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Behavioral Dyscontrol After TBI

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Behavioral Dyscontrol

- Frequently complicates care and management of individuals with TBI, particularly moderate or severe TBI.
- Clinically challenging, often interfere with rehabilitation efforts, disrupt social support networks, and compromise optimal recovery

Behavioral Dyscontrol

- Aggressive behavior poses crucial safety issues, especially when it puts patients and providers in harm's way
- Aggression may be directed outwardly (toward persons or objects in the surrounding environment), or inwardly (self-directed violence)
- Violent acts carry negative social and legal consequences, further complicating recovery and access to care

Terms and Definitions

- Literature plagued with a challenging nosology, especially regarding posttraumatic aggression
- Various terms to denote behavioral dyscontrol after injury (e.g., agitation, restlessness, impulsivity, disinhibition, irritability, lability, explosive behavior)
- Lack a standardized or universally accepted definition for even posttraumatic aggression.
- Prudent to recognize limitations, and sometimes arbitrary delineations, when trying to label innumerable emotional and behavioral presentations that may follow TBI

Agitation

- A state of restlessness and increased psychomotor activity typically reflecting underlying dysphoric emotions (e.g., anxiety, fearfulness, anger, sadness)
- Although agitation may lead to aggression, it is not equivalent to aggression (aggression can occur absent any agitation)
- No single type of behavior defines agitation; it may involve a combination of emotional, cognitive, and behavioral features (aggression, akathisia, disinhibition, emotional lability, motor restlessness, impulsivity, disorganized thinking, perceptual disturbances, and impaired attention)

Disinhibition

- Socially or contextually inappropriate nonaggressive verbal, physical, or sexual responses that are indicative of a reduced or lost ability to appreciate behavioral norms and inhibit behaviors accordingly
- Though term impulsivity is often used synonymously, it is only one, and a highly variable, feature of disinhibition
- Disinhibition may also feature deficits in patience and frustration tolerance, social cognition, and comportsment
- Emotional dysregulation (e.g., affective lability, irritability, pathological laughing and crying) may co-occur, or even share phenomenological similarities and environmental antecedents with disinhibition or aggression

Aggression

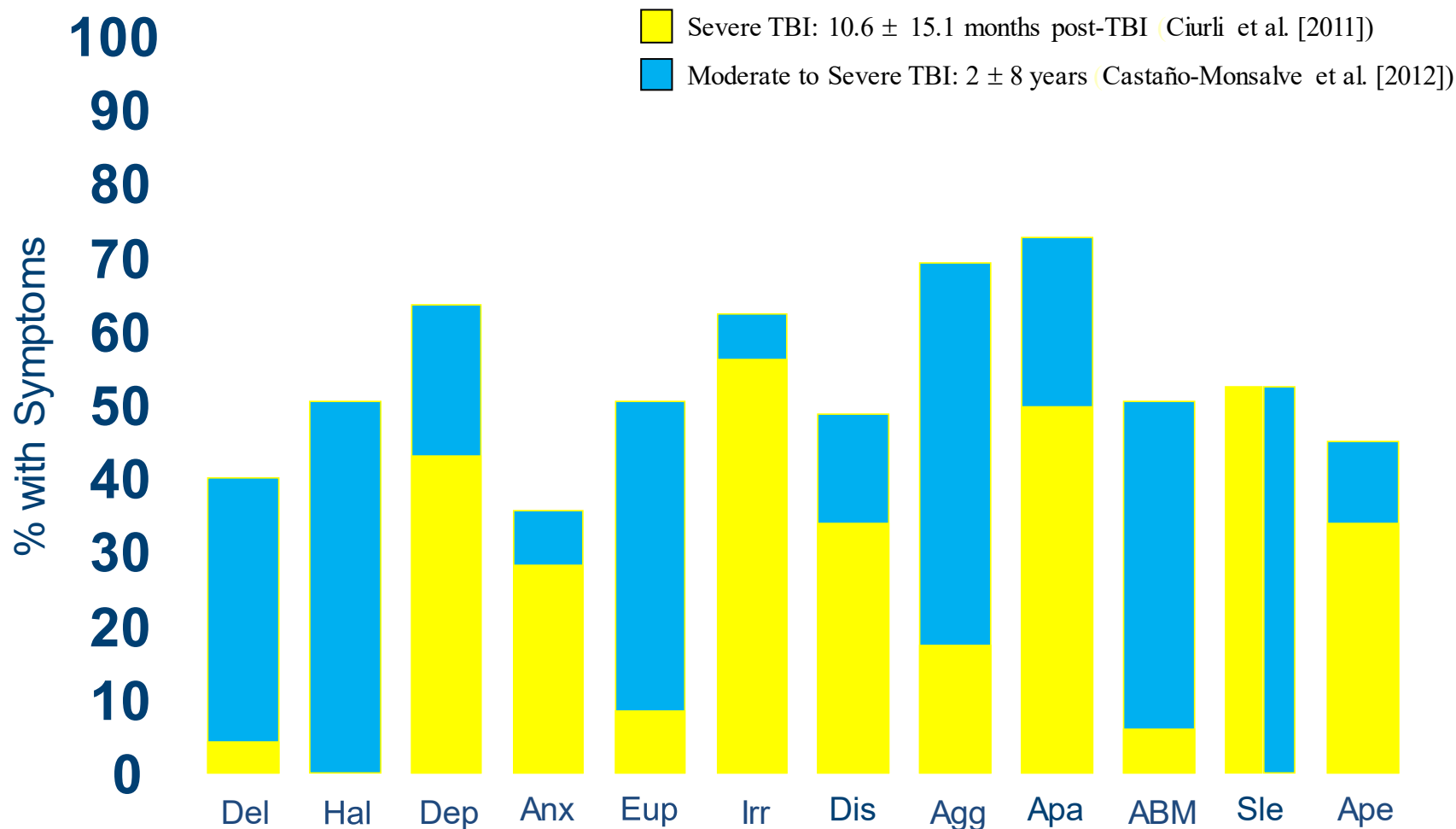
- Term has historically been applied to a broad range of problems involving emotional and behavioral dyscontrol
- However, aggression is limited to behaviors involving verbal outbursts or physical violence directed at objects or other people
- Even so defined, aggression encompasses a broad range of behaviors that vary in character, severity, and frequency

Disturbances of Emotion and Behavior

	Acute/Subacute	Chronic
Major depressive episode/disorder	6-50%	26-64%
Secondary mania (not bipolar disorder)	1-8%	<<1%
Pathological laughing and crying	5-11%	unknown
Affective lability	33-46%	14-62%
Irritability	35-71%	35-61%
Disinhibition	up to 48%	12-34%
Aggression	30-80%	15-51% (avg. 20%)

(Reviewed in Jorge RE, Arciniegas DB. Mood disorders after traumatic brain injury. *Psychiatric Clinics of North America* 37(1):13-29, 2014; Arciniegas DB, Wortzel HS. Emotional and behavioral dyscontrol after traumatic brain injury. *Psychiatric Clinics of North America* 37(1):31-53, 2014; Arciniegas DB, Wortzel HS. Emotional Dyscontrol. In Silver JM, McAllister TW, Arciniegas DB. Textbook of Traumatic Brain Injury, Third Edition. Washington DC, American Psychiatric Association Publishing, Inc., 2019, pp. 347-360; Wortzel HS, Silver JM. Behavioral Dyscontrol. In Silver JM, McAllister TW, Arciniegas DB. Textbook of Traumatic Brain Injury, Third Edition. Washington DC, American Psychiatric Association Publishing, Inc., 2019, pp. 395-411)

Neuropsychiatric Symptoms in Traumatic Brain Injury



(Castaño Monsalve B, Bernabeu Guitart M, Lopez R, Bulbena Vilassar A, Ignacio Quemada J. Psychopathological evaluation of traumatic brain injury patients with the Neuropsychiatric Inventory. Rev Psiquiatr Salud Ment. 2012;5(3):160-166; Ciurli P, Formisano R, Bivona U, Cantagallo A, Angelelli P. Neuropsychiatric disorders in persons with severe traumatic brain injury: prevalence, phenomenology, and relationship with demographic, clinical, and functional features. J Head Trauma Rehabil. 2011 Mar-Apr;26(2):116-26)

Emotion, Behavior, and TBI: Overlapping Neuroanatomies

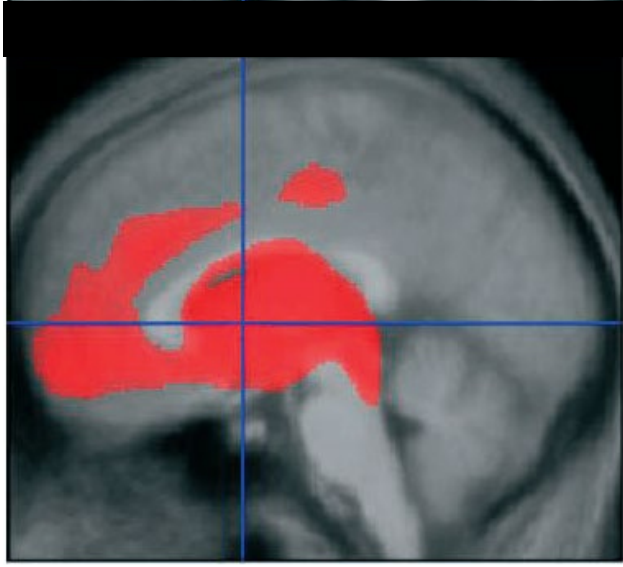
Limbic and paralimbic areas involved in the generation and expression of emotion and behavior

(Purves et al. 2001)



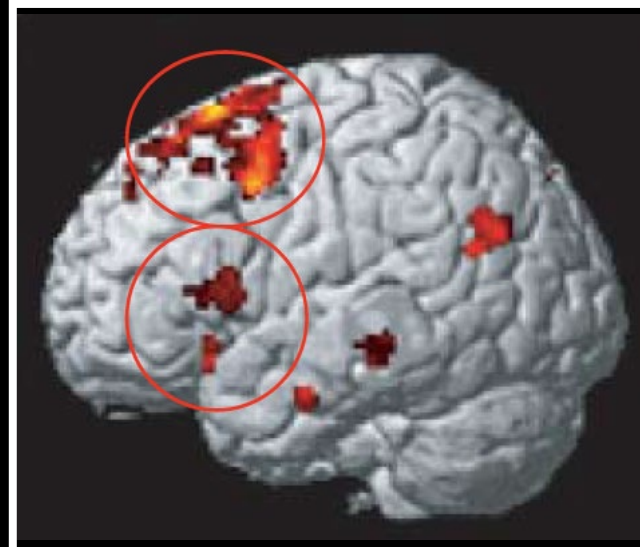
Limbic and paralimbic areas with gray matter volume reductions after moderate-to-severe TBI

(Salmond et al. 2005)



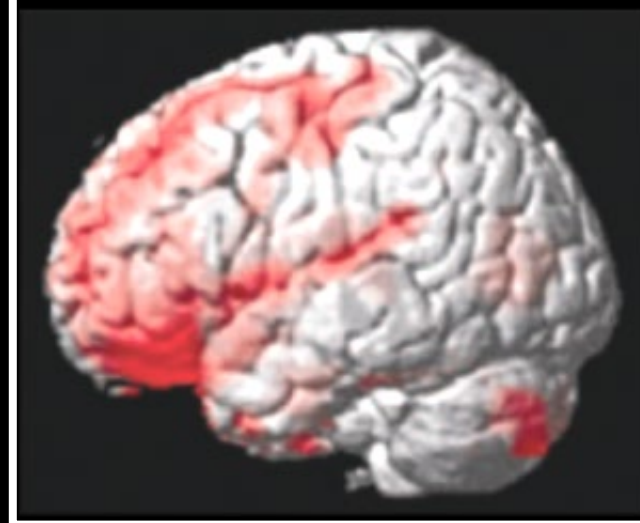
Dorsolateral and inferolateral prefrontal cortices involved in the regulation of emotion and behavior

(Ochsner and Gross 2005)



Dorsolateral, inferolateral, and anterior prefrontal cortices, anterior temporal, and cerebellar areas with gray matter volume reductions after TBI

(Yeates et al. 2007)



Neuropsychiatric Inventory: Agitation/Aggression Subscale

C. Agitation/Aggression

(NA)

Does the patient have periods when he/she refuses to cooperate or won't let people help him/her? Is he/she hard to handle?

NO (If no, proceed to next screening question). YES (If yes, proceed to subquestions).

1. Does the patient get upset with those trying to care for him/her or resist activities such as bathing or changing clothes? _____
2. Is the patient stubborn, having to have things his/her way? _____
3. Is the patient uncooperative, resistive to help from others? _____
4. Does the patient have any other behaviors that make him hard to handle? _____
5. Does the patient shout or curse angrily? _____
6. Does the patient slam doors, kick furniture, throw things? _____
7. Does the patient attempt to hurt or hit others? _____
8. Does the patient have any other aggressive or agitated behaviors? _____

If the screening question is confirmed, determine the frequency and severity of the agitation.

Neuropsychiatric Inventory - Clinician Version: Aggression Subscale

D. Aggression:

Does (S) shout angrily, slam doors, or attempt to hit or hurt others? Does (S) intentionally fall or try to harm him/herself?

(✓) Yes: No:

Responses should be based on the past 4 weeks. Description	Caregiver Interview*			Patient Interview	Clinical Impression*
	Frequency 0-4	Severity 0-3	Distress 0-5	Frequency 0-4	Severity 0-3
1. Does (S) shout or curse angrily?					
2. Does (S) slam doors, kick furniture, and throw things?					
3. Does (S) attempt to hurt or hit others?					
4. Does (S) grab, push or scratch others?					
5. Is (S) unreasonably or uncharacteristically argumentative?					
6. Is (S) intrusive, such as taking others' possessions or entering another's room inappropriately?					
7. Is (S) in covert or open conflict with staff or others?					
8. Does (S) try to do things that are dangerous, such as lighting a match or climbing out a window?					
*Do not leave blank. Enter "0" if it does not occur.				Column Total:	

Cummings et al. 1994; de Medeiros et al. 2010

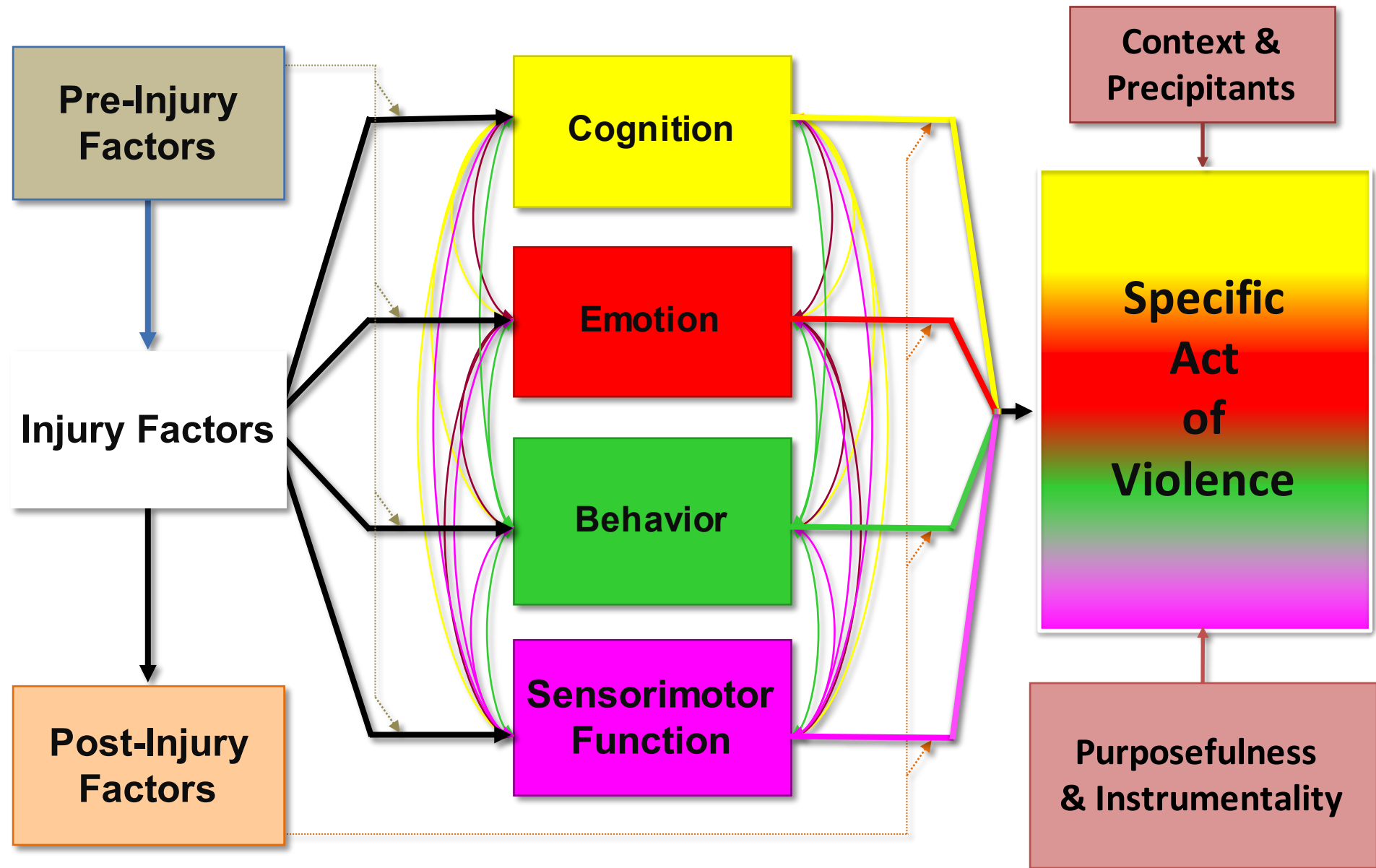
Differential Diagnosis

- There is a broad differential diagnosis for these symptoms (especially aggression) after TBI
- Tateno et al. (2003) reported aggression in 11% of individuals with no history of TBI in other-injury control group
- During acute recovery from more severe TBI, agitation and aggression features in 30%–80% of cases, with 20% involving violent behavior
- During later stages of recovery from severe TBI, rates range from 15% to 51% (Arciniegas and Wortzel 2014).
- Broad ranges bespeak methodological challenges in characterization of the problem and highly variable rates of behaviorally relevant (or explanatory) comorbid conditions

Aggression after TBI

- Neuropsychiatric approach to evaluation and management of aggression after TBI must be anchored to a conceptually and semantically clear definition of the problem
- Definition is applied to the characterization and contextualization of aggressive behaviors using standardized, valid, and reliable metrics
- Assessment of aggressive behaviors after TBI also requires consideration of the neuroanatomy of injury both in relation to the behavior itself as well as its implication on nonpharmacologic and pharmacologic interventions
- Management begins with treatment of identifiable causes and contributors

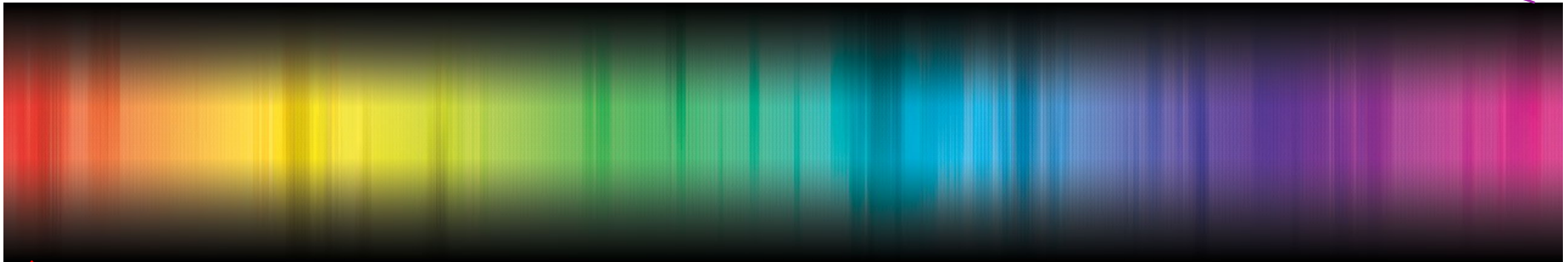
Forensic Neuropsychiatric Assessment





Not all violence is the same

Purposeful, Instrumental Violence:
Planned, deliberate act of aggression
to achieve desired end



Organic Aggressive Syndrome:
Highly impulsive and non-
instrumental violence



Psychosocial Context

- Violence can be adaptive and contextually appropriate
 - e.g., military service may warrant acts of violence that involve meticulous planning and for readily apparent objectives
- Psychosocial import of environmental precipitants will relate to some extent to prominence of pathological neuropsychiatric conditions in understanding the etiology of violence
 - Dire circumstances invoking extreme distress may precipitate aggressive behavior in individuals with otherwise modest neuropsychiatric burden
 - Relatively trivial occurrences might lead to aggressive acts among those persons suffering from substantial neuropsychiatric illness



Typologies of Violence

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
- Predatory/planned v. impulsive/reactive
- ***Typology of violence has implications in terms of both risk assessment and risk management***



Violence that is purposeful, and instrumental...

- This may even involve behaviors/statements for the purposes of disguising intent, such that it may be very difficult to detect acute risk
- Typically occurs in the setting of difficult-to-treat conditions (e.g., ASPD)
- There is very little evidence to suggest that we have good interventions to control violence of this sort
 - Seems unlikely that medication or safety planning would afford much benefit in this setting



Violence that is targeted but impulsive...

- **Impulsive acts of aggression, occurring in the setting of neuropsychiatric illness, and experienced as egodystonic, are often amenable to interventions**
 - Management of underlying conditions may mitigate risk (e.g., associated PTSD, depression, anxiety, pain, etc.)
 - Pharmacological interventions that more directly target impulsivity and aggression
 - Safety Planning, in the setting of a motivated patient, may engender increased ability to recognize an impending crisis and adjust behaviors accordingly

A Forensic Neuropsychiatric Approach to Traumatic Brain Injury, Aggression, and Suicide

Hal S. Wortzel, MD, and David B. Arciniegas, MD

Aggression is a common neuropsychiatric sequela of traumatic brain injury (TBI), one which interferes with rehabilitation efforts, disrupts social support networks, and compromises optimal recovery. Aggressive behavior raises critical safety concerns, potentially placing patients and care providers in harm's way. Such aggression can be directed outwardly, manifesting as assaultive behavior, or directed inwardly, resulting in suicidal behavior. The frequency of TBI and posttraumatic aggression and the potential medicolegal questions surround purported causal relationships between the two, forensic psychiatrists need to understand and recognize traumatic aggression. They also must be able to offer cogent formulations about the relative contribution of neurotrauma versus other relevant neuropsychiatric factors versus combinations of both to any specific violence. This article reviews the relationships between TBI and aggression and discusses neurobiological and cognitive factors that influence the occurrence and presentation of posttraumatic aggression. The heuristic is offered that may assist forensic psychiatrists attempting to characterize the relationships between and externally or internally directed violent acts.

J Am Acad Psychiatry Law 41:274–86, 2013

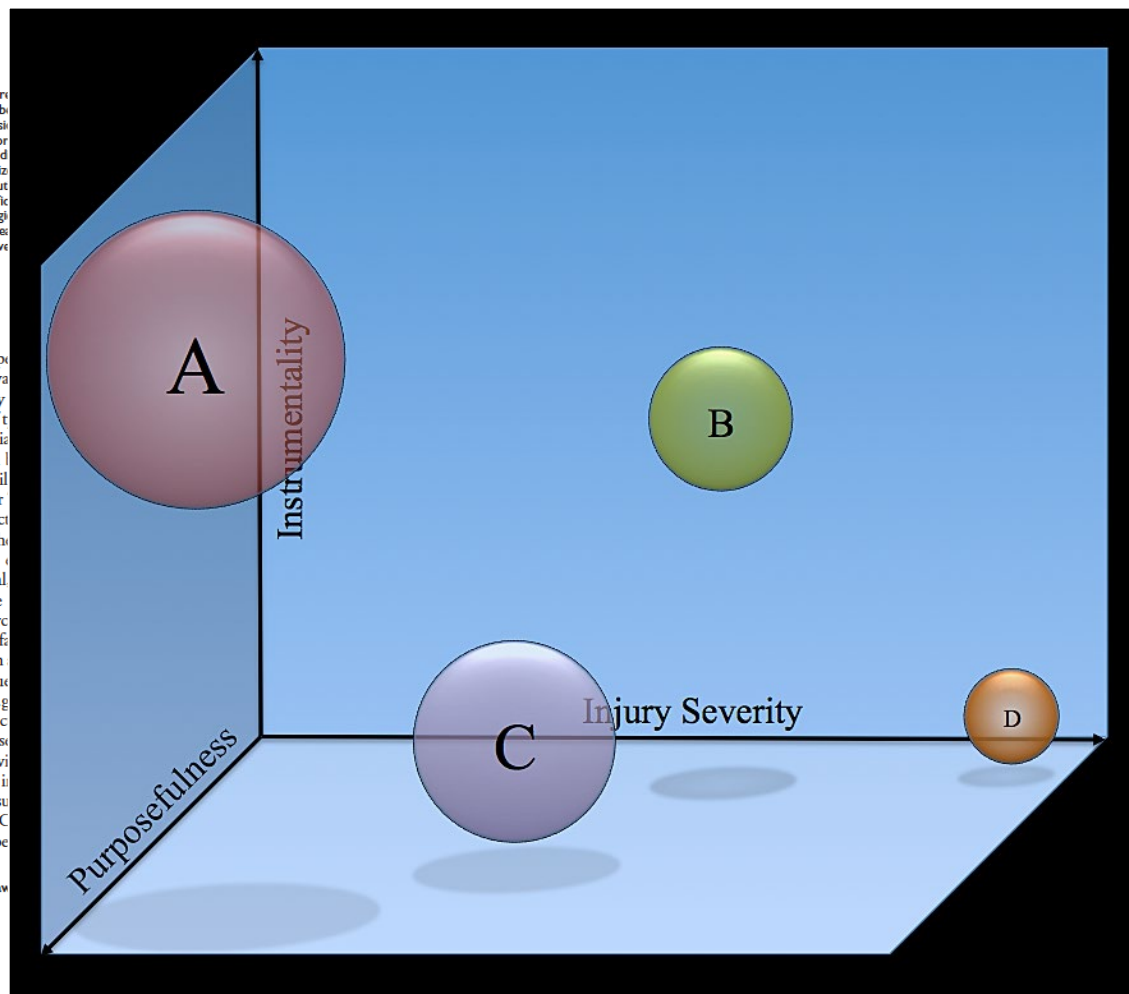
Traumatic brain injury (TBI) is a common problem in the United States. TBIs are sustained by approximately 1.5 million civilians each year,^{1,2} 124,000 of whom are expected to experience long-term disability.³ Current estimates suggest that 1.1 percent of the U.S. civilian population is living with long-term disability from TBI.⁴ TBI is also common in soldiers returning from the wars in Iraq and Afghanistan, with an estimated 15 to 20 percent of nearly 2 million deployed U.S. troops having experienced a pos-

sible mild TBI.^{5,6} The symptoms that follow TBI vary within individuals as they reflect the broad range of clinical diagnoses in this category of clinical diagnosis, the influence of and interaction between neurotrauma and neurotrauma. Variability in symptom presentation and persistence after postinjury psychosocial factors and social supports (or the lack thereof) and litigation and other legal factors can influence the outcome of traumatic cognitive, emotional, and behavioral impairments, irrespective of the frequency and substantial source of trauma for both patients and families.

Aggression is a common neuropsychiatric sequela of TBI, which can manifest as externally directed acts (e.g., physical violence toward objects or toward persons) as well as self-directed violence (e.g., nonsuicidal self-directed violence and suicide). Aggression interferes with rehabilitation efforts, disrupts social support networks, and compromises optimal recovery. As described posttraumatic be-

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ARTICLES

Mild Traumatic Brain Injury and Aggression, Impulsivity, and History of Other- and Self-Directed Aggression

Caterina Mosti, Ph.D., Emil F. Coccaro, M.D.

Mild traumatic brain injury (mTBI) is highly prevalent, with an estimated occurrence in the United States of more than 1.3 million per year. While one consequence of mTBI is impulsive aggressive behavior, very few studies have examined the relationship between history of mTBI and aggressive behavior in impulsively aggressive individuals. The authors examined the relationship between history of mTBI in a healthy control group (HC; N=453), a control group with psychiatric disorders (PC; N=486), and individuals with intermittent explosive disorder (IED; N=695), a disorder of primary impulsive aggression. Results demonstrated that IED study participants were significantly more likely to have a history of mTBI (with or without history of a brief loss of consciousness [LOC]) compared with both HC and PC participants. A similar observation was made with regard to self-directed aggression

(i.e., suicidal or self-injurious behavior), although group differences were only among those with mTBI with LOC. For both other- and self-directed aggression variables, the authors observed a stepwise increase in dimensional aggression and impulsivity scores across participants as a function of mTBI history. Given that impulsive aggressive behavior begins very early in life, these data are consistent with the hypothesis that lifelong presence of an impulsive aggressive temperament places impulsive aggressive individuals in circumstances that put them at greater risk for mTBI compared with other individuals with and without nonimpulsive aggressive psychopathology.

J Neuropsychiatry Clin Neurosci 2018; 30:220–227;
doi: 10.1176/appi.neuropsych.17070141

with a number of cognitive, physical, and emotional sequelae that typically resolve within 3 months of injury.¹ However, a growing body of research indicates that anywhere from 10% to 31% of post-mTBI patients experience symptoms, including lingering physical symptoms and mood disturbances, beyond the three-month period.^{5,6} Factors associated with more persistent post-mTBI symptoms include female gender, older age, pre-existing psychiatric issues, and medical complications.^{7,8} However, it should be noted that mTBI is a diagnostically heterogeneous condition, due to both the variability in

previous year. In comparison with those with remote or no history of TBI, those who reported a TBI within the past year exhibited greater neuropsychological deficits related to phonemic verbal fluency and mental flexibility, both of which are associated with frontal network dysfunction. Moreover, those who endorsed a recent history of TBI reported significantly higher levels of anger and aggression on the Brief Anger-Aggression Questionnaire than did control subjects. Importantly, the two groups did not differ in psychiatric disorder prevalence. Similarly, increased TBI is also



Aggression after TBI

- Although aggression can be a direct neuropsychiatric consequence of TBI, its development is influenced by pre-injury and post-injury comorbidities; mood disorders, trauma-spectrum disorders, psychotic disorders, personality disorders, substance use disorders, pain, and medications with adverse behavioral effects
- Depression and anxiety, in particular, are strongly associated with the development of aggression in the late period following TBI
- When any of these conditions are present in a person with posttraumatic aggression, their treatment may reduce behavioral dyscontrol and obviate treatment targeting posttraumatic aggression specifically

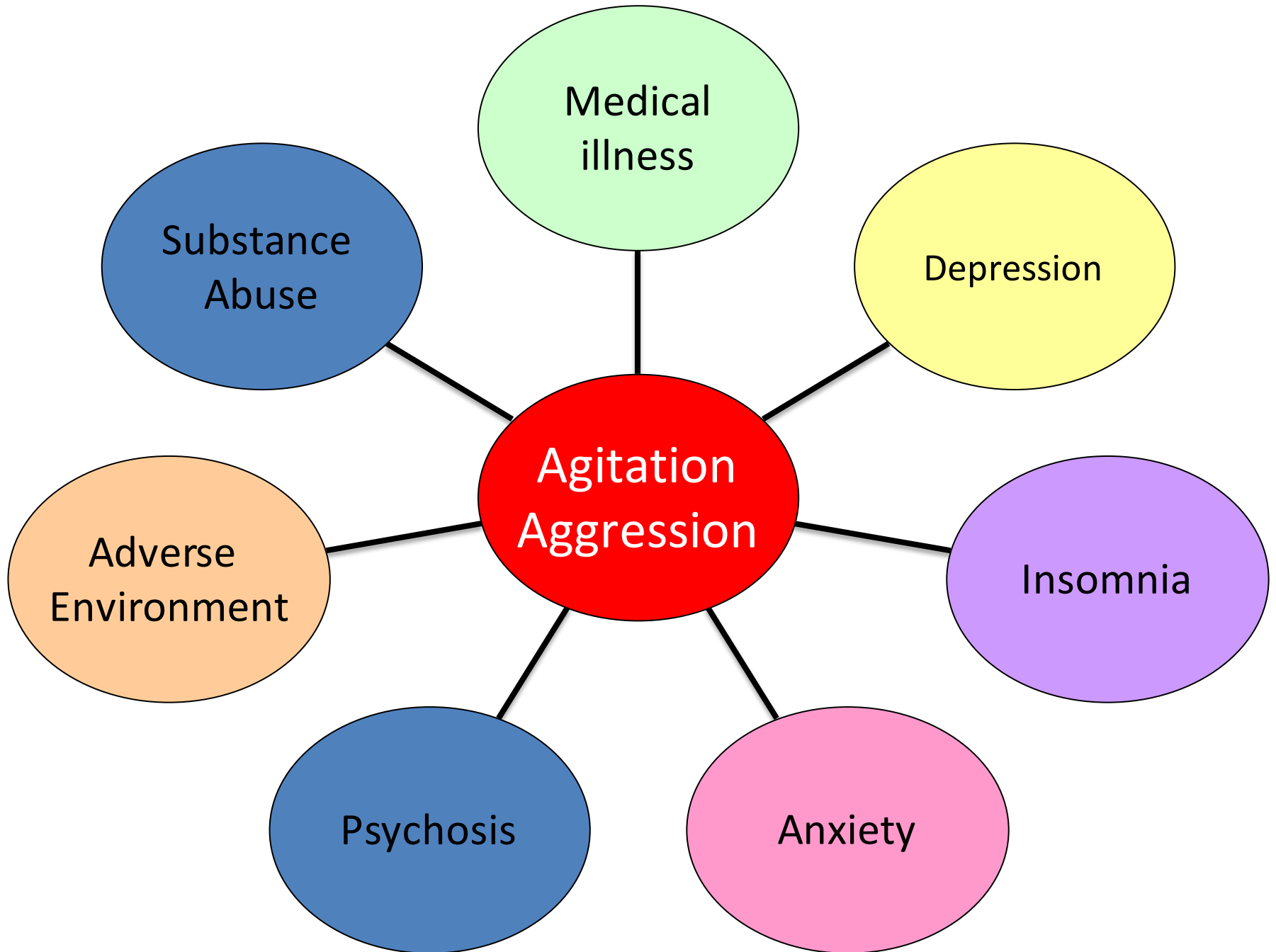


Figure adapted from Silver 2005

Adjunctive Pharmacotherapy

- **All pharmacotherapies of post-TBI neuropsychiatric disturbances – including cognitive impairments – are “off-label” and require consent as such**
- **Every intervention is an “n of 1” empiric trial**
 - apply an evidence-informed approach to treatment selection
 - emphasize use of medications with less complex dosing requirements, titration schedules, and adverse effect profiles
 - “start low, go slow, but go”
 - remain vigilant for side effects and drug-drug interactions
 - augment partial treatment responses using agents with complementary (rather than directly or indirectly identical) pharmacologic properties

R_x of Aggression after TBI

Medication	Fleminger 2003 ABI	Warden 2006 TBI	ABIKUS 2007 ABI	ERABI 2012 ABI
Beta-Adrenergic Antagonists	4 RCT	Guideline	Recommended A	Level 1
Methylphenidate	1 RCT	Option	Recommended B	Level 2
SSRIs		Option	Recommended B	No evidence
Tricyclic Antidepressants		Option (amitriptyline & desipramine)	Recommended B	Level 4 (Trazadone)
Valproate		Option	Recommended B	Level 4 (Divalproex)
Carbamazepine		Option		Level 4 evidence
Amantadine	1 RCT	Option		May not help (level 2)?
Buspirone		Option		Level 5
Typical Antipsychotics			Avoid (C)	Haldol not negative (LOE 4); Methotrimeprazine safe & effective (4)???
Lithium carbonate		Option		Level 4 evidence












Posttraumatic Agitation/Aggression

- Acute episode of aggression: abortive agents for acute treatment of a specific episode of severe posttraumatic agitation/aggression include anticonvulsants and/or atypical antipsychotics
 - only if these fail and aggression presents imminent danger to self or others are haloperidol \pm lorazepam appropriate
- Chronic/recurrent aggression: recurrence risk reduction pharmacotherapy begins with:
 - understanding of the anatomy of injury (particularly the integrity of lateral orbitofrontal cortex) and
 - consideration of co-occurring problems that may be parsimoniously treated with the minimum number of agents



Neurochemical Modulation of Aggression

Pharmacologic Class	Limbic/Paralimbic Activation	Lateral Orbitofrontal Modulation
SSRIs		
Dopamine and Norepinephrine Reuptake Inhibitors		
Uncompetitive NMDA Receptor Antagonists		
Atypical Antipsychotics		
Anticonvulsants		
Beta Adrenergic Antagonists		



Rx of Aggression after TBI

- **If the lateral orbitofrontal cortex and the subcortical elements of the circuit of which it is a part are largely intact anatomically, then catecholaminergic or cholinergic augmentation strategies may be useful for impulsivity and disinhibition**
 - methylphenidate
 - cholinesterase inhibitors
 - e.g., donepezil, rivastigmine, galantamine
 - uncompetitive NMDA receptor antagonists
 - amantadine, memantine

Effectiveness of Amantadine Hydrochloride in the Reduction of Chronic Traumatic Brain Injury Irritability and Aggression

Background: Following traumatic brain injury (TBI), individuals may experience chronic problems with irritability or aggression, which may need treatment to minimize the negative impact on their relationships, home life, social interactions, community participation, and employment. **Objective:** To test the a priori hypothesis that amantadine reduces irritability (primary hypothesis) and aggression (secondary hypothesis) among individuals greater than 6 months post-TBI. **Methods:** A total of 76 individuals greater than 6 months post-TBI referred for irritability management were enrolled in a parallel-group, randomized, double-blind, placebo-controlled trial of amantadine ($n = 38$) versus placebo ($n = 38$). Study participants were randomly assigned to receive amantadine hydrochloride 100 mg twice daily versus equivalent placebo for 28 days. Symptoms of irritability and aggression were measured before and after treatment using the Neuropsychiatric Inventory Irritability (NPI-I) and Aggression (NPI-A) domains, as well as the NPI-Distress for these domains. **Results:** In the amantadine group, 80.56% improved at least 3 points on the NPI-I, compared with 44.44% in the group that received placebo ($P = .0016$). Mean change in NPI-I was -4.3 in the amantadine group and -2.6 in the placebo group ($P = .0085$). When excluding individuals with minimal to no baseline aggression, mean change in NPI-A was -4.56 in the amantadine group and -2.46 in the placebo group ($P = .046$). Mean changes in NPI-I and NPI-A Distress were not statistically significant between the amantadine and placebo groups. Adverse event occurrence did not differ between the 2 groups. **Conclusions:** Amantadine 100 mg every morning and at noon appears an effective and safe means of reducing frequency and severity of irritability and aggression among individuals with TBI and sufficient creatinine clearance. **Key words:** aggression, agitation, amantadine, brain injuries, dopamine, irritability



R_x of Aggression after TBI

- **If the lateral orbitofrontal-subcortical circuit is not intact anatomically (i.e., posttraumatic orbitofrontal encephalomalacia, severe atrophy, etc.)**
 - serotonergic augmentation (SSRIs) is first-line
 - if SSRIs are ineffective, then anticonvulsants (especially valproate, carbamazepine)
 - if anticonvulsants are ineffective, then atypical antipsychotics
 - if atypical antipsychotics are ineffective, then consider:
 - buspirone (5HT-1a agonist), clonidine (α -2 agonist), propranolol (β antagonist), and (last-line) benzodiazepines



Law and Psychiatry

Therapeutic Risk Management for Violence: Clinical Risk Assessment

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Violence risk assessment is a requisite component of mental health treatment. Adhering to standards of care and ethical and legal requirements necessitates a cogent process for conducting (and documenting) screening, assessment, and management of other-directed violence risk. In this 5-part series, we describe a model for achieving therapeutic risk management of the potentially violent patient, with essential elements involving a clinical interview augmented by structured screening or assessment tools; risk stratification in terms of temporality and severity; chain analysis to intervene on the functions of violent ideation and behavior; and development of a personalized safety plan. This first column of the series focuses on essential aspects of the clinical interview.

(Journal of Psychiatric Practice 2020;26;313–319)





Therapeutic Risk Management (TRM) with the Potentially Violent Patient

1. Conduct and document clinical risk assessment
2. Augment clinical risk assessment with structured instruments
3. Qualitative assessment of violence; stratify risk in terms of both severity and temporality
4. Perform Chain Analysis and Develop and document a Safety Plan



Clinical Risk Assessment

Ideation → Intent → Plan → Access to Means



The addition of structured instruments can...

- Augment clinical care
- Serve an important medicolegal function
- Help to realize therapeutic risk management of the suicidal patient

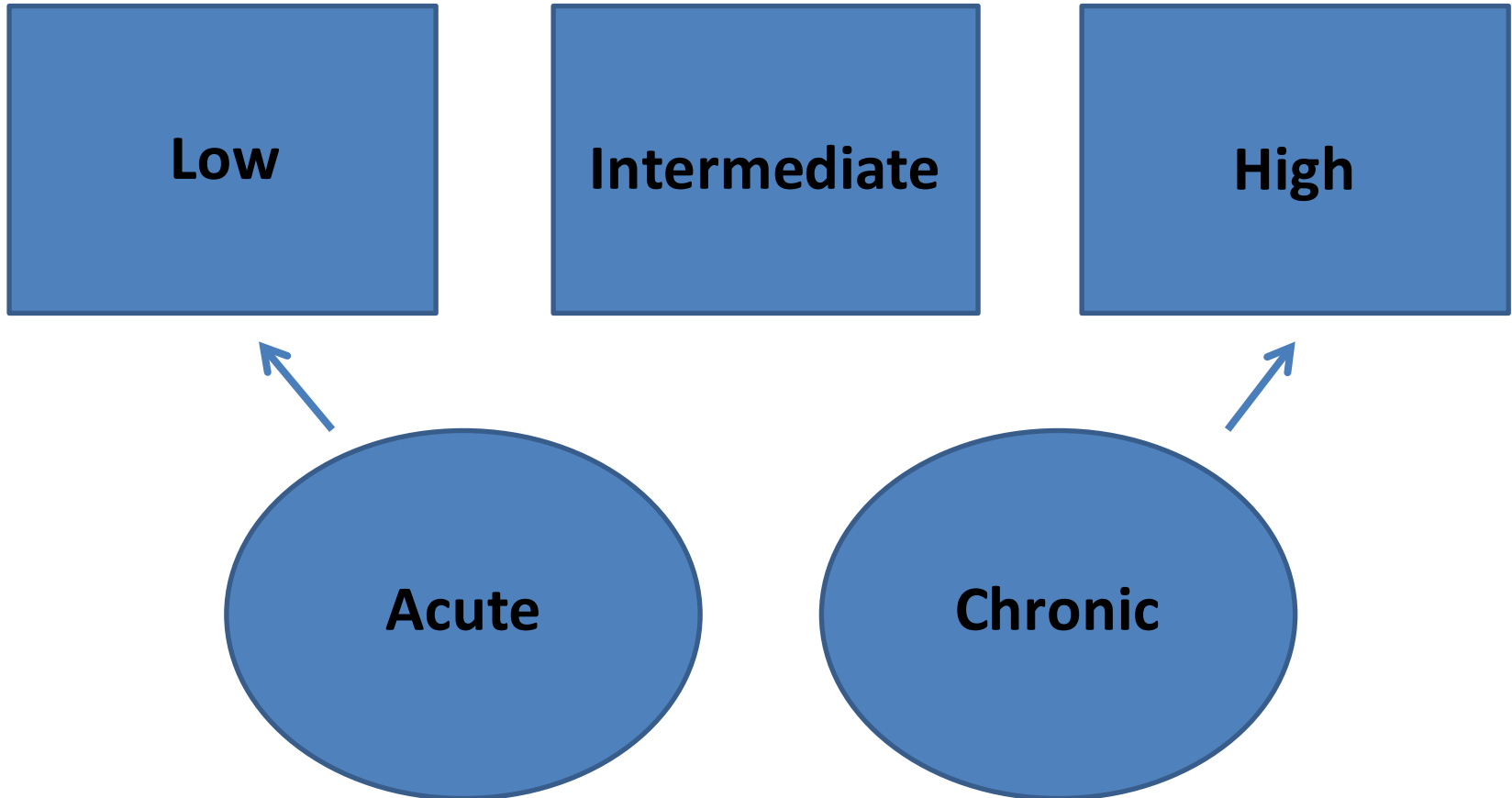
Singh JP, Grann M, Fazel S: Clin Psychol Rev. 2011 Apr;31(3):499-513.

A comparative study of violence risk assessment tools: a systematic review and metaregression analysis of 68 studies involving 25,980 participants.

<https://www.ncbi.nlm.nih.gov/pubmed/21255891>



Stratify Risk – Severity & Temporality



***Risk stratification informs risk-benefit analysis
pertaining to various interventions***



Risk Assessment and Formulation: Documentation

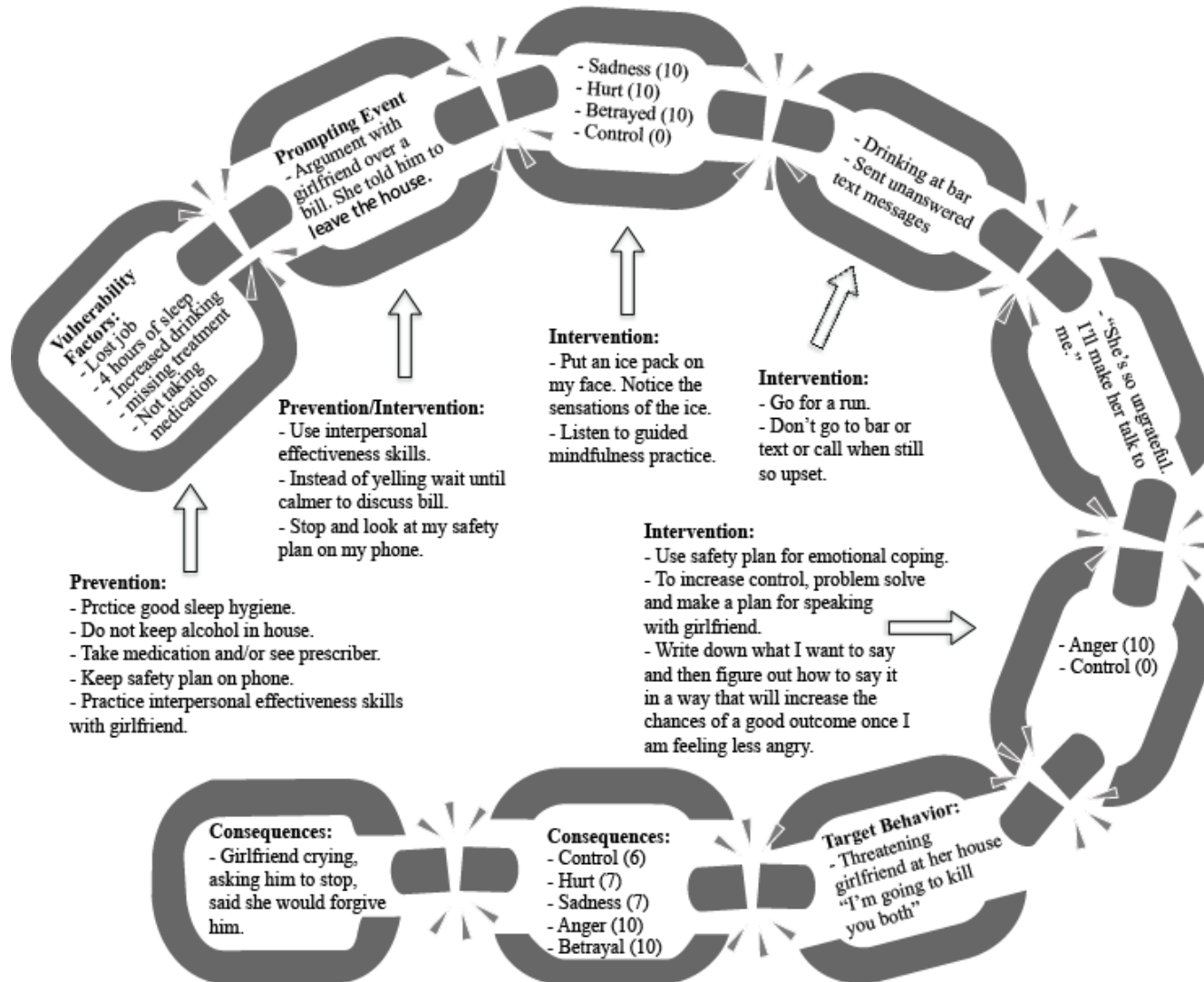
Ideation → Intent → Plan → Access to Means

X is presently considered to be at **LOW ACUTE RISK** for violence given that he is currently maintaining sobriety and enjoying fairly good control of PTSD symptoms. He is motivated to avoid future acts of violence to sustain his relationship and avoid legal consequences. Psychosocial status is presently relatively stable (e.g., stable housing, sustained sobriety). He is willing and able to use a safety plan and is actively engaged in outpatient therapy.

X is presently considered to be at **HIGH CHRONIC RISK** for violent behavior given his multiple prior instances, history of severe TBI and associated mental health diagnoses (depression, history of substance dependence), and somewhat limited coping skills.



Components of Chain Analysis: Intervention





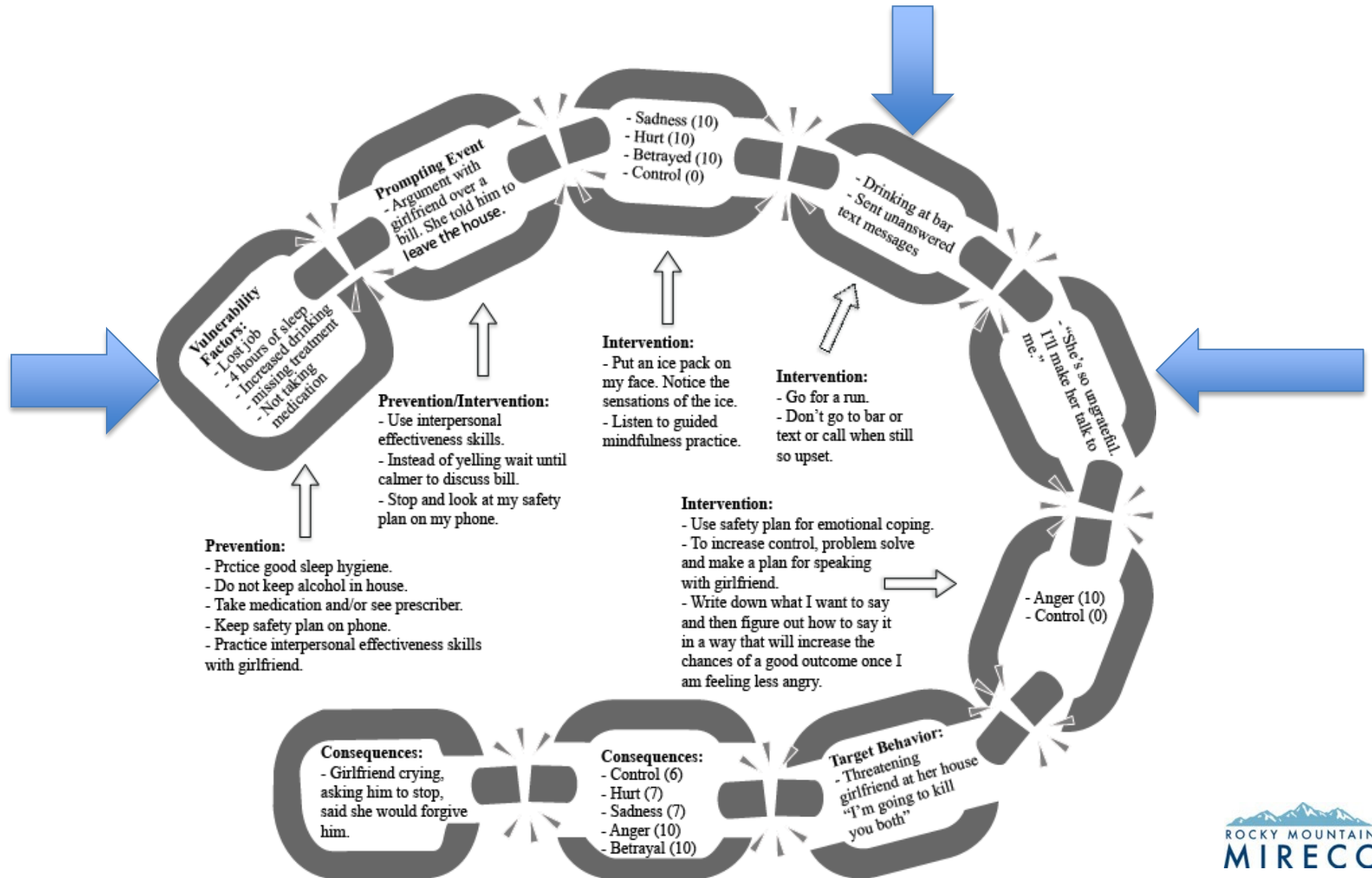
Safety Plan Steps

1. Warning Signs
2. Internal Coping Strategies
3. Social Contacts and Settings for Distraction
4. People Who I Can Ask for Help
5. Professionals and Agencies to Contact for Help
6. Making the Environment Safe

All of these may serve similar functions in relation to aggression directed towards others, especially in the context of a therapeutic relationship.



Mapping the Chain onto the Safety Plan





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