

Brain Recovery after Injury

*Kerry R. Crone, MD, FAANS
Professor of Neurosurgery
Department of Neurological Surgery
University of Cincinnati College of Medicine
Cincinnati, Ohio, USA*

TBI

- 10,000,000 TBIs serious enough that result in death or hospitalization occur annually*
- 1.4 million TBIs occur in the United States each year*

Statistics Underestimate the Incidence

- Do not include outpatient visits to physicians or clinics*
- Do not include military events*
- Do not include events that may be miscoded*

TBI: The Problem

- *Can result in long-term or lifelong physical, cognitive, behavioral and emotional consequences*
- *The injury related productivity loss is 14 times higher than spinal cord injury*
- *At least 5.3 million, approximately 2.0%, of Americans are living with a disability related to a brain injury*

Consequences Associated with TBI

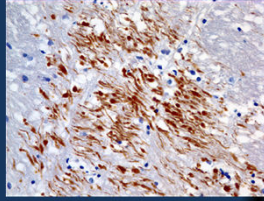
- *During the first 1-3 years post-injury*
 - *1.8 times higher probability to binge drinking*
 - *11 times higher risk for epilepsy*
 - *7.5 times higher risk for death*
- *New health issues*
 - *1.5 increased risk for depression*
 - *2.3 – 4.5 times risk for Alzheimer disease*

Requirements for Optimal Recovery

- *Accessible, available, and appropriate healthcare*
- *Wellness promotion services*
- *Difficulty when “invisible” disability is present*

Histological Changes in mTBI

- Axonal injury as seen by β -APP immunostaining was found in all five cases of mild TBI
- Located within the hippocampal fornices and corpus callosum

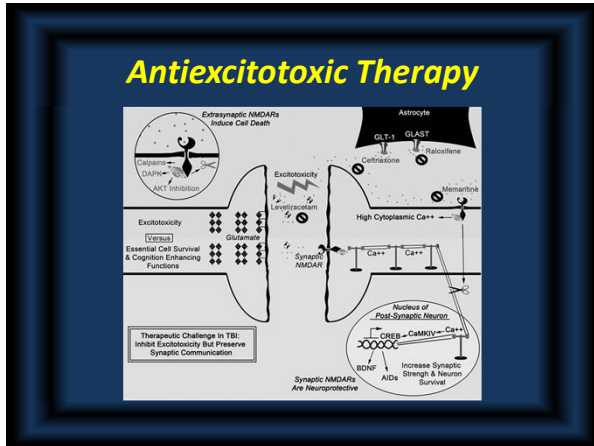


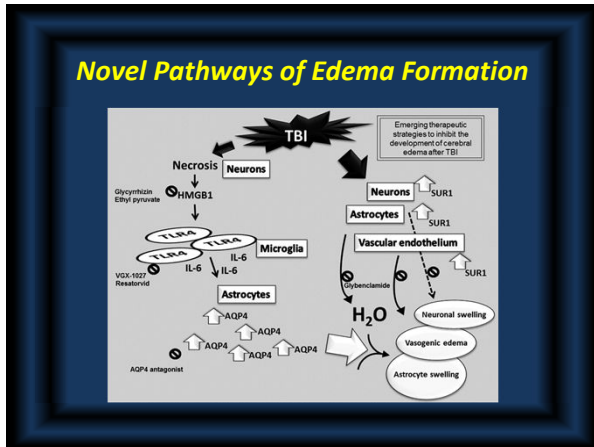
What's New

- Dementia after head trauma with loss of consciousness is doubled compared to TBI without loss of consciousness

Emerging Therapies

- Standard of Care
 - Supportive Measures
 - Studies targeted at modulation of secondary injury have failed
 - Progesterone
 - Antiepileptotoxic Therapy





- ### CSF Biomarkers
- *Tau*
 - *NFL – neurofilament light*
 - *GFAP – Glial fibrillary acidic protein*
 - *Measurement of Tau and NFL following injury correlates with the outcome at one year*

Classes of Brain Recovery

- *Restitution – neural pathways are reactivated and functions restored*
- *Substitution – refer to transfer reorganization from damaged to healthy brain*

Restitution

- *Reflects the physiological recovery of undamaged brain and is seen in days to weeks following injury*
 - *Regeneration focal at best and hindered by scar and blood clots if present.*
 - *Sprouting occurs relatively early as axons that have not been destroyed attempt to reestablish connections.*
 - *Denervation Supersensitivity*

Substitution

- *Intrahemispheric transfer is seen best in young children and diminishes with age.*
- *Restoration of function to an adjacent area may result in decreased skill over time.*

Question

- *Early plasticity vs early vulnerability*
- *There is not uniform agreement regarding the recovery from injury.*
 - *Some young children demonstrate significant improvement following injury while others do not*
 - *Bilateral uniform injury (hypoxic insult) leads to an unfavorable recovery*

Brain Maturation

- *Well established stages of brain maturation beginning in the prenatal period, continuing postnatally and proceeding through adolescence*
- *Disruption of normal maturation related to trauma may prevent further brain development*

Collective Hazard Risk

- *Severity of insult*
- *Age at insult*
- *Social disadvantage*
- *Male gender*

APOE and Genetic Susceptibility to CTE

- Cholesterol and lipids are released from damaged neurons after neuronal injury
- Astrocytes increase ApoE to scavenge the cholesterol and lipids to repair axons and dendritic membranes.
- The ApoE gene has three alleles and ApoE (4) increases the risk of neuronal damage.
- The presence of ApoE (4) decreases the recovery in children and young adults

Conclusion

- The age related outcome is dependent on the maturation of the nervous system at the time of injury
 - The less mature brain which has greater plasticity may be more vulnerable to injury
- The differences in recovery following any TBI is multifactorial, but the genetic construct of the patient may be more significant in the degree of recovery.
