

TRAUMATIC BRAIN INJURY GUIDELINES 2025

Department of Physical Medicine and Rehabilitation/UAMS IDHI Brain Injury Program

TBI Agitation

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I. I. Definition, Assessment, Diagnosis

A. Agitation Definitions: No consensus between or within fields – working definition used by medical providers and by patients/families likely to be different from one another. Recommend clearly defining terms used when speaking with patients, families, and other providers. (Sano 2024). All definitions emphasize that agitation is a diagnosis of exclusion and must not be solely attributable to another psychiatric disorder, medical condition, substance use, or environmental conditions / poor care.

1. Per INCOG guidelines: agitation is a subtype of delirium unique to TBI which may occur during the period of post-traumatic amnesia (PTA). PTA is the period of time post-TBI in which new memory formation is impaired; by this definition, agitation cannot exist outside this period and thus can no longer occur when new memory formation is restored to baseline. Agitation is characterized by a varying combination of disinhibition, emotional lability, aggression, impulsivity, and restlessness. (Ponsford, 2023)

2. Per International Psychogeriatric Association guidelines: agitation is a chronic state (2+ weeks) that may occur secondary to cognitive impairment and/or dementia, wherein TBI is a subtype of cognitive impairment. Agitation is characterized by disabling emotional distress within the context of cognitive impairment that may be displayed through excessive motor activity, reactive physical aggression, and/or reactive verbal aggression. It is specifically distinct from delirium in terms of symptoms and management.

B. Agitation Assessment:

1. Westmead Post-Traumatic Amnesia Scale (WPTAS)

A. Completed by patient - patient must be able to communicate via either speech, writing, or pointing at “yes” or “no” when prompted.

B. Validated in English and Spanish, or with use of interpreter for other languages.

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- C. Abbreviated scale (A-WPTAS) recommended at initial ER visit if within 24 hours of injury
- D. Supports clinical decision making, including decisions regarding further CT scanning
 - 2. Agitated Behavior Scale: physician-completed assessment that numerically describes level of agitation.
 - a. Helpful for monitoring patient’s recovery progression and assessing effectiveness of interventions
 - b. High inter-rater reliability
 - c. Rating of 1 to 4 (based on severity) for 14 different behaviors, where 21+ meets criteria for agitation
 - D. It is now recommended to corroborate answers for initial ABS assessment with patient family members - i.e. with reference to change from baseline.
- 3. Galveston Orientation and Amnesia Test (GOAT): [8]
 - a. Reliable and valid indicator of PTA in TBI patients [9]
 - b. Score of 78 or more on three consecutive occasions is considered to indicate that patient is out of PTA
 - c. Can be administered daily until patient is out of PTA
- 4. Rancho Los Amigos (RLA) Scale/ Levels of Cognitive Functioning Scale
 - a. Represents the typical sequential progression of recovery in TBI
 - b. Stage IV: Confused, Agitated Response
 - c. Barriers: These patients have deficits in attention, memory, initiation, problem solving, sequencing, information processing speed, and safety awareness. Anosognosia (lack of awareness of deficits) is also a challenge.

C. Agitation Diagnosis [3], [4], [5]

- 1. A diagnosis of exclusion after physical, medical, psychiatric, and neurological conditions have been ruled out
- 2. Score of 21 or greater on ABS
- 3. Can also result from physical, medical, psychiatric, and neurological conditions:
 - a. Physical:
 - i. Pain (fractures, post-operative, heterotopic ossification, spasticity, wounds, or other noxious stimuli)
 - ii. Environmental: Excessive stimulation, Temperature, Restraints
 - “ICU Syndrome” : acute state of confusion seen even in patients without primary brain pathology, secondary to constant stimulation in ICU - vital signs, alarms,

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medication administration, constant lighting, and ambient hallway noise. ^{[11],[12]}

iii. Tubes/lines

b. Medical:

- i. Metabolic disturbance (electrolytes, thyroid, hypoglycemia)
- ii. Infection
- iii. Hypoxemia, pulmonary embolism
- iv. Urinary retention/incontinence
- v. Nausea, Constipation

c. Neurological:

- i. Hydrocephalus
- ii. Seizures
- iii. Intracranial mass lesion/rebleed
- iv. Headache

d. Psychiatric:

- i. Premorbid or exacerbation of premorbid Personality/Psychotic/Anxiety/Mood disorders
- ii. Sundowning in patients with dementia

e. Substance/medication related:

- i. Iatrogenic
- ii. Acute intoxication
- iii. Withdrawal ^[6]
 - Alcohol: Hypertension, tachycardia, hallucinations, disorientation, agitation
 - Opioid: Restlessness, abdominal pain, yawning, piloerection
 - Benzodiazepine: Hypertension, tachycardia, diaphoresis, tremors, hyperthermia, and seizures

4. Work up of Agitated patient: CMP, Thyroid function tests, CBC with differential, UA, B12/Folate, Urine toxicology screen, CT/MRI of Brain, EEG, XRay

II. Management and Treatment Recommendations

A. FIRST LINE: Environmental Modification ^[6]

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1. Reduce stimuli:
 - a. Light, noise, distractions (especially at night) – place patient in bed, draw curtains, turn off television, etc.
 - b. Limit number of visitors at one time
 - c. Staff and family should speak in low volume, slowly, one at a time
2. Avoid/minimize restraints: Use non-contact restraints if able (safety net beds), padded hand mittens, one-to-one staff supervision
3. Minimize tubes and lines: May cover them (abdominal binder, etc)
 1. May be helpful to secure abdominal binders behind the patient
4. Frequent reorientation-orientation by staff and family
5. Obtain any hearing devices or vision aids from home to improve orientation
6. Consistent schedule and staff
7. Timed toileting
8. Create a familiar environment: Allow family to bring in personal possessions^[15]
9. Monitor sleep cycle and sleep quality
 - a. Consider use of Trazodone, Melatonin

B. Behavioral Modification

1. Allow patient to pace (if safe) or be walked /wheeled around by staff to address akathisia/restlessness.
2. Mobile patients may benefit from a closed unit or sensors for safety
3. De-escalation techniques (see prevention and education section below)^[14]
4. Structured behavioral programs^{[6],[15]}
 - a. Limited application depending on patient's level of cognitive and communication impairment

C. Pharmacologic Management

1. Agents which slow cognition may prolong/exacerbate agitation.^[14] Dopaminergic agents should be avoided if able as they can prolong PTA and slow cognitive recovery^[5]

2. Antipsychotics:

a. Typical Antipsychotics: Not recommended as first line, rescue only

i. Haldol:

-shown to slow cognitive recovery

-shown to slow motor recovery in rat model^[16]

-associated with longer time in PTA^[17]

-Easily accessible in the hospital and can be given IM, IV: useful for patients who are imminently a danger to self or others.

ii. Droperidol:

-Also available in IM

-Found to be faster and superior to Haldol, Ativan, and Benadryl in controlling acute agitation^[18]

iii. Cognitive improvement seen after discontinuing typical antipsychotics^[19]

iv. Associated with extrapyramidal side effects, dystonic reactions, restlessness, Neuroleptic Malignant Syndrome, QTc prolongation

v. Not recommended as long term agents

b. Atypical antipsychotics

i. Quetiapine:

-Shown to be effective in treating agitation^[20]

- available PO and rapidly absorbed, short half-life (7hrs)

- Better side effect profile compared to typical agents

- lower risk for QTc prolongation

ii. Olanzapine:

- Shown to have effect in treating agitation
- Favorable side effect profile when compared to other antipsychotics^[21]
 - lower risk of Qtc prolongation, longer half life (30hrs)
- Available orally or IM

iii. Risperidone Others: Risperidone, Ziprasidone ^[52]

- Associated with significant impairment in motor function
- Continuous administration may impede cognitive recovery

IV. Noted that observational studies report reduction in agitation, however no controlled studies to evaluate efficacy other than olanzapine

V. antipsychotics may increase length of PTA

3. Anxiolytics

a. Benzodiazepines

i. Impair cognition ^[22]

ii. May cause paradoxical agitation ^[22], anterograde amnesia ^[23], disinhibition, respiratory depression, impaired coordination

iii. Useful for rapid resolution of violent agitation (rapid onset of action)

iv. Lorazepam preferred

-Less effect on cardiovascular and respiratory centers than other benzodiazepines ^[23]

-Doses of 0.5-1mg q8h, titrating up to maximum of 8-12mg/day ^[22]

-Start long-term agents concurrently ^[22]

-Discontinue as soon as possible to minimize chances of delaying cognitive recovery ^[22]

b. Buspirone ^{[6],[14],[32]}

i. Preferred anxiolytic in TBI patients

ii. No significant adverse neurological or cognitive effects, non-sedating, non-addictive, does not interact with other CNS agents, not a respiratory depressant ^[14]

- iii. Side effects: Lowers seizure threshold, light-headedness, headache
- iv. Disadvantage: Delay in therapeutic action. Rapid neuropsychiatric effects, but 2-3 weeks for anxiolytic effects^[45]
- v. Dosing: 60mg/day is maximum, but as high as 180/day seen^[14]. Usual dose of 5-20mg TID

4. Beta blockers

a. Propranolol

- i. Best evidence for efficacy in treating post-traumatic agitation with minimal side effects per Cochrane review^[24]
- ii. shown to reduce agitation intensity and need for physical restraints^[25]
 - However no change in frequency of episodes
- iii. Also improves restlessness and disinhibition^[14]
- iii. Also helpful for treating hyperadrenergic/dysautonomic state after TBI
- iv. Also used to treat drug-induced akathisia, EtOH withdrawal, mania, generalized anxiety disorder, lithium induced tremor^{[31],[27]}
- iv. Side effects
 - Hypotension and bradycardia are limiting side effects
 - May also cause depression and lethargy^{[31],[27]}
 - No adverse effect on motor recovery^[14]
- v. Dose:
 - Starting dose: up to 40-60mg/day divided into BID –QID dosing^[25]
 - Maximum dose of 420 mg/day has been used, reports of bradycardia and hypotension at 520mg/day
- vi. Lipophilic properties
 - More effective CNS penetration
 - Propranolol is the most lipophilic beta blocker

b. Moderately lipophilic beta blockers

i. Metoprolol and pindolol

5. Anticonvulsants

a. Mood-stabilizing AEDs reduce agitation ^[29]

b. Valproic acid ^{[30],[32], [33]}

i. Initial dose of 250mg BID, may be titrated up 250mg every 2-3 days to maximum of 1000-2500mg/day ^[20]

ii. Serum levels of 40-100 ug/mL with positive effects ^[34]

iii. Limited, if any, adverse effects on cognition^[31]

iv. Side effect limitations: hepatotoxicity, thrombocytopenia.

-More common side effects of sedation, nausea, and vomiting, are limited by meal time administration and gradual titration

v. Less likely than carbamazepine to have negative impact on cognition and has safer side effect profile^{[35],[32]}

vi. Potential for rapid loading

c. Carbamazepine ^{[35],[36]}

i. Dose to therapeutic effect with titration up. Aggression-limiting doses seen starting at 300-400mg/day ^[14]. Other studies with effective doses 400-900 mg/day (BID-TID dosing).^{[36],[37]}

ii. Side effects: Hyponatremia, renal impairment, imbalance, sedation. Rarely, aplastic anemia, and Steven-Johnson syndrome^[20]

iv. Monitor serum levels for toxicity

iii. Rapid onset of action makes it useful in trauma critical care setting^[37]

d. Others

i. Gabapentin, Lamotrigine

-Not as well studied

-Reports of negative effects, such as anxiety and agitation
[38],[39],[40]

ii. Phenytoin, Topiramate

-Negative cognitive impact [38],[41],[42]

6. Neurostimulants

a. Amantadine

i. Can be effective for both acute [44] and chronic [43] TBI agitation

- Studies however with inconsistent results
- Can be cautiously considered for chronic nonpenetrating TBI

ii. Shown to improve cognition: Attention, concentration, processing time, initiation, orientation, sequencing, verbalization, and participation [40], [41], [32]

iii. Dosing from 50-400 mg/day, in divided doses [44],[46]

iv. Therapeutic effects typically seen within several days [14]

v. Side effects:

-Overstimulation, irritability, hypomania, agitation

- Increased HR and BP, use with caution in patients with dysautonomia and cardiovascular complications

-Lowers seizure threshold, so use with caution in seizure history patients and early stage TBI when increased intracranial pressure also lowers the threshold [45]

-Some side effects potentiated when combined with anti-cholinergic agents: hallucinations, confusion, nightmares [47]

-Side effects are generally mild, dose dependent, and reversible [32]

b. Methylphenidate

i. Useful in both acute and chronic TBI agitation [31] [32], [34], [35]

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- Controlled studies demonstrate effect on agitation are either nonsignificant or can worsen agitation
- May improve anger measures
- ii. Improves cognition similarly to Amantadine
- iii. Quick onset of action ^[32]
 - 30min-2hrs after administration
- iv. Relatively benign side effect profile ^[32]
- v. Dosing: 10-60 mg/day in divided doses, usually at 8AM and noon ^[14]
- c. Bromocriptine: Dopaminergic neurostimulator similar to Amantadine
- d. Dextroamphetamine: Sympathomimetic neurostimulator similar to Methylphenidate

7. Antidepressants

a. Selective Serotonin Reuptake Inhibitors (SSRIs)

- i. Useful for behavioral syndromes in TBI
- ii. Trazodone
 - Helpful for sleep-wake cycle regulation
 - Starting dose: 50-100 mg.
 - Side effects: Anticholinergic, Rare priapism
- ii. Others: Sertraline ^[48], Fluoxetine, Paroxetine, Citalopram
- iv. Side effects: Serotonin syndrome, QTc prolongation, anxiety, sexual dysfunction, excessive weight loss

b. Tricyclic Antidepressants (TCAs)

- i. Amitriptyline ^{[14], [54]}
 - Dosing: 10-75 mg/day
- ii. Side effects: Anticholinergic, QTc prolongation, potential seizure threshold lowering ^[55]

c. Bupropion

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i. Useful for restlessness at 150mg daily ^[51]

8. Lithium

i. Has been suggested to reserve its use in patients with mania and cyclic mood disorders ^[57]

ii. Dosing: Start at 300mg BID and titrate by serum levels (0.6-1.2 mEq/L is therapeutic and >1.4 mEq/L is toxic level) and side effects ^[6]

iii. Side effects: sedation, movement disorders, hypothyroid, seizures, bradycardia, vomiting, QTc prolongation, renal impairment. ^{[6], [58]}

9. Summary:

a. Choose agent based on clinical presentation. Every TBI is different.

i. Restlessness/Akathisia: Frequent ambulation, Beta-blocker

ii. Hyperadrenergic state: Beta-blocker

iii. Episodic Behavior Dyscontrol / Mood Lability:
Anticonvulsants/Mood stabilizers; possibly Atypical antipsychotics, SSRI, Neurostimulator

iv. Anxious/fearful: Buspar, SSRI/TCA, Trazodone

v. Paranoid: Atypical antipsychotic

b. Start low, go slow

c. Ideal agent is non-sedating, not affecting cognitive recovery, low side effect profile

d. May need to discontinue drugs which may amplify agitation:

i. Narcotics

ii. Benzodiazepines

iii. Dopamine agonists (e.g. metoclopramide)

iv. H₂-receptor antagonists (e.g. famotidine)

v. Anticholinergic medications (e.g. oxybutynin)

III. Prevention and Education ^[50]

A. Educate staff and family on how to approach an agitated patient

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- A. Warning Signs of Agitation
 - a. Decreased Compliance
 - b. Increased Restlessness
 - c. Increased Physical Movement (i.e., pacing)
 - d. Impatience
 - e. Pressured Speech (i.e., loud, rapid, forceful)
 - f. Outbursts of Anger (i.e., verbal or physical)
 - g. Increased Anxiety/Changes in Mood
- B. Non-Pharmacological Interventions
 - a. Verbal De-escalation[60]
 - i. Monitor body language.
 - 1. Enter the room with non-threatening posture
 - 2. Avoid sudden grabbing or touching of the patient.
Approach from the front.
 - ii. Use social greetings and introduce yourself: these are cues to relax
 - iii. Clearly express the intent of the interaction and explain what you are going to do before you do it (e.g. vitals, procedures, physical exam, etc.)
 - iv. Speak calmly, slowly, briefly, clearly, and directly
 - v. Speak in simple terms and break down tasks into steps
 - vi. Give the patient time to process and respond
 - vii. Ask open-ended questions
 - viii. Instead of disagreeing, make a neutral statement or re-direct attention to another topic
 - ix. Be empathetic
 - x. Avoid judgement
 - xi. Formally end the interaction as patient may not be aware of normal social cues
 - b. Environmental Management[61]
 - i. Limit staff to no more than 2 at a time when possible
 - ii. Regulate the environment when possible (i.e., do not disturb hours)
 - iii. Reduce noise/distractions when interacting with the patient (i.e., turn TV off)
 - iv. Balance stimulation with rest
 - v. Redirect and reorient patients to the environment and what is being done if they become confused
 - vi. Prioritize the safety of yourself and the patient
 - vii. Provide intervention in a quiet area, such as at bedside
 - viii. Use positive reinforcement to encourage positive interactions
 - ix. Try to increase structure/routine as is feasible
- C. Patient Resources
 - a. PM&R inpatient consult services and outpatient TBI clinic
 - b. Brain Injury support group
 - i. In-Person Survivor Support Group at Baptist Health Rehabilitation Center the 2nd Wednesday of each month from 11:30 AM to 1 PM

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- ii. Online Survivor Support Group meets every Tuesday from 1-2 PM.
 1. <https://v.ringcentral.com/join/894179693>
- iii. Information on other local/online support groups can be found at: <https://idhi.uams.edu/brain-injury-program/resource-directory/support-groups/>
- c. UAMS Brain Injury Program[61]
 - i. Outpatient resources and support (i.e., 24/7 Brain and Spine Hotline)
 - ii. The Holistic Rehabilitation Intervention Experience (THRIVE): A multi-faceted interventional group that focuses on educating and helping participants manage cognitive/functional/emotional changes after a brain injury.
 - iii. Can help you get connected with relationship counseling
- d. Services through UAMS Walker Family Clinic
 - i. Individual Cognitive Rehabilitation
 - ii. Neuropsychological Testing
 - iii. Individual Psychotherapy
- e. Online Resources
 - i. Brain Injury Association of America (BIAA): www.biausa.org
 - ii. Brainline: www.brainline.org
 - iii. The Stroke Network: www.strokenetwork.org
 - iv. Arkansas Rehabilitation Services: <https://dws.arkansas.gov/ar-rehabilitation-services/>

A. Educate staff and family on how to approach TBI pt

-Use social greetings: these are cues to relax

-Speak calmly, slowly, briefly, clearly, and directly

-Do not need to correct confused statements. Instead of disagreeing, make a neutral statement or re-direct attention to another topic

-Explain what you are going to do before you do it (e.g. vitals, procedures, physical exam, etc)

-Avoid sudden grabbing or touching of the patient. Approach from the front.

-Do not crowd patient

-Formally end the interaction as patient may not be aware of normal social cues

-Provide patient with choice instead of command.

-Therapies in quiet area, at bedside

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-Positive reinforcement

-Give patient ample time to process information and formulate responses

-Break down difficult tasks into small steps

B. Patient Resources

-PM&R inpatient consult services and outpatient TBI clinic

-Brain Injury support groups (e.g. Baptist Rehabilitation Institute)

-Online Resources, such as Brainline.org

-Arkansas Trauma Rehabilitation Program: <https://atrp.ar.gov/>[59]