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Traumatic Brain Injury – Behavioral Health ECHO

UW Medicine | Psychiatry and Behavioral Sciences

Assessment and Management of Agitation after TBI

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UW SCHOOL OF MEDICINE

Project ECHO

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Speaker disclosures

No conflict of interest

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Objectives

1. Understand definition of agitation after TBI
   - Recognize subtypes of agitation
2. Identify evaluation methods:
   - Agitated Behavior Scale
3. Identify treatment tools/plans for managing agitation following TBI

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Cases

Case 1

- 20 year-old who fell
- CT head demonstrated bilateral frontal lobe contusions
- Admitted to the hospital

Case 2

- 20 year-old who was in a motor vehicle collision
- CT head with left frontal and temporal lobe contusions and SAH
- Admitted to the hospital

- What additional information would you like to know about them?

Reminder: TBI Severity Determination

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0-30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/mental state	Up to 24 hours	>24 hours; severity based on other criteria	
Post-traumatic amnesia duration	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	<9

TBI Severity Classification Update

- Goal to move away from the mild, moderate, and severe by using CBI-M pillars:
  - Clinical
  - Biomarker
  - Imaging
  - Modifiers

A new characterisation of acute traumatic brain injury: the NIH-NINDS TBI Classification and Nomenclature Initiative

Prof Geoffrey T Manley, MD [a,*] · Prof Kristen Dams-O'Connor, PhD [b,*] · Michael L Alosco, PhD [c] · Hibah O Awwad, PhD [d] Prof Jeffery J Bazarian, MD [e] · Prof Peter Bragge, BPhysio [f] · et al. Show more

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New TBI Classification System Aims to Improve Diagnoses and Treatment

MAY 20, 2025

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Agitation

- Subtype of delirium occurring during the state of **posttraumatic amnesia**

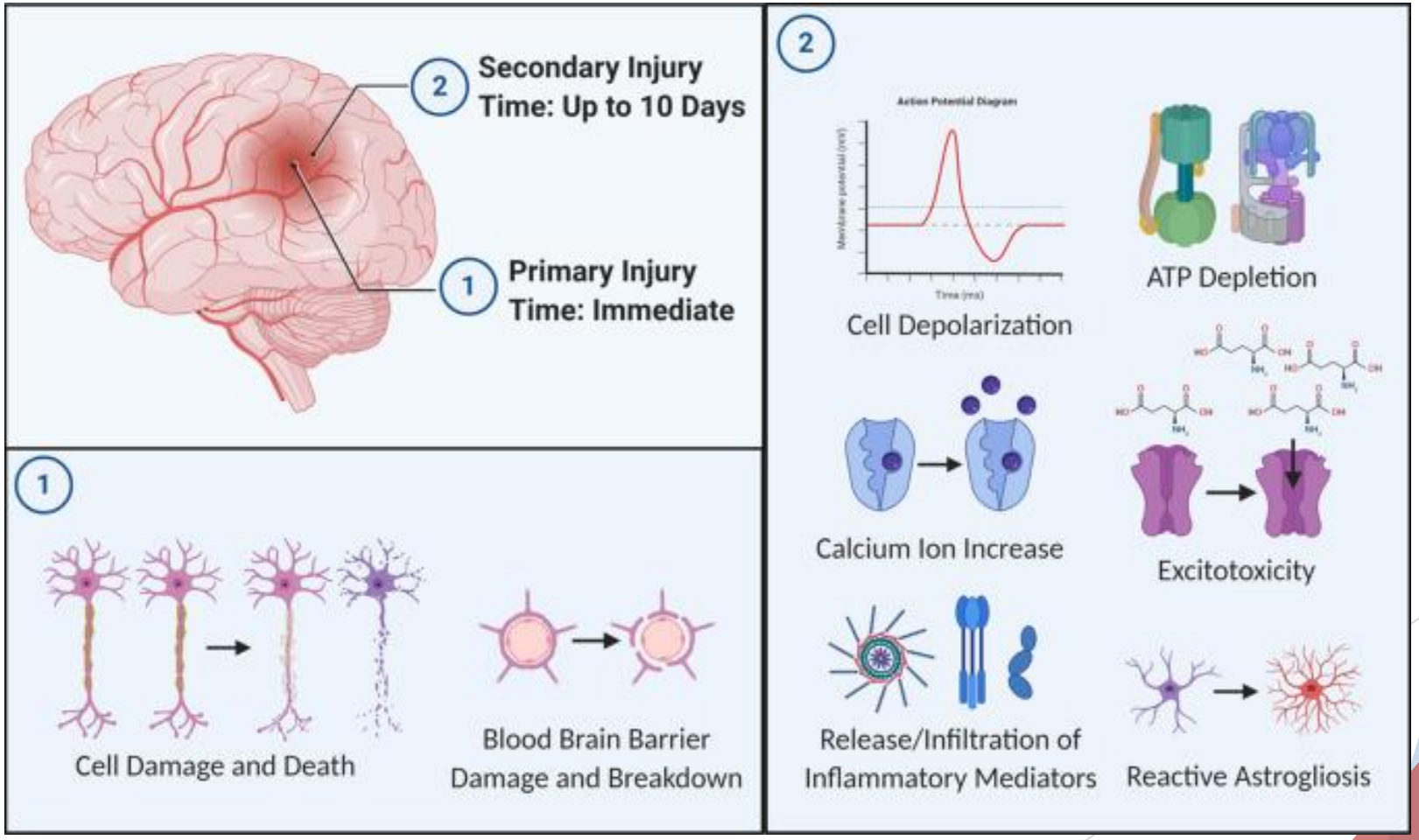
- Characterized by **excesses** of behavior:
  - Aggression
  - Akathisia
  - Disinhibition and/or
  - Emotional lability

- 35-96 % exhibit during acute recovery phase

Rosenthal and Mortimer, 2013

TBI Pathophysiology – what's leading to agitation?

- Primary and Secondary Injury



Finkel, 2022

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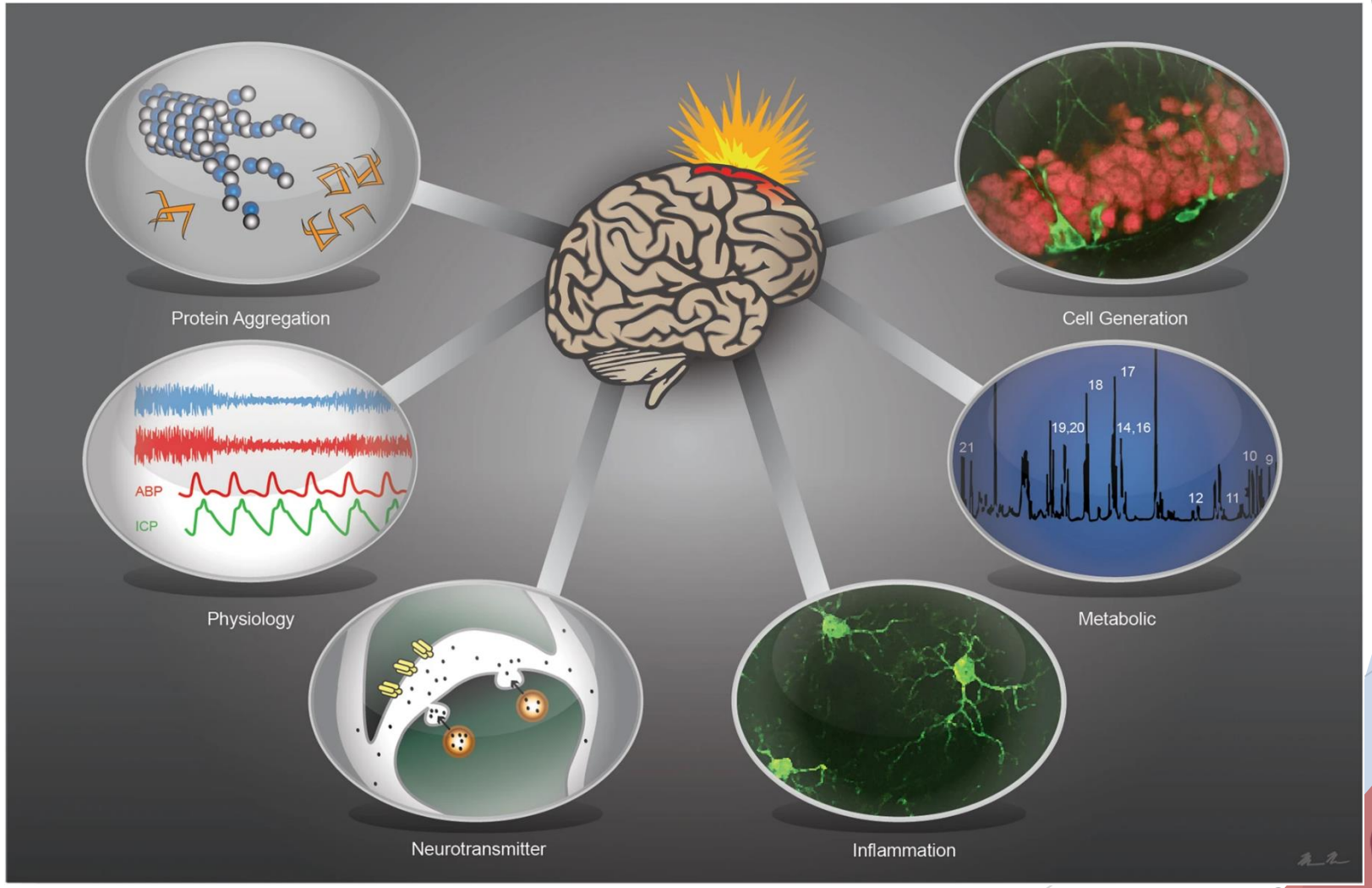
TBI Pathophysiology – what's leading to agitation?



McGuire, 2019

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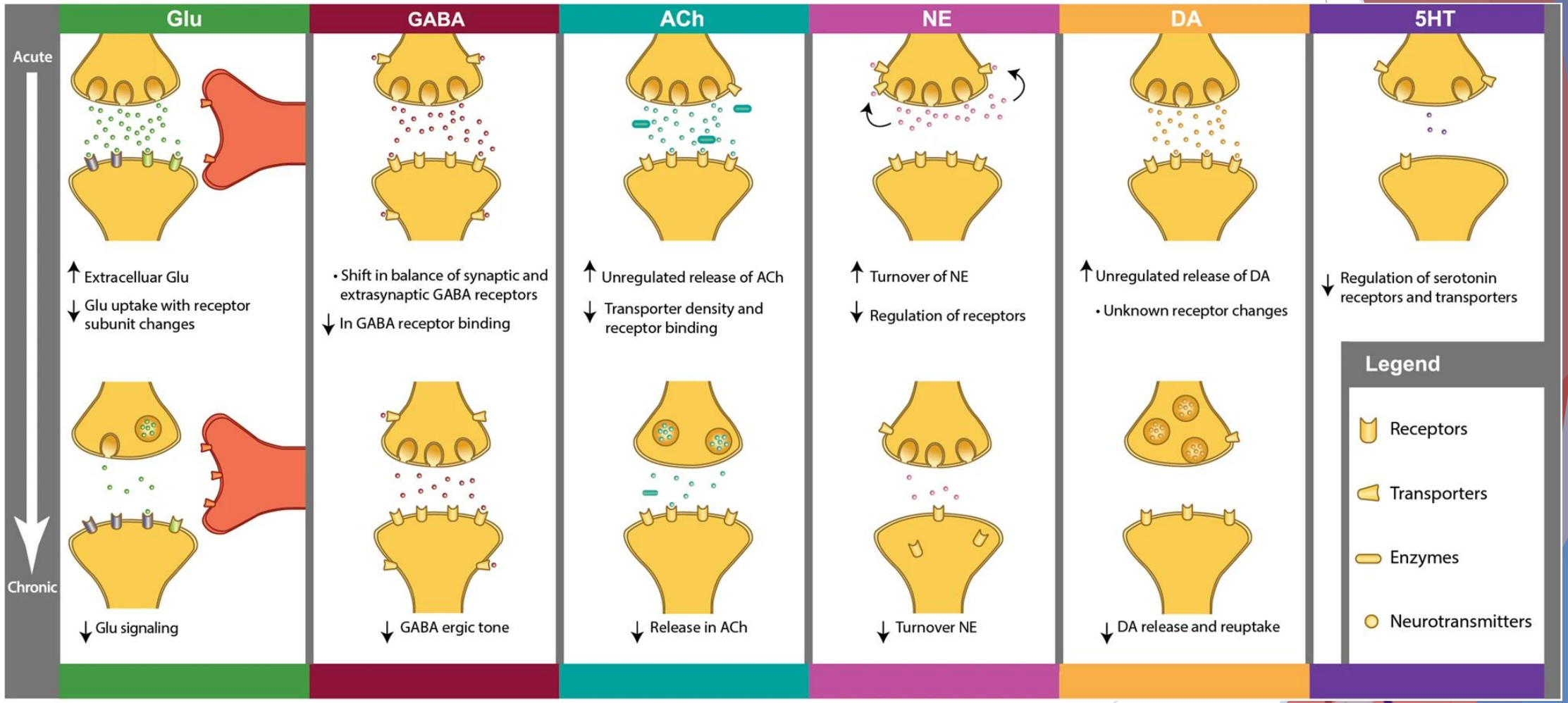
TBI Pathophysiology – Neurotransmitter changes



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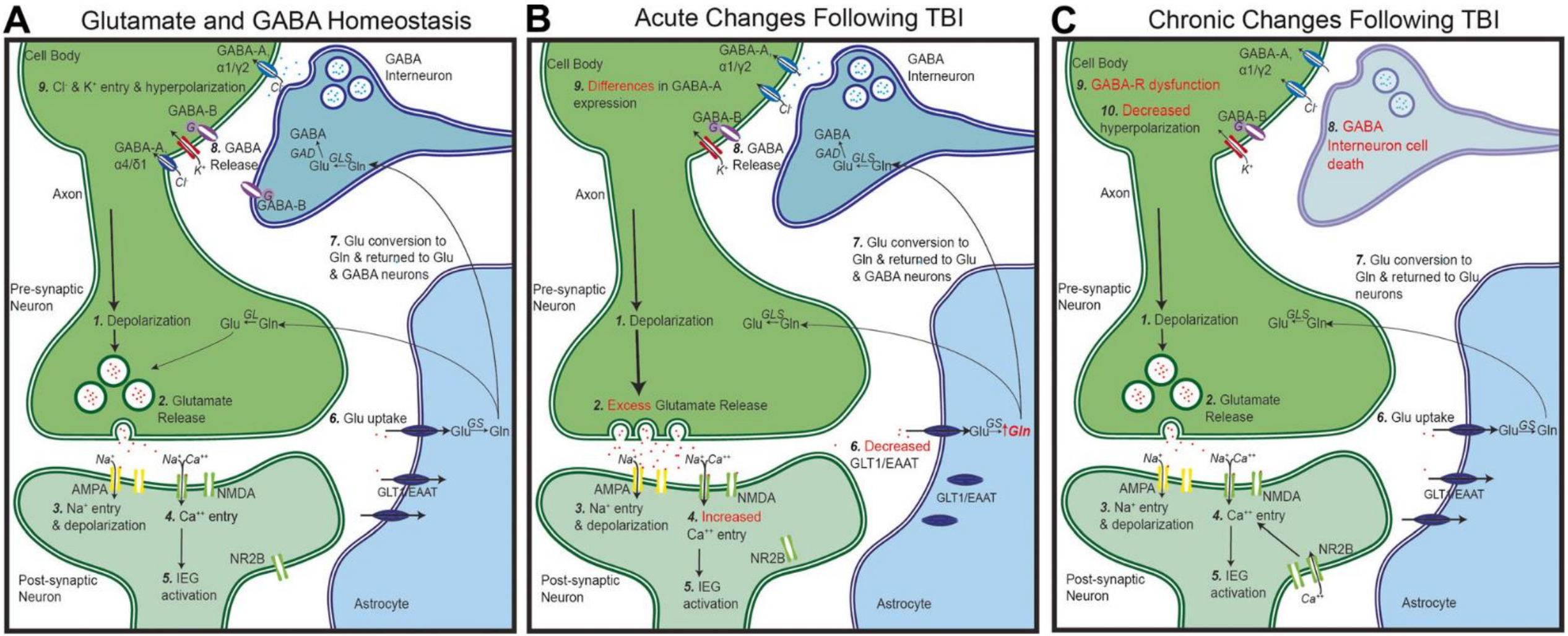
McGuire, 2019

TBI Pathophysiology – Neurotransmitter



Guerriero, Giza, and Rotenberg, 2015

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Neuropathology

Locus	Activity
Hypothalamus	Orchestrates neuroendocrine response via sympathetic arousal, monitors internal status
Limbic system	Mediates impulses from prefrontal cortex, adds emotional content to cognition
Amygdala	Activates and/or suppresses hypothalamus, input from neocortex
Temporal cortex	Associated with aggression (also in both ictal and interictal status)
Frontal neocortex	Modulates limbic and hypothalamic activity, associated with social judgement aspect of aggression

Reminder: Post-traumatic Amnesia (PTA)

- A loss of memory for events surrounding the injury, disorientation, confusion and significant cognitive impairment
- Resolution: working memory returns
- Multiple assessment tools:
  - Galveston Orientation and Amnesia Test (GOAT)
  - Orientation-log (O-log)
  - Abbreviated Westmead Post Traumatic Amnesia Scale (A-WPTAS)

Reminder: Irritability and Aggression

- Long-term sequelae of TBI
- Non-specific term

- Irritability: Tendency to be easily upset[1] and poorly controlled brief, external displays of temper
  - Third most commonly reported symptoms
  - 30-35% after mild TBI reported it one year after the injury[2]

- Aggression:
  - Reflection of irritability
  - Physical and verbal
  - 12-41% after severe TBI reports 1-15 years after the injury[3]

1. Prigatano, 1992
2. Alderman, 2003
3. Malec, 2018

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Risk or Associated Factors

- **Major depression**: can present with irritability in TBI
- **Frontal lobe lesions**: can result in impulsivity, disinhibition
- **Poor premorbid social functioning**: people with impulse control issues may be more likely to sustain TBI
- **Alcohol or substance use disorder**: people undergoing withdrawal, craving by be irritable or agitated
- **PTSD**: exposure to triggers may cause agitation, irritability

Evaluation

- Differential diagnosis:
  - Pain
  - Sleep disorder
  - Medication side effects
  - Delirium
  - Infection
  - Epilepsy
  - Metabolic disorders
  - Drug withdrawal
  - Hypoxia
  - Depression
  - PTSD

Agitated Behavior Scale (ABS)

- 14 behaviors

- Each behavior is scored 1 – 4:
  - 1: absent
  - 2: present to slight degree
  - 3: present to moderate degree
  - 4: present to extreme degree

- Excellent test-retest (same day) reliability, interrater reliability, internal consistency, and face validity

ABS – 14 behaviors

1. Short attention span, easy distractibility, inability to concentrate
2. Impulsive, impatient, low tolerance for pain or frustration
3. Uncooperative, resistant to care, demanding
4. Violent and or threatening violence toward people or property
5. Explosive and/or unpredictable anger
6. Rocking, rubbing, moaning or other self-stimulating behavior
7. Pulling at tubes, restraints, etc.
8. Wandering from treatment areas
9. Restlessness, pacing, excessive movement
10. Repetitive behaviors, motor and/or verbal
11. Rapid, loud or excessive talking
12. Sudden changes of mood
13. Easily initiated or excessive crying and/or laughter
14. Self-abusiveness, physical and/or verbal

ABS – Subscale

1. Short attention span, easy distractibility, inability to concentrate
2. Impulsive, impatient, low tolerance for pain or frustration
3. Uncooperative, resistant to care, demanding
4. Violent and or threatening violence toward people or property
5. Explosive and/or unpredictable anger
6. Rocking, rubbing, moaning or other self-stimulating behavior
7. Pulling at tubes, restraints, etc.
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Disinhibition: 1, 2, 3, 6, 7, 8, 9, and 10

Aggression: 3, 4, 5, and 14

Lability: 11, 12, and 13

ABS - Scoring

- 14-20: no agitation
- 21-27: mild agitation
- 28-34: moderate agitation
- 35+: severe

ABS – rating example

8. Restlessness, pacing, excessive movement

Score 2: engages in random movements or fidgets occasionally. The **behavior does not threaten safety and terminates spontaneously**.

Examples:

a. fidgets in bed but remains in place

b. occasionally fidgets in the chair but the chair remains stable

ABS – rating example

8. Restlessness, pacing, excessive movement

Score 3: engages in random movements or fidgets frequently. There is **some threat to safety** but the behavior **terminates** with verbal or physical cueing or redirection

Examples:

a. frequently slips down in bed, needing replacement

b. fidgets in the chair, threatening stability, stops at least briefly after redirected

ABS – rating example

8. Restlessness, pacing, excessive movement

Score 4: random movements or fidgets frequently, threatening safety. Does **not** terminate with verbal or physical cueing or redirection and must be moved frequently or allowed free movement with **constant supervision**

Examples:

a. cannot stay in bed, must be moved to wheelchair and allowed to move about

b. fidgets in the chair, threatening stability. The caregiver must push the chair, move the patient to bed, or allow the patient to walk with assistance

Cases

Case 1

- 20 year-old who fell
- CT head demonstrated bilateral frontal lobe contusions
- Admitted to the hospital
- Staff and family notes that the patient is pulling out lines, getting out of bed often, and wandering

Case 2

- 20 year-old who was in a motor vehicle collision
- CT head with left frontal and temporal lobe contusions and SAH
- Admitted to the hospital
- Staff and family notes that the patient is yelling at people for waking him or that they're not helping him. Has been throwing objects in the room.

- What additional information would you like to know?

- Case 1: ABS of 27
- Case 2: ABS of 35

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Treatment Option – Limitation in Literature

- Literature is limited and **does not discriminate well among behavioral phenotypes** (irritability, verbal or physical aggression, or lability) and research using samples
- Varies on definition of agitation and scales used
- Level of evidence is not strong and often old
- Many treated with **multiple medications**

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- Admitted to the hospital
- Staff and family notes that the patient is yelling at people for waking him or that they're not helping him. Has been throwing objects in the room.

- What could be helpful in this setting?
- Would these change in the community setting?

Reviews of non-pharmacological treatment approaches

- Carrier SL, Ponsford J, Phyland RK, Hicks AJ, McKay A. Effectiveness of Non-Pharmacological Interventions for Agitation during Post-Traumatic Amnesia following Traumatic Brain Injury: A Systematic Review. *Neuropsychol Rev.* 2023;33(2):374-392.
- Carrier SL, Ponsford J, McKay A. Managing agitation during early recovery following traumatic brain injury: qualitative interviews with clinicians. *Disabil Rehabil*. 2023;45(22):3686-3695.

Evidence for non-pharmacological treatments

- Focus on adults with agitation during post-traumatic amnesia
- 12 studies: two randomized cross-over trials, three quasi-experimental, fours case series, three case reports
- Four music studies; exposure to preferred music live or taped for 15-80 minutes per day significantly reduced agitation compared to no music and classical music; caveat that in several cases exposure to strong beat, fast rhythm (heavy metal or rap music) increased agitation
- Five studies used behavior management and environmental modifications (positive/negative reinforcement, ignoring disruptive behaviors, token economy) and found they were generally associated with reduced agitation
- Four studies (CBT, restraint, ECT) ignored for our purposes

Carrier SL, Ponsford J, Phyland RK, Hicks AJ, McKay A. *Neuropsychol Rev.* 2023;33(2):374-392.

Agitation: Multi-level Influences

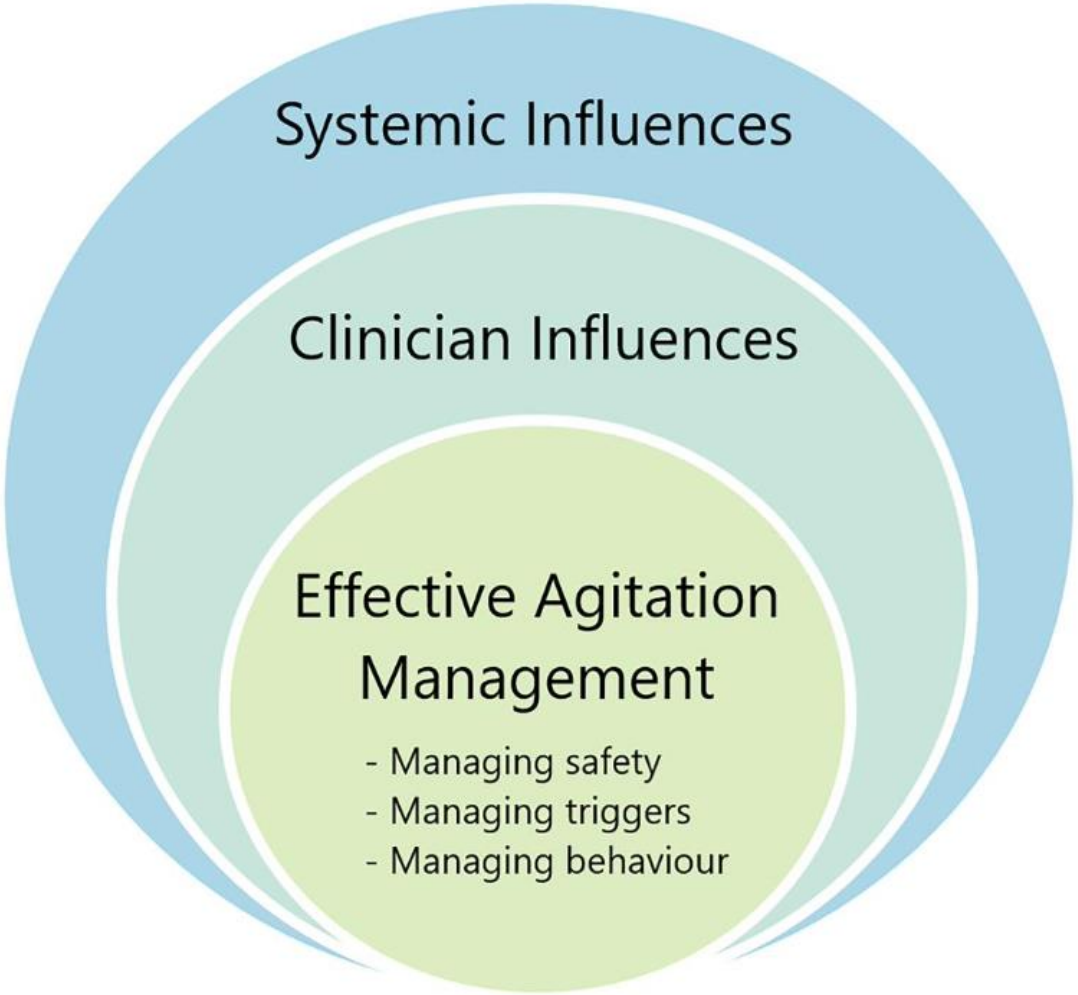

Figure 1. Visual representation of thematic analysis.

Carrier et al Disabil Rehabil 2023

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Systemic influences: Staff and Family

- Having dedicated, experienced staff with hands-on training to manage TBI-related agitation and who deal with this problem frequently is important
- Availability of behavioral health specialists
- Family participation can make or break agitation management programs depending on their presence and willingness to participate in a coordinated effort
- The lack of high-quality research and evidence-based guidelines on non-pharmacological management is a major limitation

Carrier et al Disabil Rehabil 2023

Clinician Influences

- Develop rapport and trust. Difficult when patient is in PTA
- Think classical conditioning. What experiences and emotions are you being paired with?
- Process: Meet with patient frequently, briefly, in calm times, engineer and highlight successful moments, one speaker, calm voice, simple questions they can answer, simple information, error-free learning
- Content: Find and affirm strengths, sources of pride, shared interests, hobbies, and things to reinforce; answer questions; give sense of control/choice e.g., Do you want me to leave now? May I check back later? Express gratitude for any positive patient efforts

Clinician Influences

Team Approach

- Develop written interdisciplinary behavioral plan in which everyone has an opportunity to contribute and to which everyone has buy-in

Flexibility and adaptability

- For example, have OT/PT sessions in preferred location (in patient room, side room, outdoors rather than in the noisy gym)
- Give patient limited choices to enhance sense of control e.g., what do they want to do first, when do they want a break, which variations (on same exercise) do they prefer

Carrier et al Disabil Rehabil 2023

Nonpharmacological Management of Agitation after TBI

- Managing safety
- Managing triggers
- Managing behaviors

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Managing Safety

- Safe space where patient cannot harm themselves or others
  - Locked ward (benefits of being able to move around but not leave)
  - Floor mattresses, low beds, netted beds, Craig beds, bed rails)
  - Remove objects that can be thrown; tubes or lines that can be pulled
  - Sitter: One-to-one human or virtual to avoid need for restraint
  - Physical restraints ranging from mittens, to waist, to 2-5 point

Carrier et al Disabil Rehabil 2023

Managing Triggers

- Patient related triggers
  - Pain: Premedicate for therapies
  - Fatigue: Space out therapies, allow short naps
  - Insomnia: Predicts next day agitation; restore normal sleep cycle via sunlight exposure, daytime activity, prevent long naps; minimize nighttime cares, allow family to sleep-over; treat nightmares
  - Anxiety: Trauma informed care, restart psych meds, access to familiar/comfort items (pictures, blankets, stuffed toys, music, lighting), cue use of prior coping strategies e.g., controlled breathing
  - Craving: Meds to reduce craving for tobacco, opioids
  - Conflict: Avoid engaging in pre-existing maladaptive interpersonal patterns

Managing Triggers

- Environmental triggers
  - Over-stimulation: Reduce/titrate: visitors, noise, light, screens, crowding, cognitive demands, level of challenge in therapies
  - Under-stimulation (no schedule, minimal therapies, long periods in bed, left alone, bored, stuck in room): Provide written schedule of activities, spaced therapies, regular time OOB, walking/moving around unit, access to preferred (calming) music, drawing, simple board/therapy games
  - Therapy demands: Break down goals, increase sense of success, soft start, limited choices, brief break then restart when refuses, chart progress on patient's wall
  - Unfamiliar setting: Visible clock, nightlight, simple schedule on wall, frequent re-orientation, and reassurance of care
  - Unfamiliar people: Consistent staff, warm handoff, know patient preferences,

Managing Behaviors

- Engage nursing staff in measuring agitation with ABS to:
  - identify triggers
  - have agreed upon definition
  - monitor progress and response to treatment

Carrier et al Disabil Rehabil 2023

Responding to Agitation-General Strategies

- Introduce self and role
- Explain what you need to do and why (benefits)
- Use low voice, speak slowly, keep it simple
- Open posture, being below eye level may help
- Ask simple questions. Give simple choices
- Use redirection, distraction, or ignoring; not reasoning
- If agitations escalates, ask to take a break
- Come back and start over in a few minutes
- In many ways follows trauma informed principles

Agitation Management Plan for Case 1

Context

- Right now he cannot remember what you tell him or his situation
- He is not always able to use the call button
- ABS = 30, mostly disinhibition
- Agitation triggers:
  - when it is dark and he's more confused
  - when he is incontinent
  - when he needs to urinate
  - when he is challenged, frustrated, or confronts impairment

Agitation Management Plan for Case 1

- Frequent, time-contingent nursing check-ins to address needs
- Nightlight, visible clock, sign on wall to re-orient to what happened and hospital situation, door open
- Offer urinal every two hours
- Small goals, high rate of success in therapies, error-free learning
- Frequent reminders of progress
- As last resort, call his mom especially at night to have her speak to him if needed help calm him down

Agitation Management Plan for Case 2

Context

- Still in PTA; sometimes thinks he is incarcerated
- He is over-using the call button
- ABS = 30, with significant verbal agression and threats
- Agitation triggers:
  - being woken up at night (for meds) and in AM (for therapies),
  - blood draws
  - restraints
  - being told what to do

Agitation Management Plan for Case 2

- Minimize meds at night and blood draws; move therapies to late AM
- Explain what you need to do and why; get his OK to proceed
- Negotiate: "You want me to do this... I need you to do that."
- Give limited choices: "Want blood draw now or after I get you some juice?"
- Label agitated behavior: "You are yelling at me."
- Reminders of incentives: "If you always put your helmet on before getting out of bed, we can take off waist restraint."
- Reminders of consequences: "If you yell at me, I will end the session."
- Treat patient in pairs for safety
- Use time-out to de-escalate: Leave the room stating that you will return in a few minutes and resume work if he can remain calm
- Verbally recognize it when patient remains calm, cooperative, engaged

Cases

Case 1

- 20 year-old who fell
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Case 2

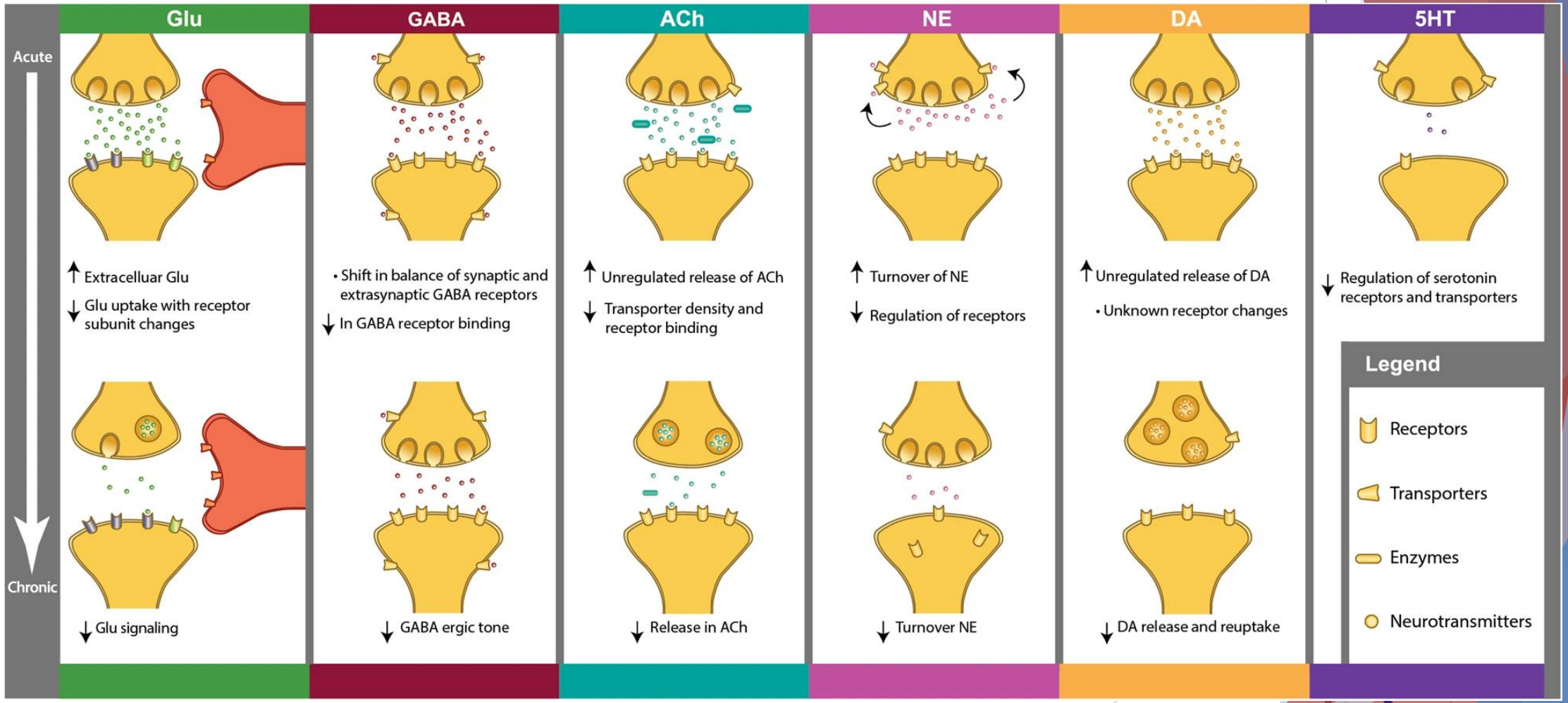
- 20 year-old who was in a motor vehicle collision
- CT head with left frontal and temporal lobe contusions and SAH
- Admitted to the hospital
- Staff and family notes that the patient is yelling at people for waking him or that they're not helping him. Has been throwing objects in the room.

- Upon evaluation, both are found to be in post-traumatic amnesia.
- In addition to environmental and other treatment options, what could be helpful?
- Would these change in the community setting?

Pharmacological Management

- What class of medication would you recommend at this time?
  - Beta blockers
  - Antipsychotics (neuroleptics)
  - Antiepileptics
  - SSRI
  - Stimulants/dopaminergic

TBI Pathophysiology – Neurotransmitter changes



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McGuire, 2019

Beta Blockers

- Most amount of evidence (Cochrane and ABIKUS) for Agitation
  - Propranolol
    - Start 10 mg tid; up to 300 mg/day
  - Pindolol
    - Start 5 mg bid; up to 30 mg/day
  - Nadolol
- May help to treat hyperadrenergic state in Agitation
- Weak evidence for reduction in anger/aggression

Hicks, 2021

Antiepileptics

- Valproic acid (VPA)
  - 250mg daily; then increase to bid
  - Adverse effects: hepatotoxic, thrombocytopenia, teratogenic, rash, GI upset, fatigue, weight gain
  - RCT: reduction in irritability without serious adverse events[1]

- Carbamazepine (CBZ)
  - Start 100-150mg BID
  - Adverse effects: aplastic anemia, hyponatremia (SIADH), hepatic impairment, teratogenic, renal failure, fatigue, dizziness
  - RCT for chronic irritability/aggression: improved but no statistical difference between placebo and CBZ groups[2]

1. Beresford, 2022
2. Hammond, 2021

Stimulants and Amantadine

- Improvement in speed of processing, attentiveness that helps with agitation
- Also shown to improve anger particularly in setting of concentration deficits

- Amantadine 100 mg twice daily (morning and noon)
  - Mixed but overall positive for reducing both irritability and aggression

- Methylphenidate 5 to 10 mg twice daily (morning and noon)

Hicks, 2021

Antidepressants

- May be more helpful in those with aggression or violent behavior
- Sertraline 100 – 200 mg/day for both Agitation and Irritability/Aggression
- Amitriptyline is not commonly used and not efficacious

Antipsychotics

- Risperidone
- Ziprasidone
- Quetiapine
- Olanzapine
- Clozapine
- Aripiprazole

- To protect the patient from harming self or others
- Need for quick sedation
- + delirious symptoms

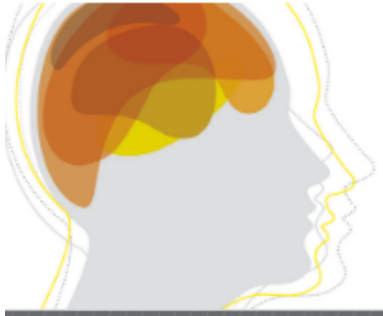
Choosing Antipsychotics

- Olanzapine, Clozapine, Quetiapine, Ziprasidone[1]
  - Expert opinion:
    - Shortest possible course
    - Consider in case of associated delirious symptoms but otherwise avoid
    - Preferable to use atypical antipsychotics

- No clear evidence of benefit with antipsychotics[1, 2]
- Choose based on side effect profile

1. Plantier, 2016
2. Elovic, 2008

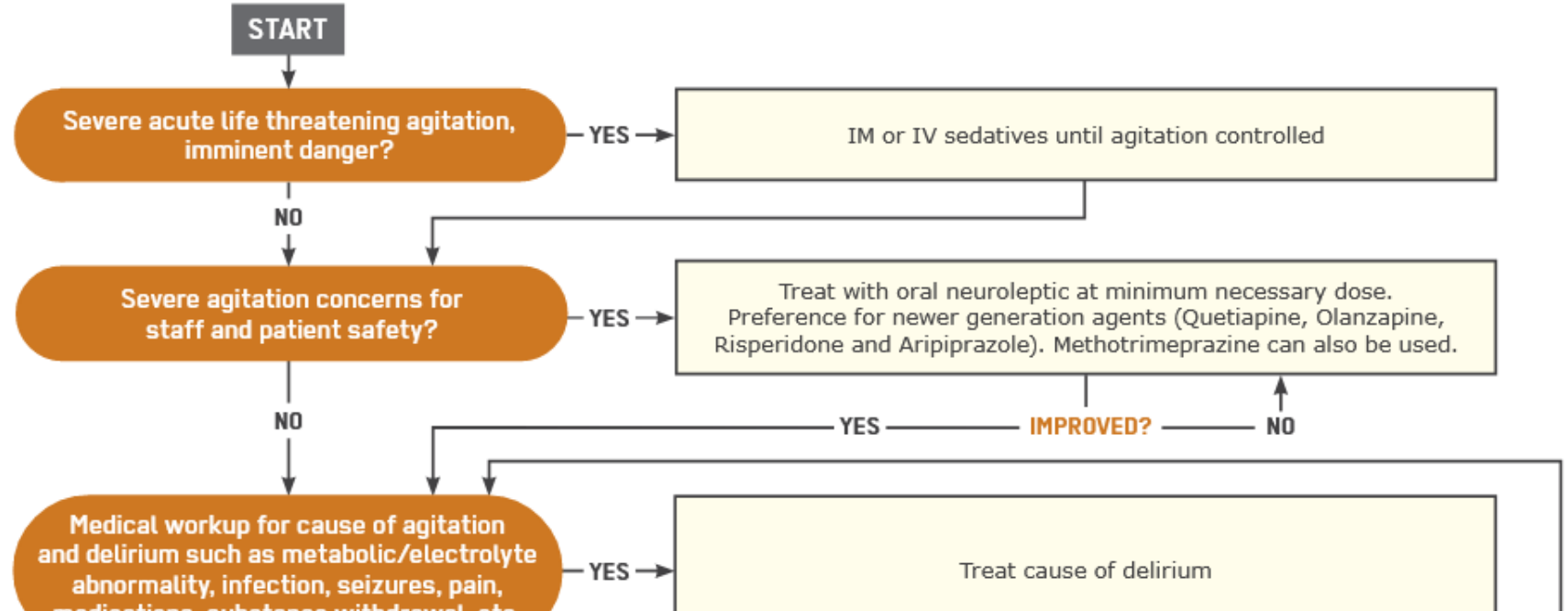
Clinical Practice Guideline – Moderate to Severe TBI



CLINICAL PRACTICE GUIDELINE

FOR THE REHABILITATION OF ADULTS WITH MODERATE TO SEVERE TBI

Pharmacological Management of Agitation and Aggression Following TBI



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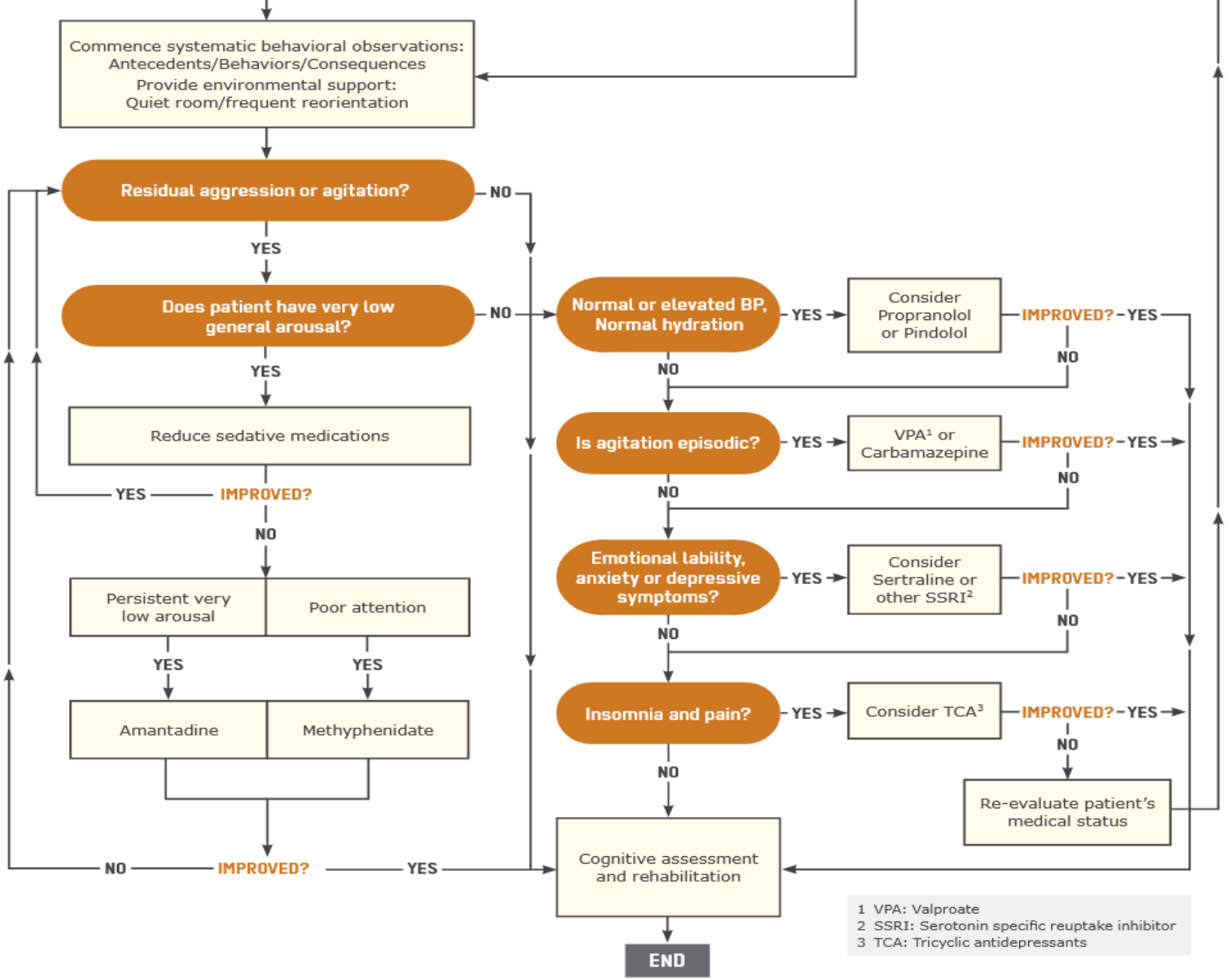

Ontario Neurotrauma Foundation
Fondation ontarienne de neurotraumatologie

Institut national d'excellence en santé et en services sociaux
Québec

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- Admitted to the hospital
- Staff and family notes that the patient is yelling at people for waking him or that they're not helping him. Has been throwing objects in the room.

- What medication would you consider at this time?

Summary

- Agitation, irritability, and anger are common after TBI
- Objective measurement is necessary:
  - Agitated Behavior Scale
- Start with environmental and behavioral management once other possible causes have been ruled out
- Agitation: beta blocker has most evidence. AEDs & anti-depressants are useful. Consider stimulant
  - Avoid antipsychotics unless risk for harm
- Irritability/Aggression: amantadine, methylphenidate, VPA, CBZ are potential options

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