover quickly and others have lasting deficits.
  - Biochemical and cellular changes occur days and even years after a traumatic event (Kovac, 2016)

- There are still no FDA approved treatments or therapies for TBI (Hack, 2016)

- Inadequate classification system for TBI
  - Are concussions on the same spectrum as coma?
  - Does type of concussion matter? Blast vs. impact, etc.

- No shared mental model of pathophysiology
Concussion is complex

- Traumatic brain injury has been called “the most complicated disease of the most complex organ of the body” (Marklund and Hillered 2011).

- The human brain has:
  - Billions of neurons with trillions of connections
  - Billions of nonneuronal cells, too:
    - Neuroglia & blood vasculature

(Image: Martijn van den Heuvel, Journal of Neuroscience.)
Concussion is complex

- Heterogeneity
  - In individual brains, modes of injury, length of recovery, and signs, symptoms, and deficits

- Dynamic: factors throughout recovery period affect outcomes

- Involves many stakeholders, and subfields:
  - In medicine: neurotrauma, neurosurgery, neurology, psychiatry, sports medicine, rehabilitation, speech therapy, neuroscience, etc.

- In research: animal, human, post-mortem; molecular, cellular, systems, computational; academia, sports, military, and more
Taking a systems approach

• TBI researchers approached us looking for a new method. Project led by systems scientists in collaboration with large team of investigators from many subfields of medicine.

• Methods: extensive review of relevant literature; interviews with key researchers, clinicians, and athletic trainers. Facilitated focus group with young athletes experiencing prolonged recovery.

• Created two conceptual models for concussion: multi-scale conceptual framework and causal-loop diagram (CLD)

• Drafted conceptual models, collected information, and reviewed model with experts in iterative process
Multi-scale framework for concussion

Social
- family
- community
- work or school
- norms
- social reserve
- social pressure or support
- relationships

Experiential
- psychological
- emotional
- attention
- social functioning
- pain
- gait/balance
- coping/adaptation
- feeling “out of sync”
- sense of self
- fatigue
- daily tasks
- cognitive reserve

Network
- neuroplasticity
- processing speed
- sleep/wake cycle
- intrinsic connectivity networks
- neuronal population dynamics
- predictive brain state
- loss of consciousness
- neural reserve

Cellular
- ionic flux
- axonal injury
- neuroinflammation
- glymphatic clearing
- neuron function
- glia & astrocytes
- metabolic cascade

Increasing size; longer time-scale
Emergence across scales
Exogenous drivers and cross-scale feedback in the multi-scale framework

Injury context

Social

Ongoing environment

Personal characteristics (e.g., genetics, age, sex, history, prior concussions, resilience, etc.)

Experiential

Behavioral interventions

INJURY

Injury biomechanics (e.g., force, direction, linear and rotational acceleration/deceleration, head/neck kinematics etc.)

Network

Cellular

Pharmacological interventions
Causal-loop diagram of concussion
Next steps

• In process of submitting first conceptual model for publication

• Complete CLD with collaborators this summer, and prepare for publication

• Create an operational system dynamics model, with the goal of generating individual recovery trajectories to aid understanding and classification