



TRAUMATIC BRAIN INJURY, AGGRESSION AND SELF- DIRECTED VIOLENCE

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TBI: The Scope of the Problem

- Approximately 1.7 million TBIs suffered in the United States alone each year¹
- Nearly 1.1% of the U.S. civilian population, or 3.17 million, is living with long-term disability from TBI²
- Common among soldiers returning from the wars in Iraq and Afghanistan; estimated 15-20% have experienced a probable mild TBI^{3,4}

1. Faul et al. 2010; 2. Zaloshnja et al 2008; 3. Hoge et al. 2008; 4. Tanielian et al. 2008



*1.9 million warriors
have deployed for
Operation Iraqi
Freedom (OIF) and
Operation Enduring
Freedom (OEF)*

OEF/OIF and TBI

- TBI is most common physical injury for combatants in Afghanistan and Iraq
- Explosion or blast injury is most common
- 2006 survey of more than 2,500 recently returned army infantry soldiers: 5% reported injuries with LOC during a yearlong deployment, 10% reported injuries with altered mental status
- RAND report with even higher rates: 19% with probable TBI on survey of almost 2,000 previously deployed service personnel.
- Terrio et al. with similarly high rate (23%) of clinician-confirmed TBI in a U.S. Army brigade combat team with at least one deployment

Mental Health Problems Post Deployment

	OIF (n=222,620)	OEF (n=16,318)
Combat Experiences (Any)	144,978 (65.1%)	7,499 (46.0%)
Any MH Concern	42,506 (19.1%)	1,843 (11.3%)
Suicidal Ideation	Some – 2,411 (1.1%) A lot – 467 (.2%)	Some – 107 (.7%) A lot – 20 (.1%)
Psychiatric Hospitalization in the First Year Post Deployment	1,214 (5.9%) (Distinct Individuals)	45 (2.9%) (Distinct Individuals)

Hoge, Auchterloine, &
Milliken 2006



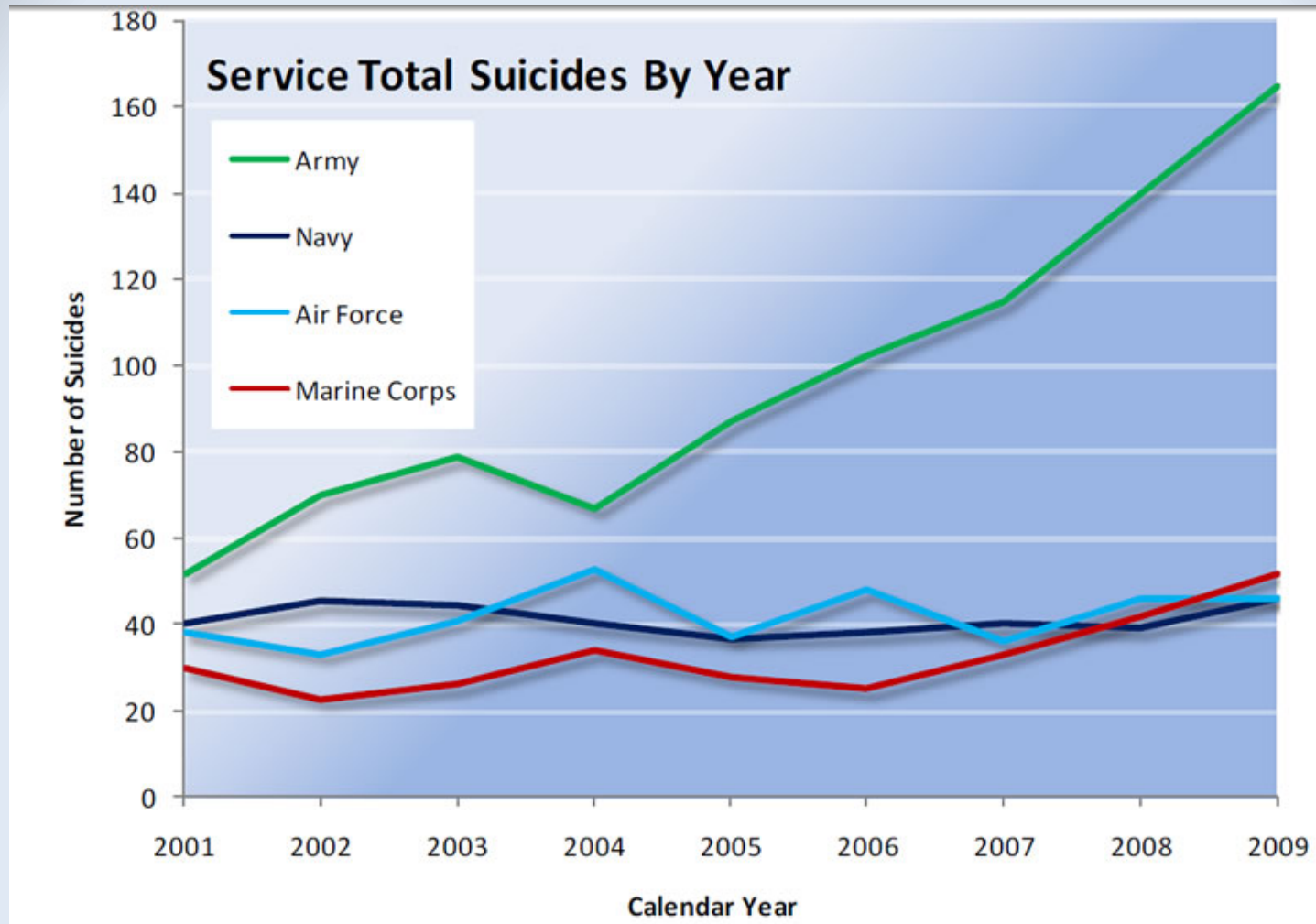
**5 years from 2005 to 2009,
more than 1,100 members of
the Armed Forces took their
own lives, an average of 1
suicide every 36 hours**

*Army Suicides more
than doubled*



[HTTP://WWW.PRNEWSWIRE.COM/NEWS-
RELEASES/JOINT-DOD-TASK-FORCE-
RELEASES-REPORT-ON-PREVENTING-
SUICIDE-IN-US-MILITARY-101313419.HTML](http://www.prnewswire.com/news-releases/joint-dod-task-force-releases-report-on-preventing-suicide-in-us-military-101313419.html)





<http://www.health.mil/dhb/downloads/Suicide%20Prevention%20Task%20Force%20final%20report%208-23-10.pdf>



Suicide and Army

- Suicide rate has continued to climb despite increased efforts and programs for suicide prevention and intervention
- Historically, being in the military was a protective factor for suicide
 - Military rate being well below the civilian rate
- Since 2005, the Army's suicide rate has exceeded that of the U.S. civilian population

<http://www.health.mil/dhb/downloads/Suicide%20Prevention%20Task%20Force%20final%20report%208-23-10.pdf>



“Across America, Deadly Echoes of Foreign Battles”

January 13, 2008



Matthew Sepi, left, shot two people, one fatally, after he was confronted in a Las Vegas alley in 2005. Seth Strasburg, right, is serving a prison term of 22 to 36 years for shooting and killing Thomas Tiffany Varney on Dec. 31, 2005.

Cases, Victims, and Charges

Branch of military



Where they served*



*Two Iraq war veterans also served in Afghanistan.

The victims



Charges

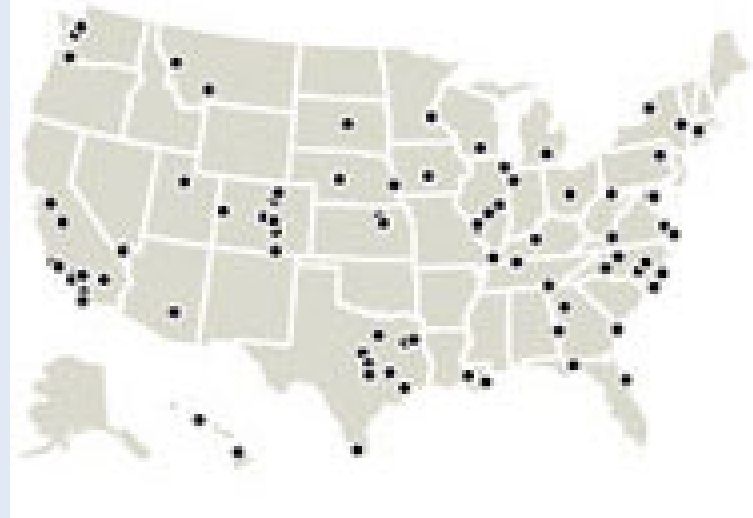


No charges (*suicides, killed by the police*)

* In four cases, the victim was also in the military.

The Cases

The New York Times found 121 cases in which veterans of Iraq and Afghanistan committed a killing in this country, or were charged with one, after their return from war.



Intimate Partner Aggression Among Combat Veterans

- 236 male combat vets seeking services at VA for PTSD
- 33% of those in intimate relationship reported perpetrating partner physical aggression in previous year
- 91% reported partner psychological aggression

Objectives

- Key concepts in evaluating/identifying TBI
- Identify the relationship between TBI and aggression as depicted in the medical literature
- Review neurobiological and cognitive relationships that appear to influence posttraumatic aggression
- Elaborate a relationship connecting TBI, aggression, and self-directed violence

General Definition of TBI

- Application to the brain of an external physical force or rapid acceleration and/or deceleration forces
 - not due to congenital, degenerative, vascular, hypoxic-ischemic, neoplastic, toxic-metabolic, infectious, or other causes
- Produces an immediately apparent physiological disruption of brain function manifested by cognitive or neurological impairments
- Results in partial or total functional disability (regardless of the duration of such disability)

American Congress of Rehabilitation Medicine Definition of Mild TBI:

- A traumatically induced physiological disruption of brain function, as manifested by at least *one* of the following:
 - any period of loss of consciousness (LOC)
 - any loss of memory for events immediately before or after the accident (posttraumatic amnesia, PTA)
 - any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, or confused)
 - focal neurologic deficit(s) that may or may not be transient

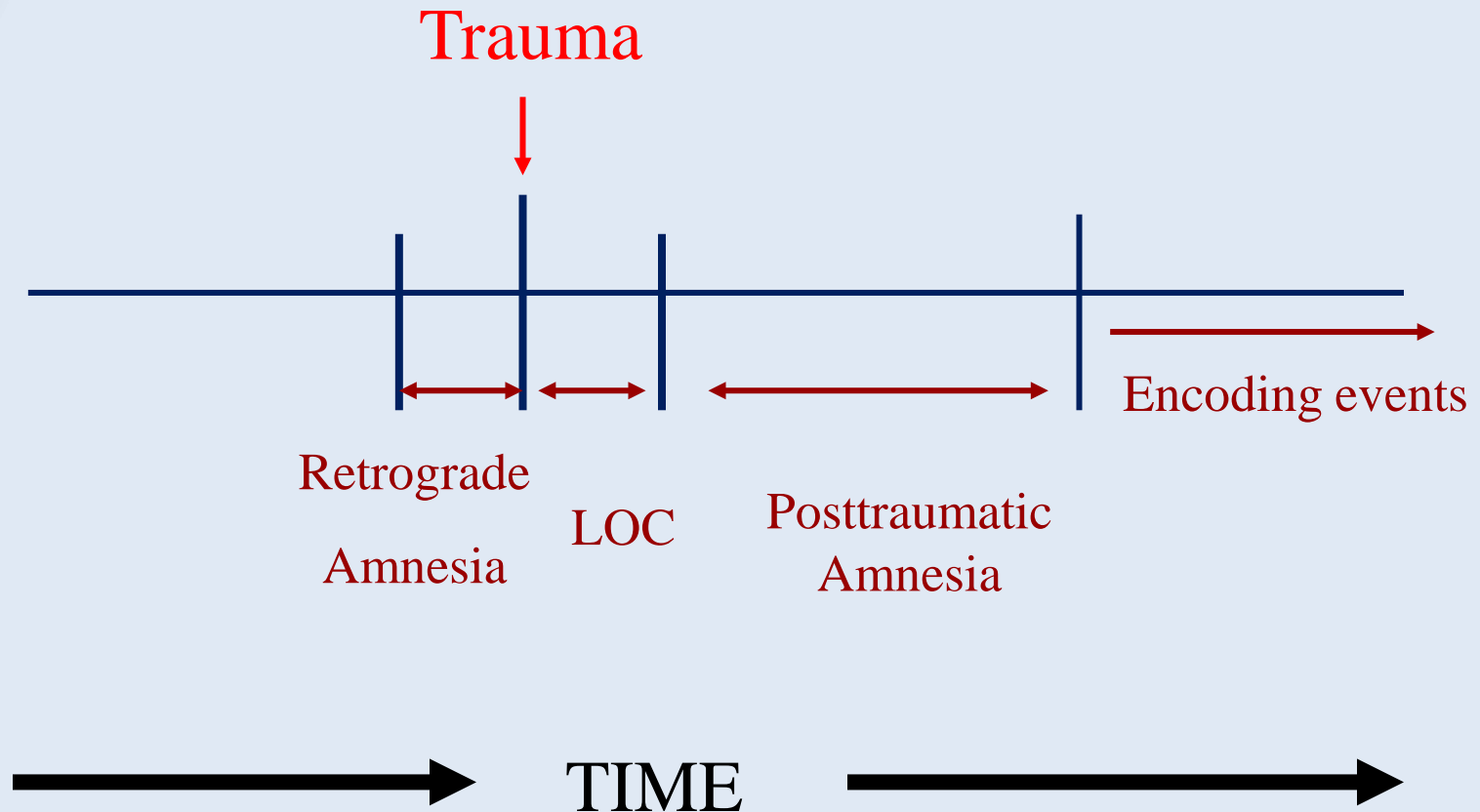
Kay, T., Harrington, D. E., Adams, R. E., Anderson, T. W., Berrol, S., Cicerone, K., Dahlberg, C., Gerber, D., Goka, R. S., Harley, J. P., Hilt, J., Horn, L. J., Lehmkuhl, D., & Malec, J. (1993). Definition of mild traumatic brain injury: Report from the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine. *Journal of Head Trauma Rehabilitation*, 8(3), 86-87.



American Congress of Rehabilitation Medicine Definition of Mild TBI:

- The severity of the injury does not exceed the following:
 - LOC \leq 30 minutes
 - after 30 minutes, Glasgow Coma Scale = 13-15
 - PTA \leq 24 hours
- TBI producing disturbances that exceed these criteria is classified as moderate or severe

Posttraumatic Amnesia



Self-diagnosis of TBI

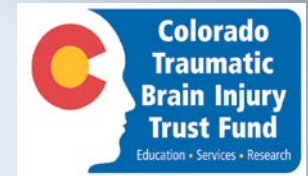
- “Gold standard” for diagnosis of TBI remains self-report and requires caution:
 - under-reporting vs. over-reporting
 - poor understanding of TBI
 - misunderstanding symptoms as reflective of TBI when other diagnoses offer better explanations
 - stigma vs. secondary gains
- Avoid missed opportunities to target other treatable conditions (PTSD, MDD, etc.)

Self-diagnosis of TBI

- Reports of mild TBI without evidence in the medical record require careful evaluation of the history and other available evidence
 - use ACRM definition of mild TBI as an anchor for the clinical history
 - interview witnesses, if any, to the purported injury
 - review medical, neurological, and neuropsychological evaluations (including comparison to pre-injury whenever such data can be obtained)
 - review (by visual inspection, not just reports) any structural neuroimaging (CT, MRI) for findings consistent with *traumatic* brain injury
- !! Biomechanical trauma frequently co-occurs with psychological trauma, especially in combat settings

TBI in a VA Mental Health Setting

TBI – 4 (n=509)

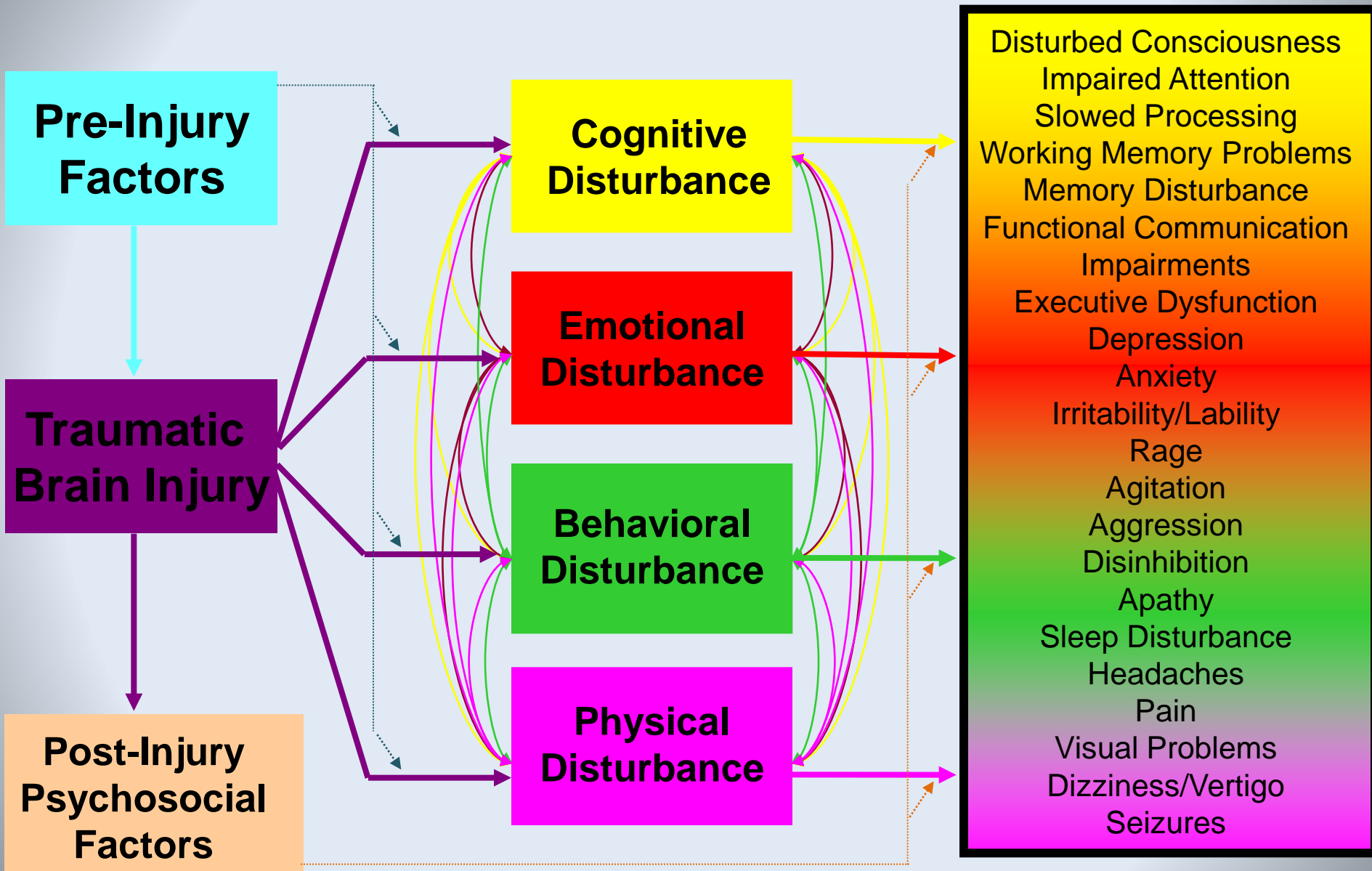


Question	Have you ever been hospitalized or treated in an emergency room following an injury? (If yes) Did you injure your head or neck?	Have you ever been knocked out or unconscious following an accident or injury?	Have you ever injured your head or neck in a car accident or from some other moving vehicle accident?	Have you ever injured your head or neck in a fight or fall?
# Yes	207	226	169	210
% Yes	41%	44%	33%	41%

Brenner, L., Homaifar, B., Huggins, J., Olson-Madden, J., Harwood, J., Nagamoto, H.
 Use of a Traumatic Brain Injury Screen in a Veteran Mental Health Population: Prevalence,
 Validation and Psychiatric Outcomes



A Model of Influences on Neurobehavioral Outcome after TBI



(Adapted from Silver and Arciniegas 2006)

"In order to understand the effects of brain injury, we must undertake full study of the individual's constitution. In other words, it is not just the kind of injury that matters, but the kind of brain that is injured."

Sir Charles Symonds, c. 1937



Recovery from Mild TBI

- 1st week post-TBI: 90% (or more) endorse postconcussive symptoms
- 1 month post-TBI: ~50% are recovered fully
- 3 months post-TBI: ~66% are recovered fully
- 6-12 months post-TBI: ~10% still symptomatic
- Those who remain symptomatic at 12 months are likely to continue experiencing postconcussive symptoms thereafter

Recovery from Moderate-to-Severe TBI

- About 35-60% of persons with moderate to severe TBI will develop chronic neurobehavioral and/or physical symptoms related to TBI
 - more severe initial injury increases the likelihood of incomplete neurological, neurobehavioral, and functional recovery
- Successful return to work and/or school is inversely related to the severity of persistent neurobehavioral and physical symptoms

Posttraumatic Cognitive Impairments

- In the acute and late periods following TBI, the domains of cognition most commonly affected by TBI include:
 - arousal/disturbances of consciousness
 - processing speed/reaction time
 - attention (selective, sustained, alternating, divided)
 - working memory
 - memory (new learning, retrieval, or [usually] both)
 - functional communication (use of language)
 - executive function

(Reviewed in: Bigler 2007; Arciniegas and Silver 2006; Nuwer 2005;
Meythaler et al. 2001)



Common Posttraumatic Emotional and Behavioral Problems

- Depression
- Mania
- Pathological Laughing and Crying
- Anxiety
- Irritability or loss of temper (“rage episodes”)
- Disinhibition
- **Agitation/Aggression** (“socially inappropriate behavior”)
- Apathy (loss of drive to think, feel, and/or behave)
- Psychosis
- Sleep disturbance



Common TBI Symptoms –
NOT to be confused with
the injury itself

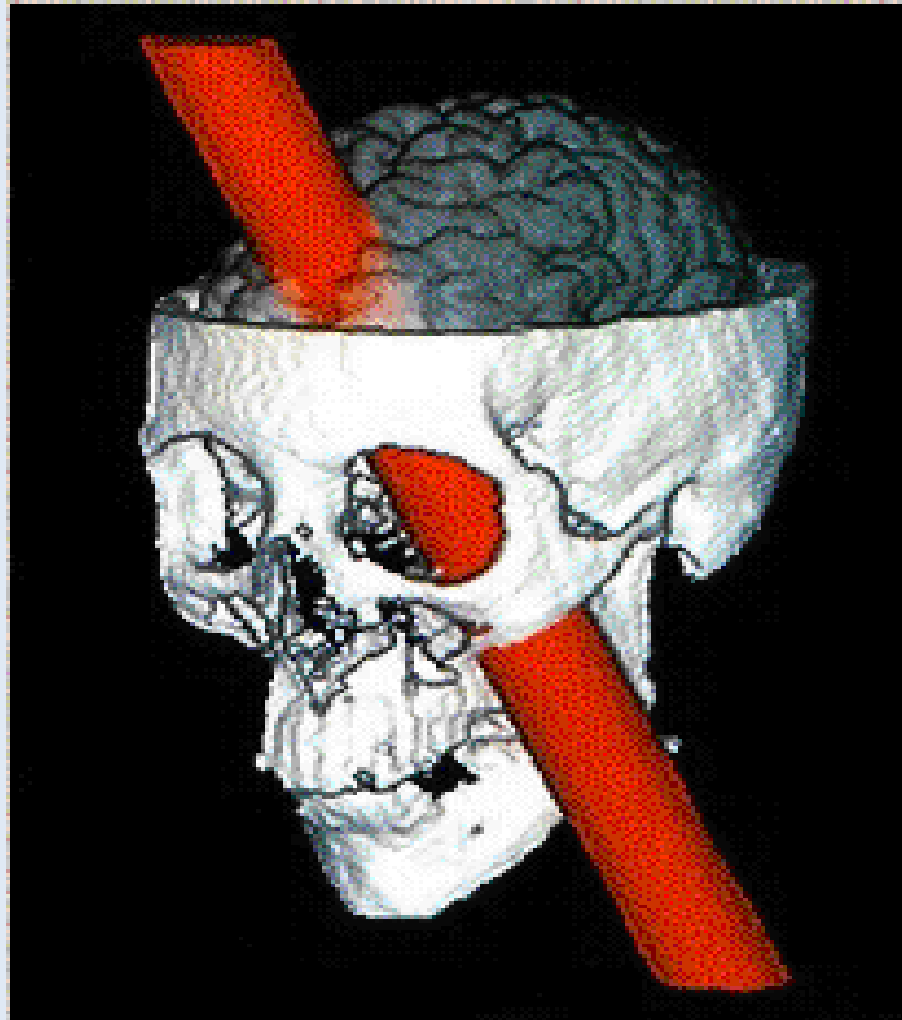
TBI is a historical
event



The Case of Phineas Gage (Harlow, 1848)

- 25 year old railroad foreman
- cognitively, emotionally, and behavioral normal
 - “a man of temperate habits, and possessed of considerable energy of character”
- while working tamping gunpowder into a blasting hole, he is momentarily distracted by coworkers
- an explosion occurs, blasting the tamping rod out of his hands and upwards through his face and skull

Phineas Gage



Reconstruction by H. Damasio and A.R. Damasio, University of Iowa

Phineas Gage

- Gage suffered a penetrating brain injury affecting the orbitofrontal lobes bilaterally
 - dramatic change in behavior occurs
 - becomes “childish, capricious, obstinate”
 - poor social judgment
 - frequently profane
 - sexually inappropriate
 - impulsive
 - loss of empathy for others
 - miraculously, he survives his injury and lives for 13 years
 - however, “Gage was no longer Gage.”

Posttraumatic Aggression

- Generally regarded as a common problem
- Literature is lacking and requires cautious interpretation
- ANPA Committee on Research Critical Review
 - Nosology of aggression and agitation particularly problematic with lack of rigorous definition
 - Minimal use of DSM diagnosis of personality change due to general medical condition, aggressive type
 - “Existing epidemiological studies... offer little insight into the prevalence and incidence of posttraumatic aggression... more research is needed to establish a consistent operational definition of posttraumatic aggression.”

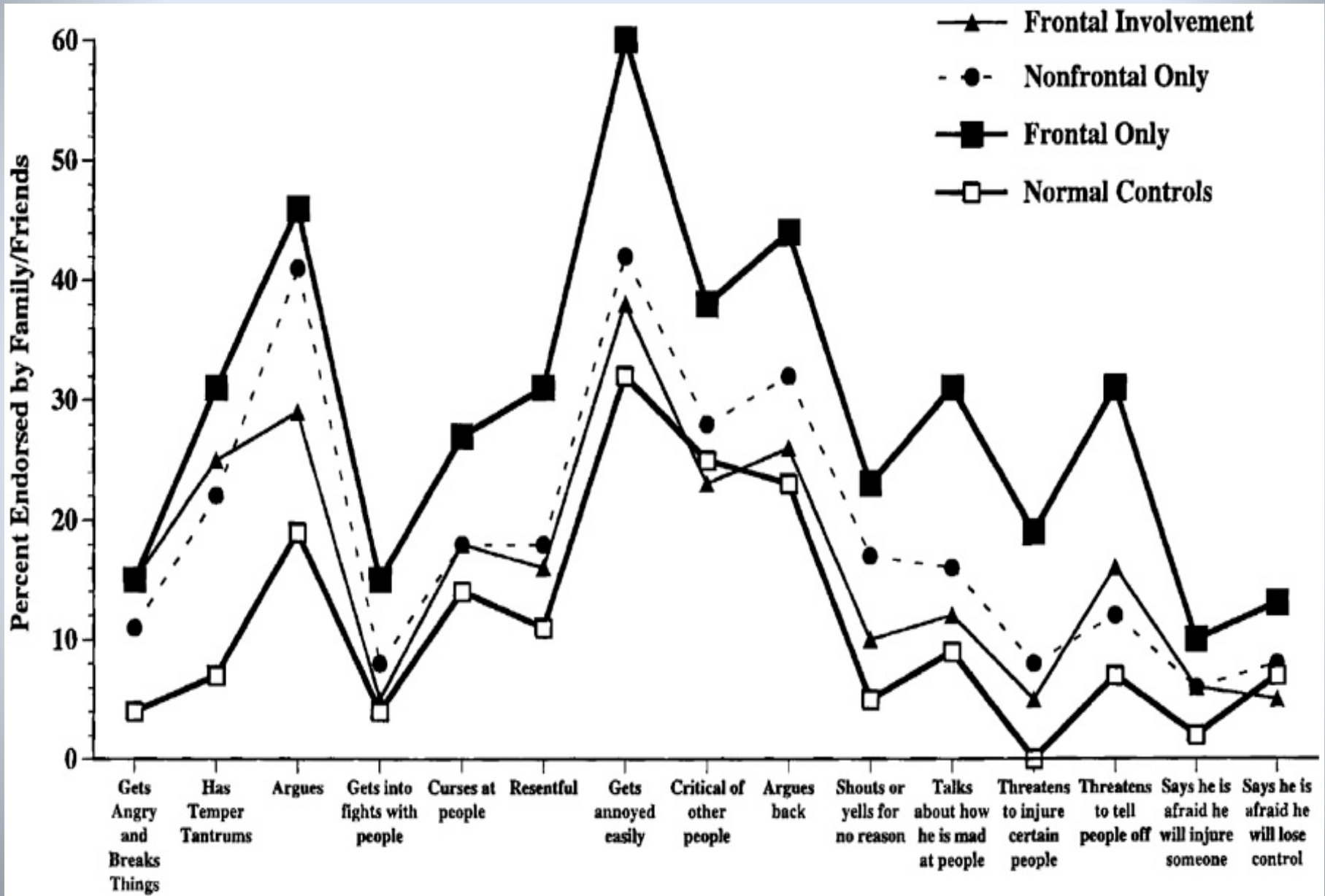
Kim et al. (2007)



Grafman et al. (1996)

- Examined relationship between frontal lobe lesions and aggressive/violent behavior
- 279 Vietnam vets with penetrating TBIs matched v. matched controls
- Family observations and self-reports
- Frontal ventromedial lesions significantly associated with higher scores for aggression and violence
- Higher aggression violence scores generally associated with verbal confrontations rather than physical assault

Percentage of items on aggression and violence endorsed by friends and family members of controls and patients



Max et al. (1998)

- Prospectively studied children with oppositional defiant disorder (ODD) in 2 years after TBI
- 50 children hospitalized after TBI assessed for injury severity; preinjury psychiatric, socioeconomic, family functioning, and family psychiatric history status
- Only at 2 years after injury was severity of injury a predictor of change in ODD symptomatology
- Patients with more severe injury, lower socioeconomic status, preinjury ODD symptoms, and preinjury family dysfunction develop more severe aggressive symptoms

Max et al. (2001)

- Investigated personality change (PC) in children after TBI
- Ninety-four subjects assessed with standardized interview, Neuropsychiatric Rating Schedule
- PC occurred in 59% of severe (22/37) and 5% of mild/moderate (3/57) TBI subjects.
- For severe TBI, labile subtype of PC most common (49%), followed by aggressive and disinhibited subtypes (38% each), apathy (14%), and paranoia (5%)
- 38% of the subjects developed aggressive behaviors

Marschark et al. (2000)

- Investigated college students with history of mTBI
- 79 students with mTBI history, 75 students with a history of general anesthesia, and 93 students with neither
- Tests of verbal memory, nonverbal memory, verbal fluency, nonverbal fluency, and Symptom Checklist-90-Revised
- Students with mTBI produced similar scores on the cognitive tests
- mTBI group with significantly higher levels of emotional distress on the SCL-90-R, included higher hostility and interpersonal sensitivity

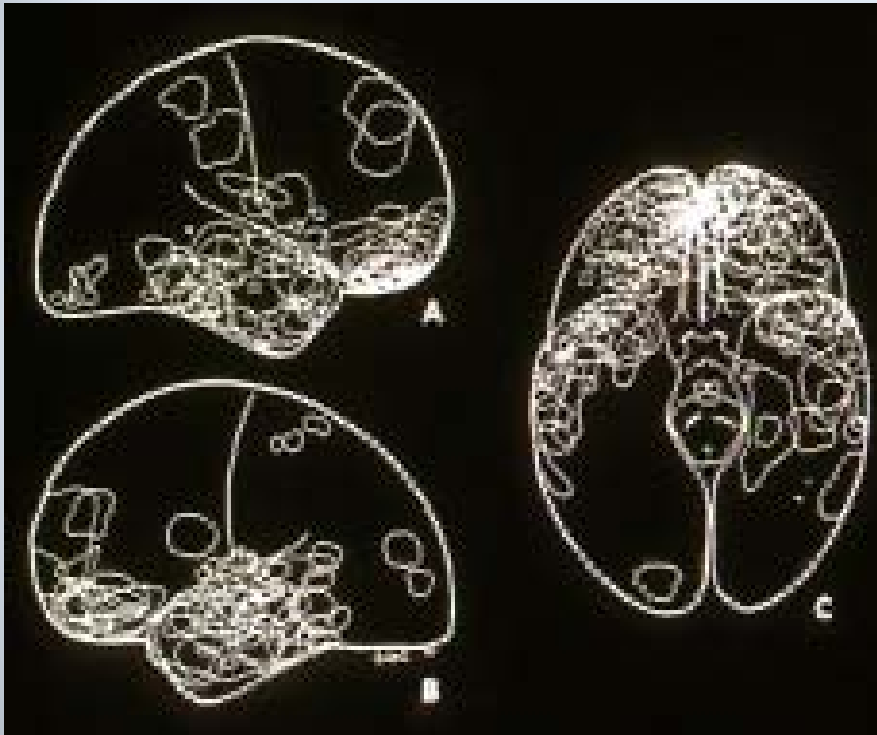
Tateno et al. (2003)

- Assessed aggressive behavior in 89 TBI patients and 26 patients with multiple trauma but no TBI using the Overt Aggression Scale and examined its clinical correlates
- Aggressive behavior in 33.7% of TBI patients and 11.5% of no TBI patients during first 6 months post-TBI
- Aggressive behavior significantly associated with presence of major depression, frontal lobe lesions, poor premorbid social functioning, and history of alcohol and substance abuse
- Suggest that interventions aimed at treatment of depression and substance abuse and enhancing social support may help reduce severity of disruptive behavior

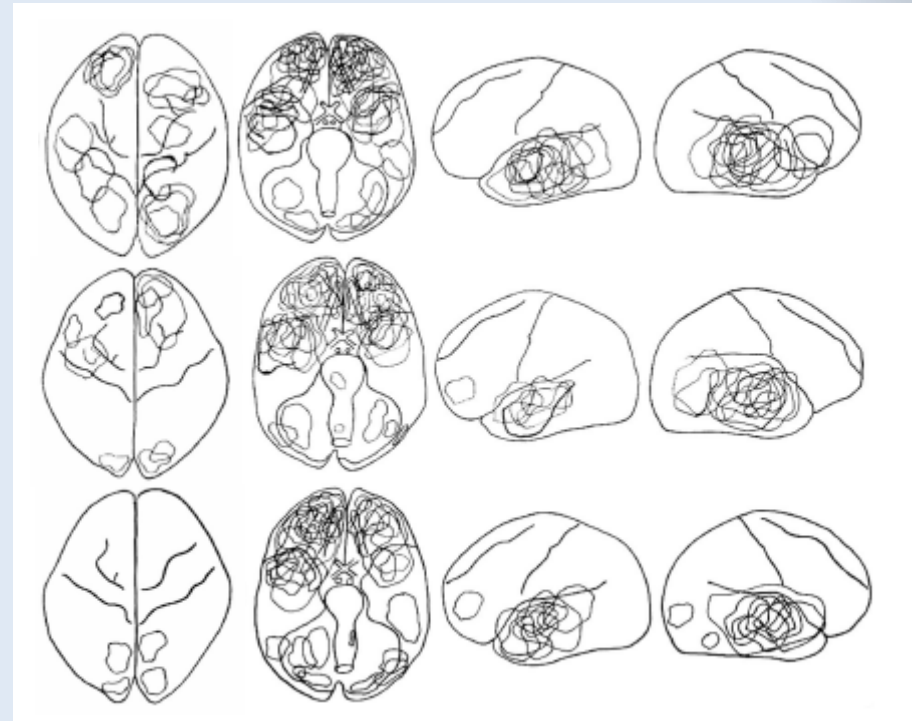
Posttraumatic Aggression

- Common problem after TBI, usually on setting in 1st year post-injury
- Associated with frontal lobe lesions
- Associated with presence of major depression
- Patients with pre-injury substance abuse or impulsive aggression at greater risk
- Some studies demonstrate increased aggression in context of normal cognitive testing
- Neuropsychological batteries may be unable to detect subtle executive dysfunction and impaired social intelligence mediated by frontal lobes.

Typical Locations of Cortical Contusion after Severe TBI

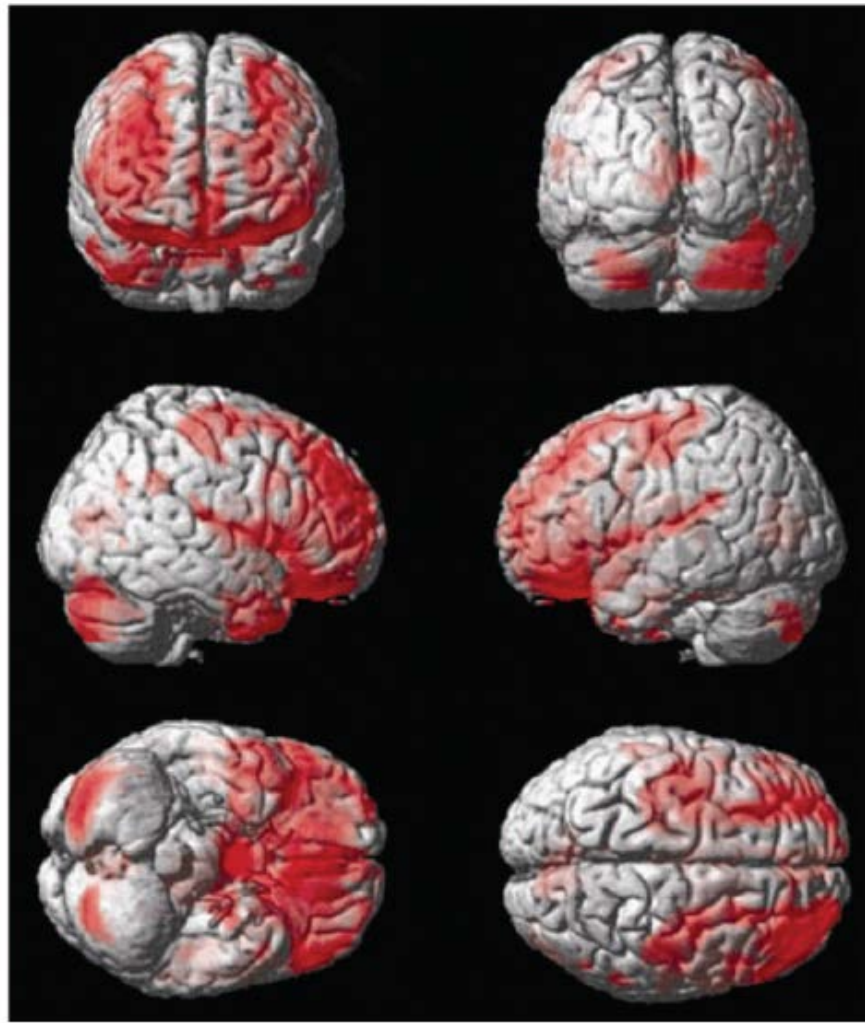


Coureville 1937; image courtesy of Thomas W. McAllister, MD (Dartmouth-Hitchcock Medical Center)

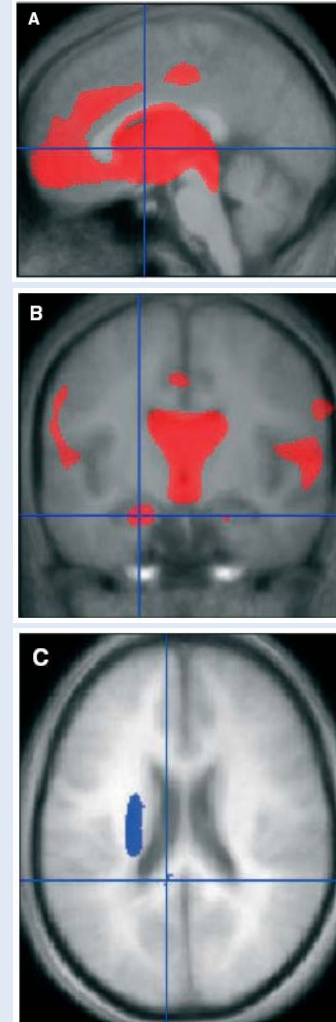


Coureville 1950 and Gurdjian 1975; adapted from Bigler 2007

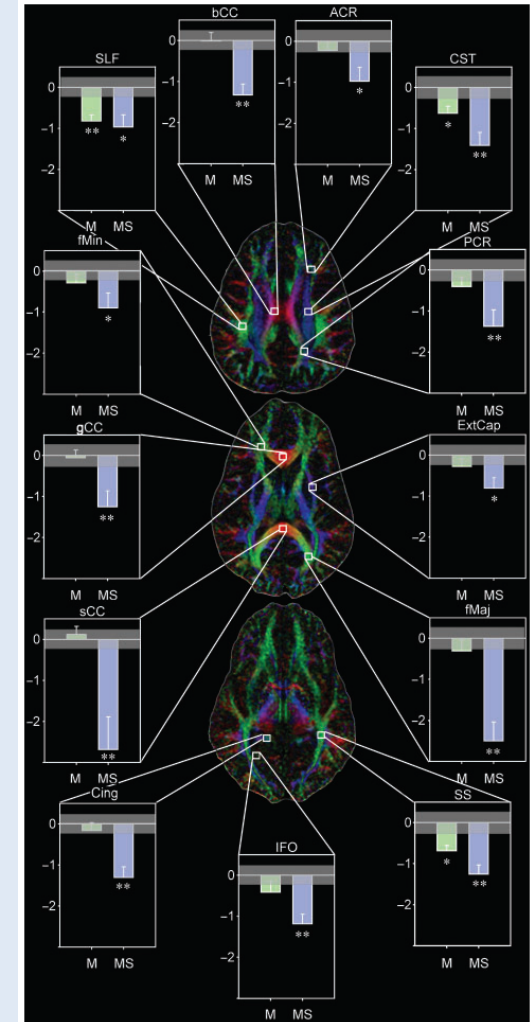
Regional Vulnerability to TBI



Yeates et al. 2007

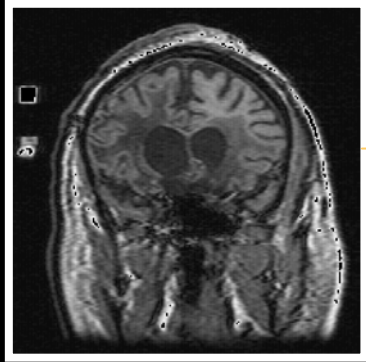


Salmond et al. 2005

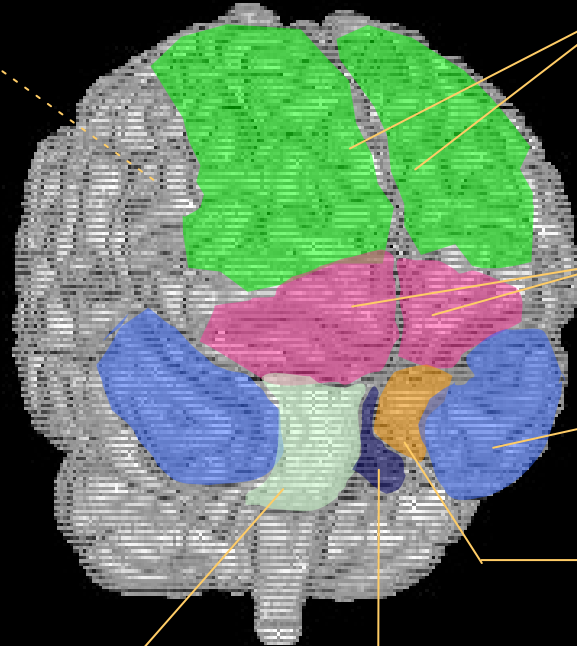


Kraus et al. 2007

Regional Vulnerability to TBI and Brain-Behavior Relationships



White matter
(processing speed/efficiency)



Dorsolateral prefrontal cortex
(executive function, including sustained and complex attention, memory retrieval, abstraction, judgement, insight, problem solving)

Orbitofrontal cortex
(emotional and social responding)

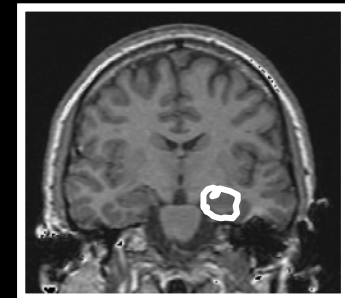
Anterior temporal cortex
(memory retrieval, sensory-limbic integration)

Amygdala (emotional learning and conditioning, including fear/anxiety)

Ventral brainstem
(arousal, ascending activation of diencephalic, subcortical, and cortical structures)

Hippocampal-Entorhinal Complex (declarative memory)

Viewed on coronal MRI →



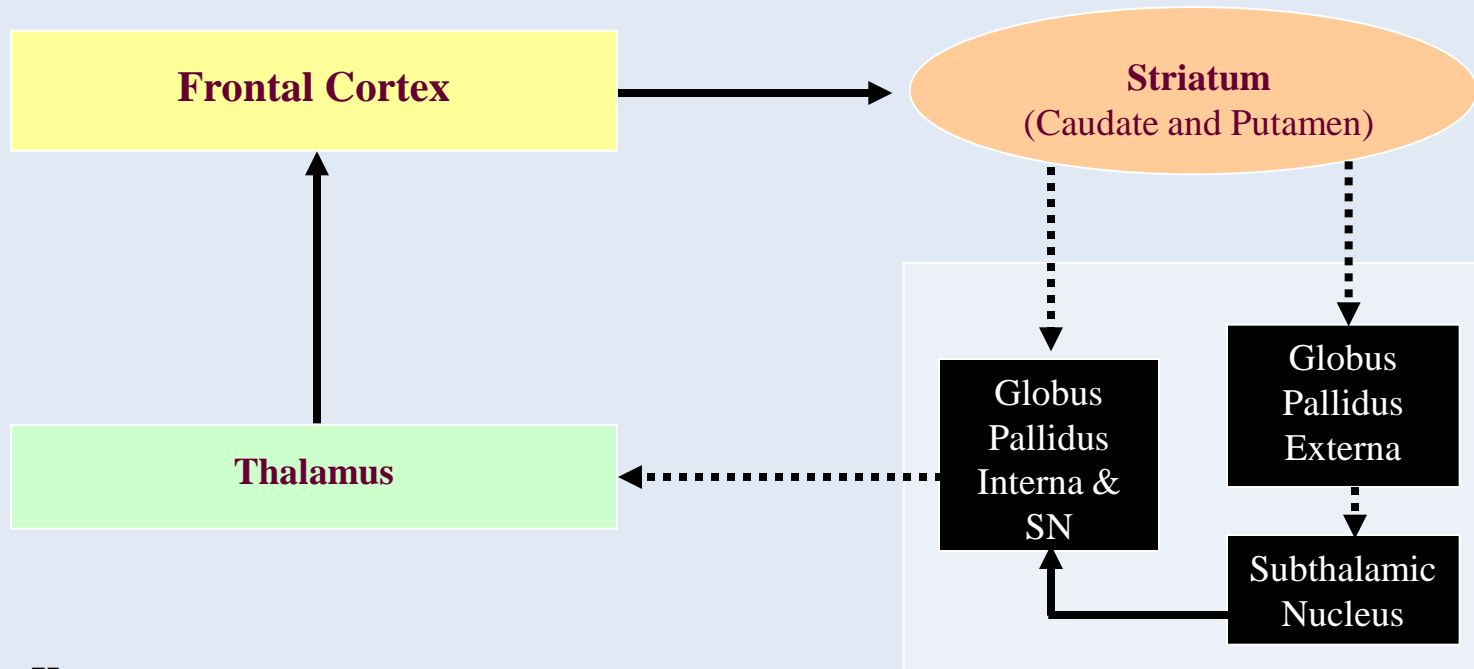
(Figure adapted from Arciniegas and Beresford 2001)

Frontal-Subcortical Circuits

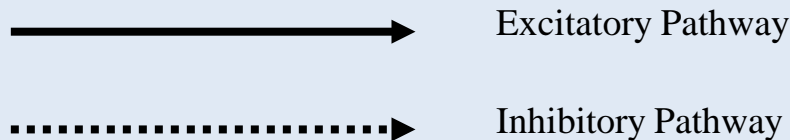
- Five major circuits
 - Motor
 - Frontal eye fields
 - **Dorsolateral prefrontal (executive)**
 - **Lateral orbitofrontal (“social intelligence”)**
 - Anterior cingulate (motivation)

All share the same fundamental circuits, and hence dysfunction in one is often associated with dysfunction in one or more of the others

Schematic Anatomy of the Frontal-Subcortical Circuits



Key:



(Arciniegas and Beresford 2001)

Dorsolateral Prefrontal Circuit

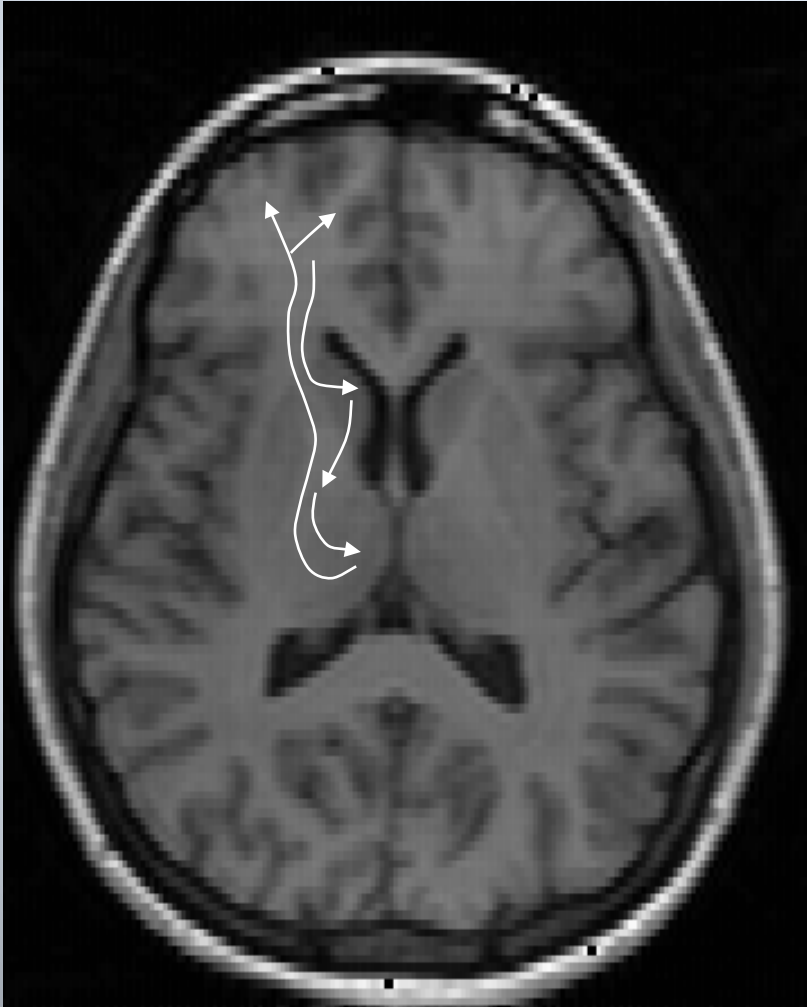


Figure 4.5 A schematic depiction of the dorsolateral prefrontal circuit. This axial MRI depicts the approximate pathway of this circuit, from right dorsolateral prefrontal cortex (DLPFC, superior and middle frontal gyri) to striatum (caudate), to globus pallidus (not shown) to thalamus and back to the DLPFC.

The DLPFC subserves executive function.

(Arciniegas and Beresford 2001)

DLPFC Circuit: Executive Function

- Refers to a collection of abilities including:
 - categorization and abstraction
 - systematic memory searching
 - information retrieval
 - problem solving
 - self-direction
 - independence from external environmental contingencies
 - generating, maintaining, and shifting cognitive, emotional, and behavioral sets and patterns

Lateral Orbitofrontal Circuit

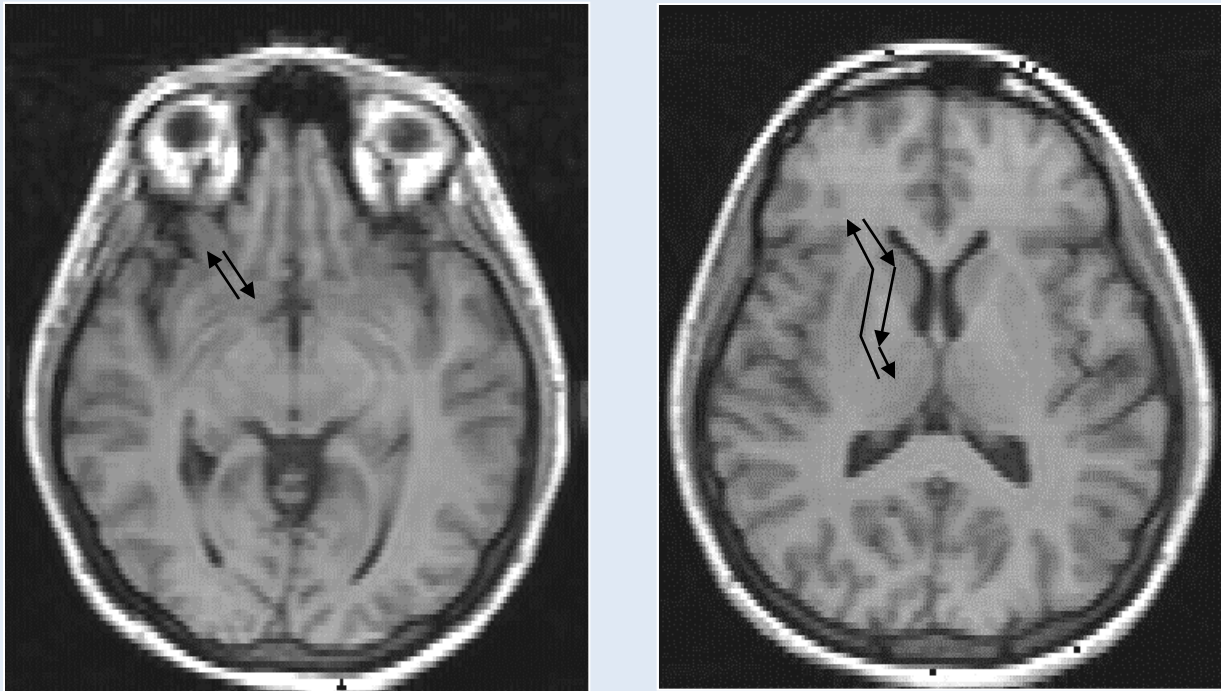
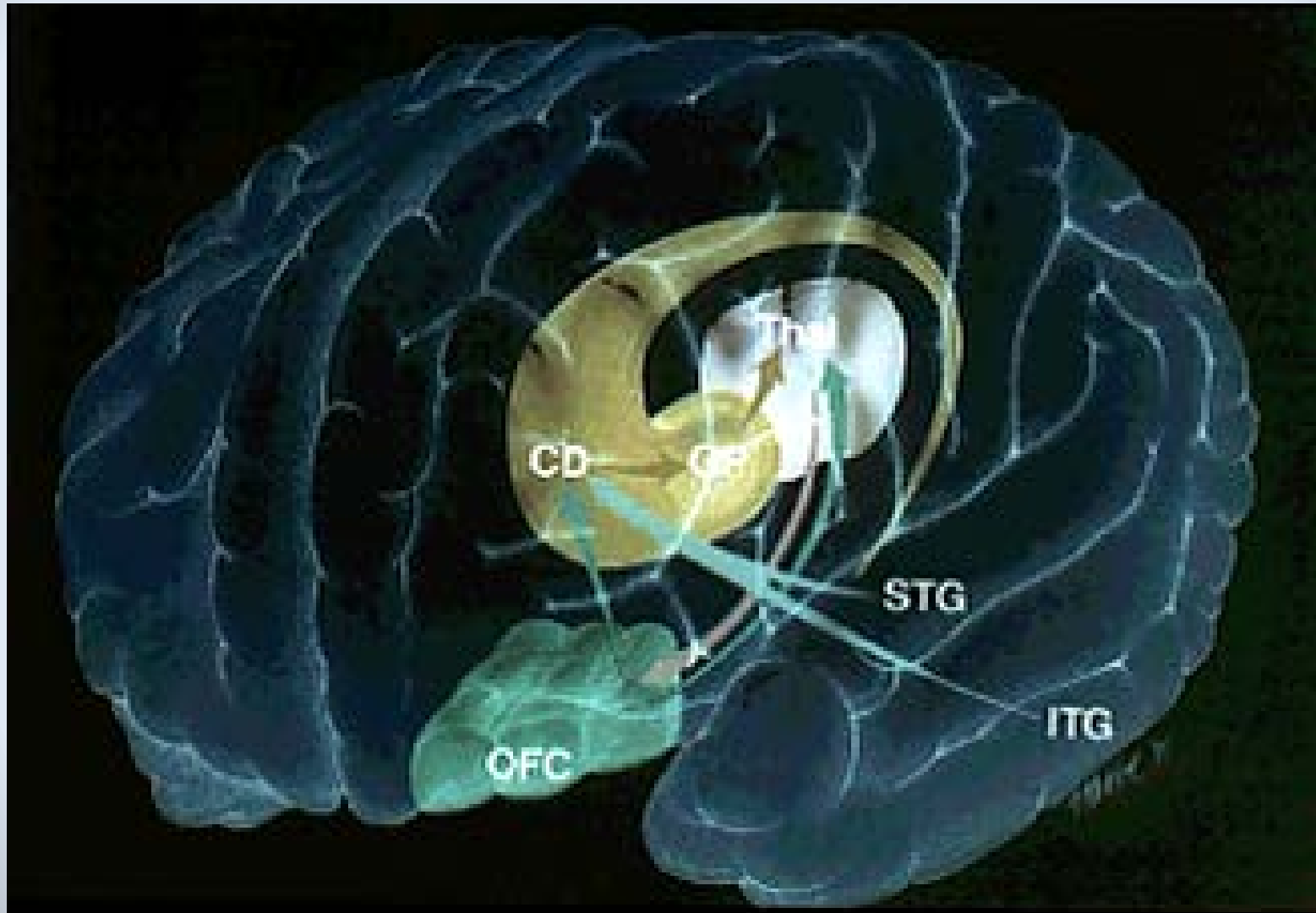


Figure 4.8 The lateral orbitofrontal-subcortical circuit. These axial MRI slices depict the approximate pathway of this circuit. The image on the left is about mid-level through the orbits, between which are the orbitofrontal cortices. The dashed arrows in the left image indicate the input and output from the right orbitofrontal cortex, which ascends to the circuit depicted in the right image. As with the dorsolateral prefrontal-subcortical circuit, the circuit follows the same basic pathways, proceeding from cortex to striatum (caudate), to globus pallidus (not shown), to thalamus, and back to cortex

Lateral Orbitofrontal Circuit



(Figure adapted from Salloway 2001)

OFC: “Social Intelligence”

- Refers to a collection of abilities including:
 - appropriate use or inhibition of “limbic” functions (survival functions and emotion)
 - anger/aggression
 - anxiety/flight
 - sexual behavior
 - appetitive (feeding) behavior
 - empathy/nurturance
 - integration of limbic drives with social context
 - social insight and judgment

Simpson & Tate (2007)

Suicide risk compared to general population...
Standardized Mortality Ratios and 95% CI

Males with TBI	3.9	3.13-4.59
Females with TBI	4.7	3.06-7.06
Age at injury < 21	3.5	1.92-6.27
21-40	4.7	3.35-6.50
41-60	5.2	3.73-7.17
>60	2.5	1.55-4.01
Concussion	3	2.82-3.25
(Severe) Lesion	4.1	3.33-4.93
Comorbid Substance Abuse	7.4	4.32-12.82

Aggression → Suicide

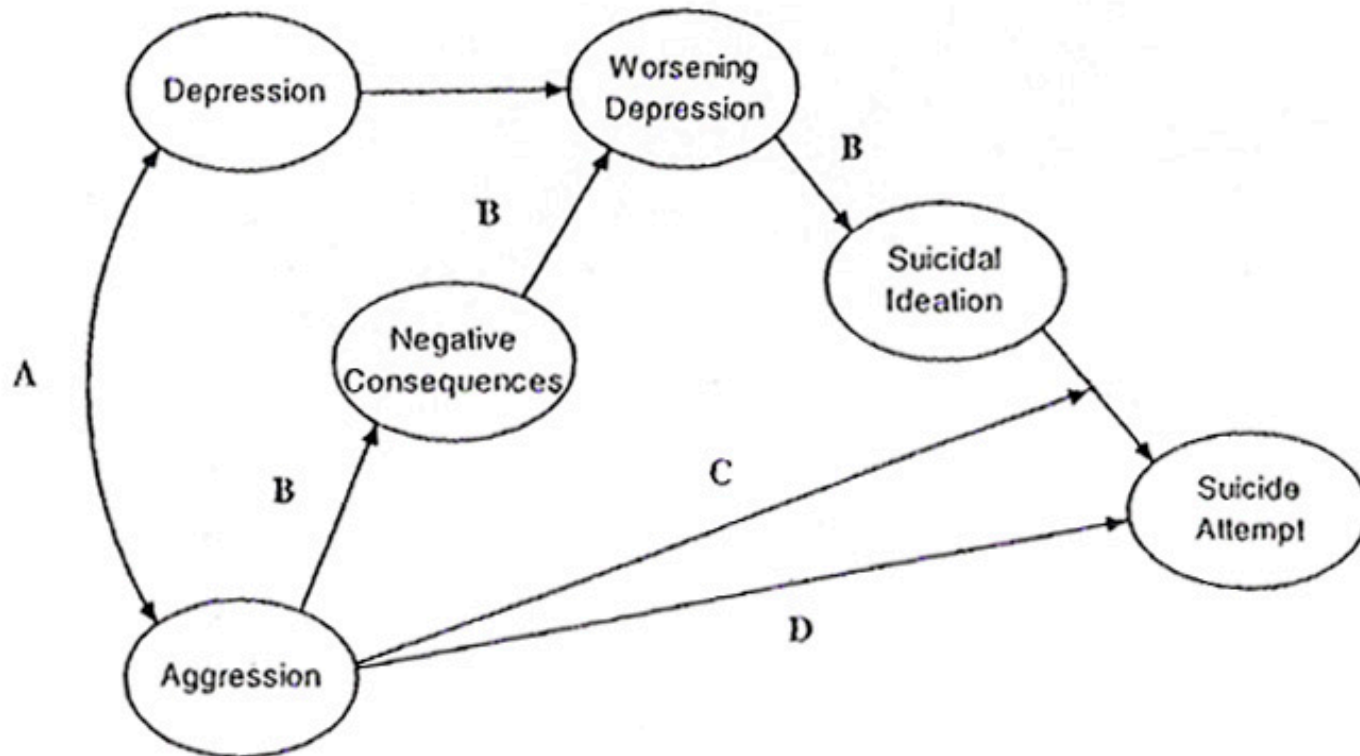
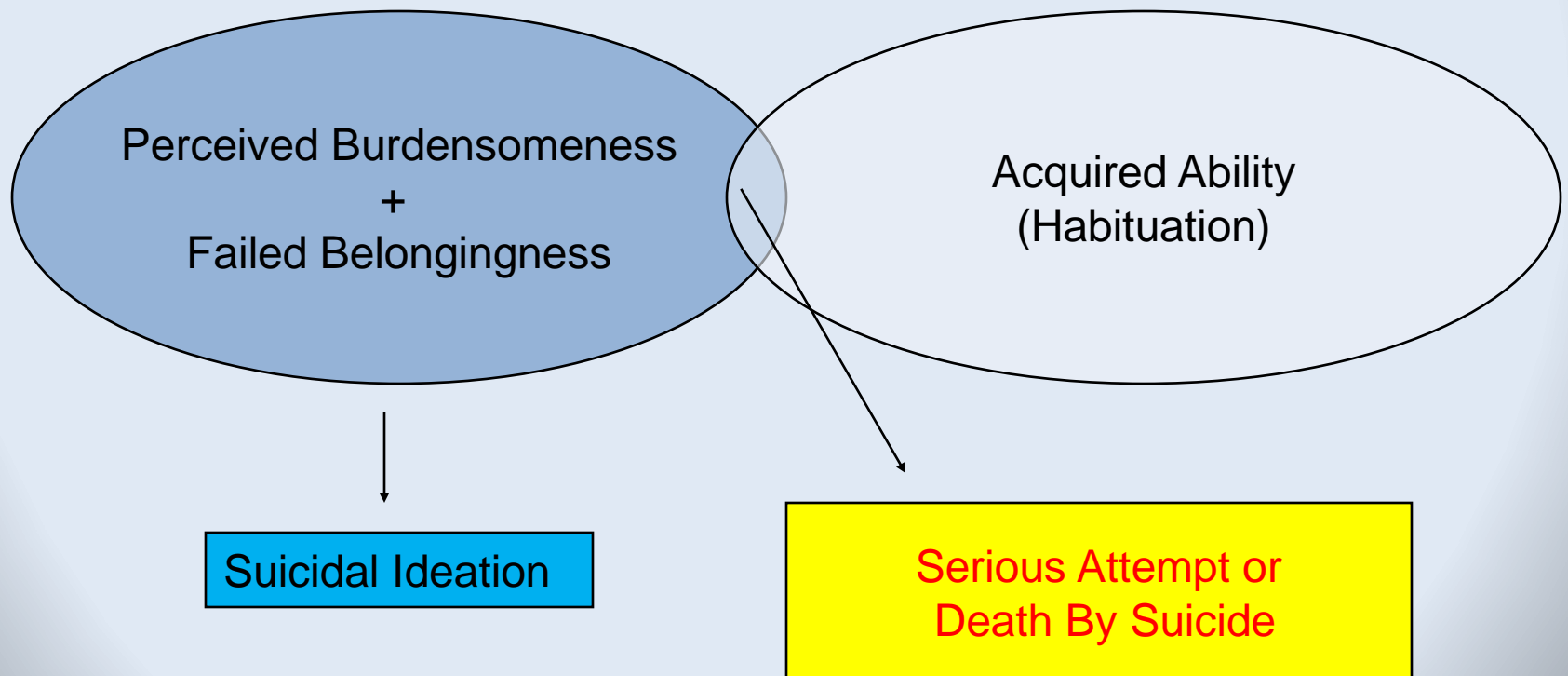


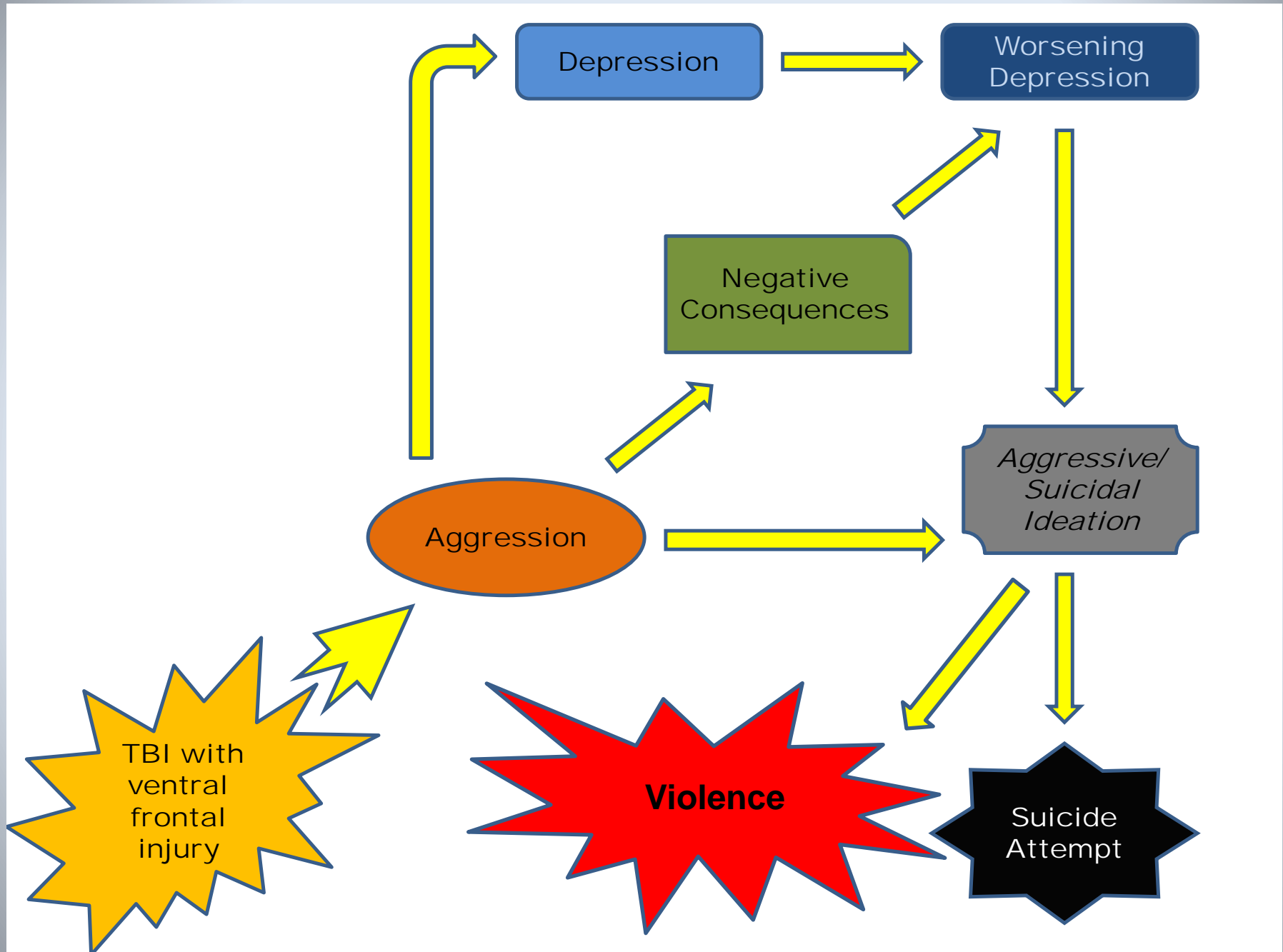
Fig. 1 Theoretical model of non-causal (*Path A*), indirect (*B*), moderating (*C*), and direct (*D*) effects of aggression on risk for suicidal thoughts and behavior

Interpersonal-Psychological Theory of Suicide Risk Joiner 2005

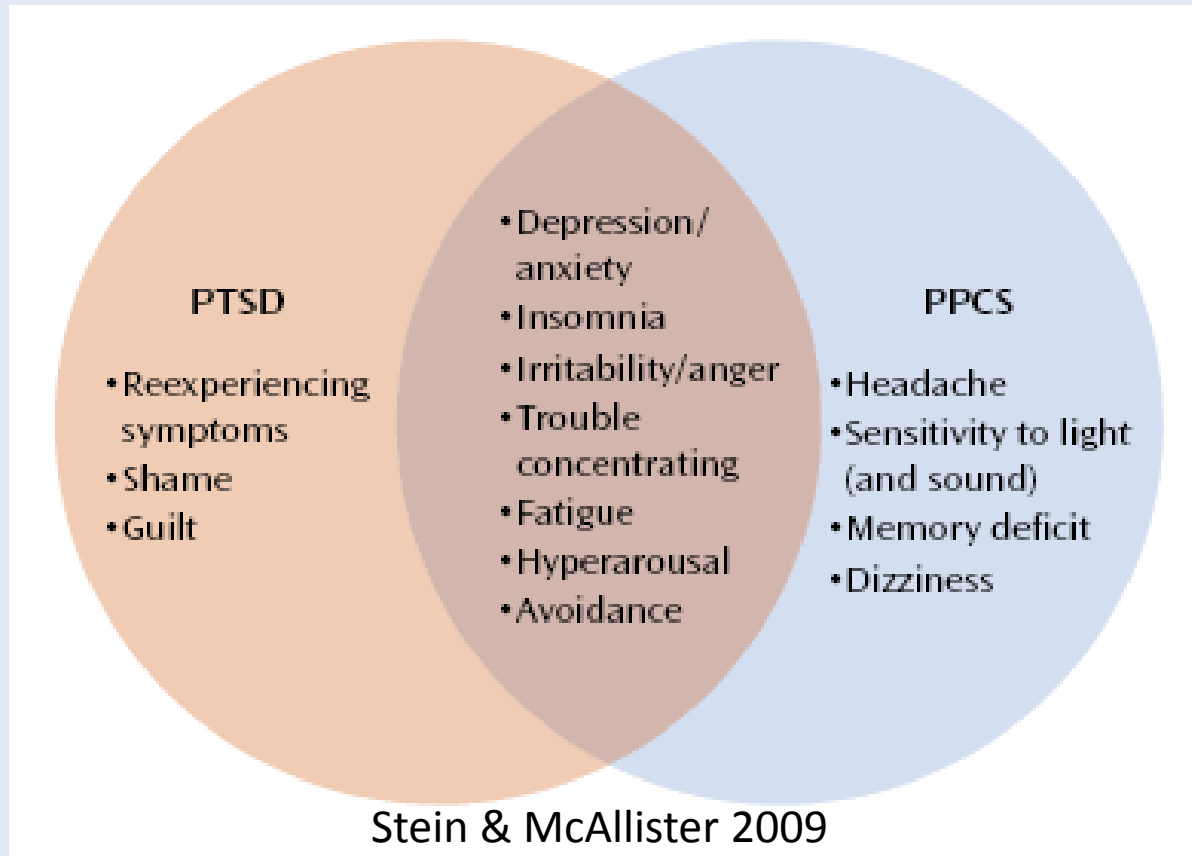
**Those who
desire death**

**Those capable
of suicide**



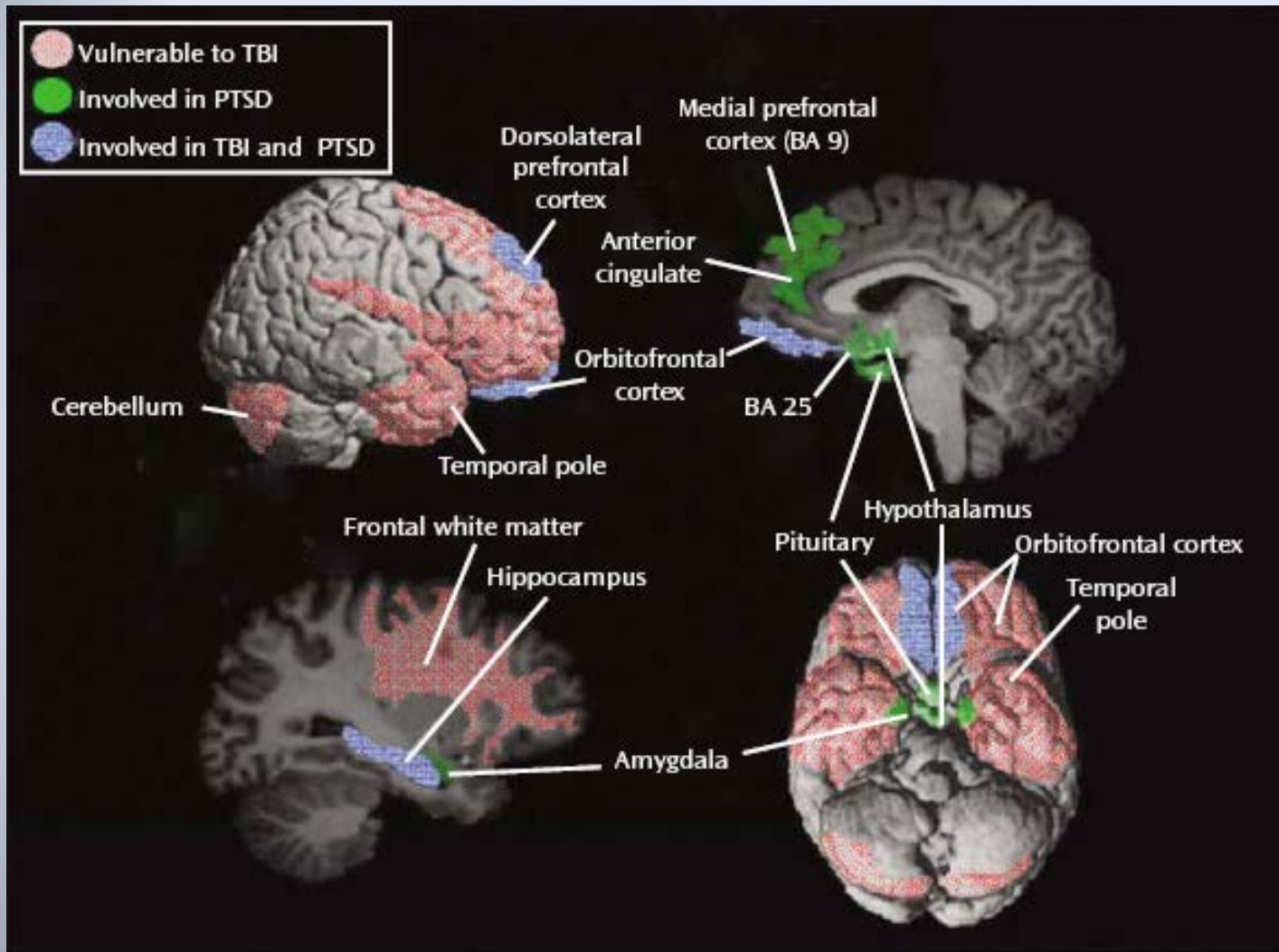


Interface of TBI and PTSD



Unfortunately, the overlap also seems to involve aggression.

Shared Anatomy of TBI & PTSD



This shared anatomy also implicates aggression

Stein & McAllister 2009

Toward and Understanding of Violence...

Aspen Neurobehavioral Conference Consensus Statement

- Behavior is variably governed by interaction of factors... genes, early life experience, acquired brain damage, learned behavior patterns, and situational contingencies.
- “Aggression and violence, like any behaviors, ultimately derive from the normal or abnormal operation of the brain.”
- TBI is associated with increased risk of aggression and violence
- TBI with frontal dysfunction appears to threaten the capacity to inhibit violent behavior
- “Illness is not destiny”

Not All Violence is Alike

- The nature and quality of violent behavior guides formulations regarding relationship to TBI
- Aggression of any kind may arise among persons with TBI as a function of issues with no direct relation to TBI
 - States of intoxication, medical conditions (e.g., delirium due to other non-TBI causes), pre-morbid personality traits/disorders (especially antisocial, borderline, narcissistic), or as a premeditated, purposeful, instrumental violent act
- Attribution of aggressive behaviors to TBI should be undertaken with caution, and only after careful consideration of the totality of the circumstances surrounding behaviors
 - Including (but not limited to) specific details of the TBI, pre-and-post psychosocial factors, the context in which the particular violent act occurred, and any potential precipitants and/or possible objectives

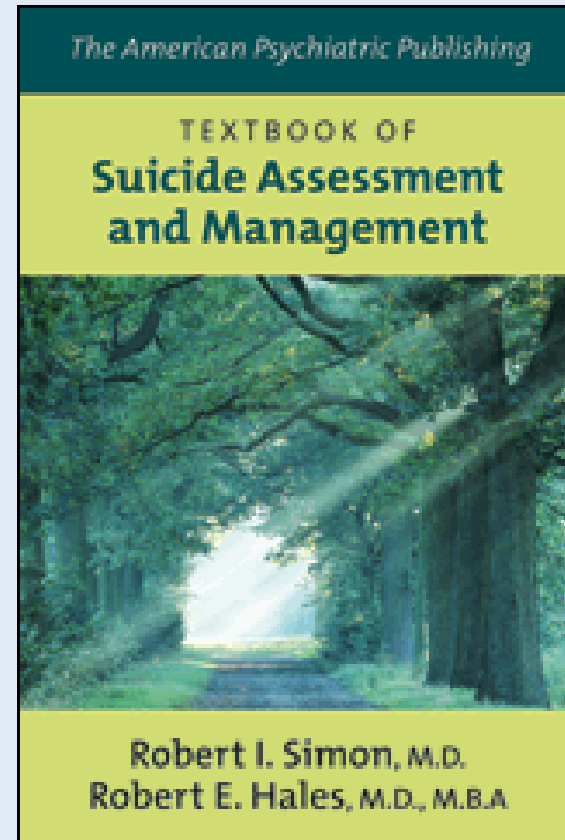
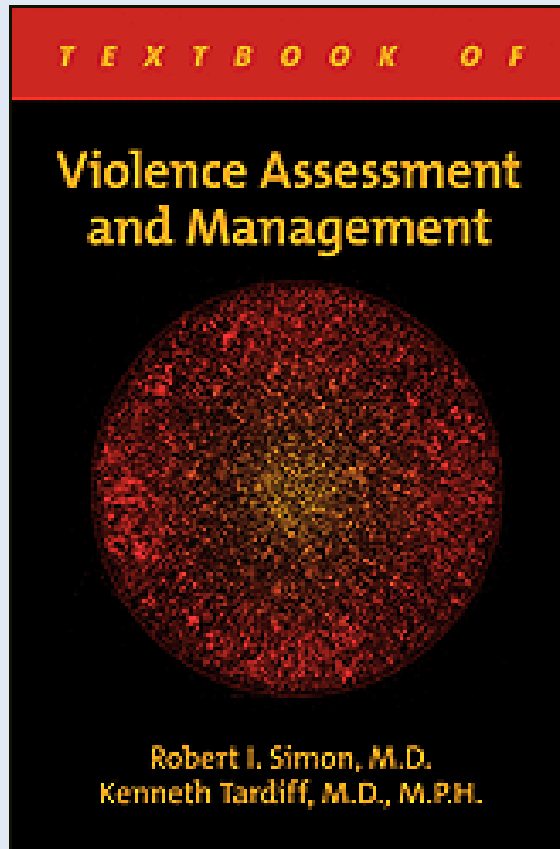
Organic Aggressive Syndrome

- **Reactive**
 - Triggered by modest or trivial stimuli
- **Nonreflective**
 - Usually no premeditation or planning
- **Nonpurposeful**
 - No obvious long-term goals or aims
- **Explosive**
 - Buildup is not gradual
- **Periodic**
 - Brief outbursts punctuated by long periods of relative calm
- **Ego-dystonic**
 - Patients upset, concerned, embarrassed by outburst as opposed to blaming or justifying behavior

Typologies of Violence

- In purposeful, instrumental violence aggressive behavior used as means to consciously achieve gainful ends, or to intimidate or manipulate another into some desired behavior
 - violence for revenge or violence for hire
- Somewhere on the middle of this proposed spectrum of aggressive behavior is targeted but impulsive violence, wherein unplanned aggressive behavior is directed at a specific person in response to a perceived threat
- The further we get from OAS, the more tenuous any causal relationship between TBI and a specific violent act
- Typologies of self-directed violence?

Need for Integrated Approaches...



In Summary...

- Accumulating evidence suggests that ventral frontal injury in TBI may impair the ability to inhibit aggressive behaviors and formulate prosocial responses
- All behavior, aggressive or not, is predicated upon a multitude of circumstances
- Neuroanatomical explanation for posttraumatic aggression, while compelling, is ultimately only a portion of the story that explains any given violent act committed by a person with TBI
- Optimal assessment and management will require conjoint attention to externally and self-directed violence, particularly among our patients with history of TBI

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All Done!