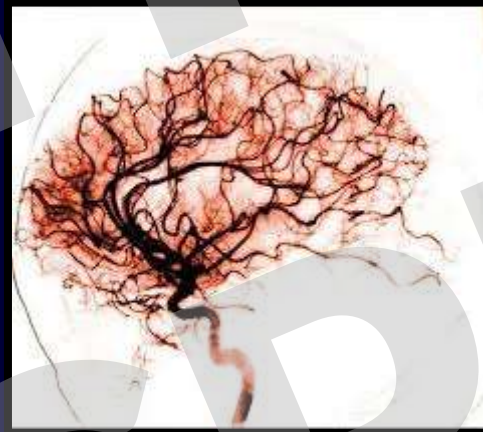

Agitation Management Following Acquired Brain Injury



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My Background



Hometown



MD

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Disclosures

- Board Member of the Brain Injury Alliance of Oregon

Objectives

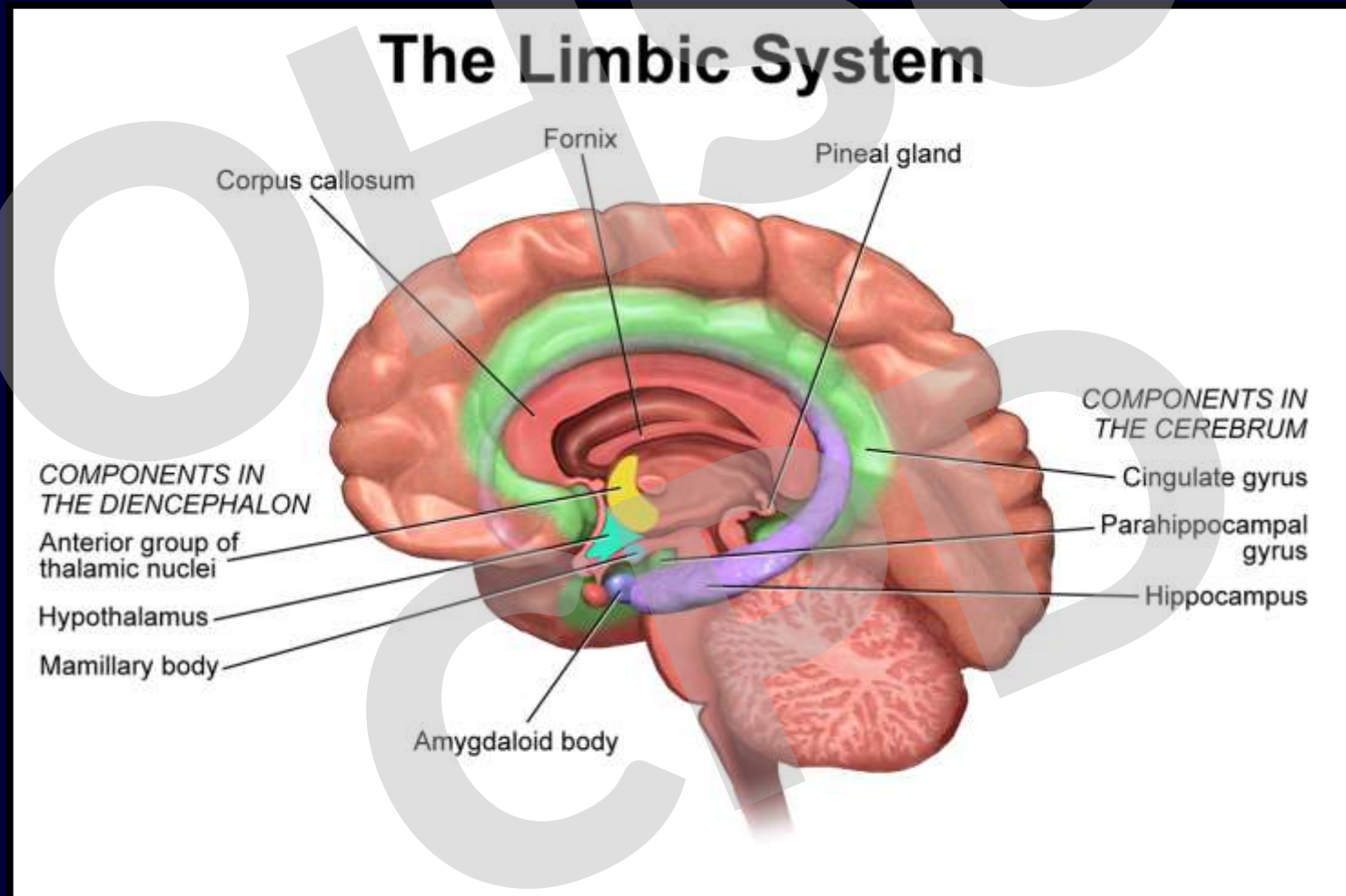
- Definition
- Types of agitation
- Underlying anatomy and pathophysiology
- Approaches to management:
 - Non-pharmacologic
 - Pharmacologic

What is Agitation?

- Mood, cognition, and behavior closely intertwined.
- Brain Injury Specialist Interest Group of AAPMR
 - Physical aggression
 - Explosive anger
 - Akathisia
 - Impulsivity
 - Verbal aggression
 - Disorganized thinking
 - Perceptual disturbances
 - Post-traumatic delirium

ANATOMY & PATHOPHYSIOLOGY

Limbic System



Limbic System

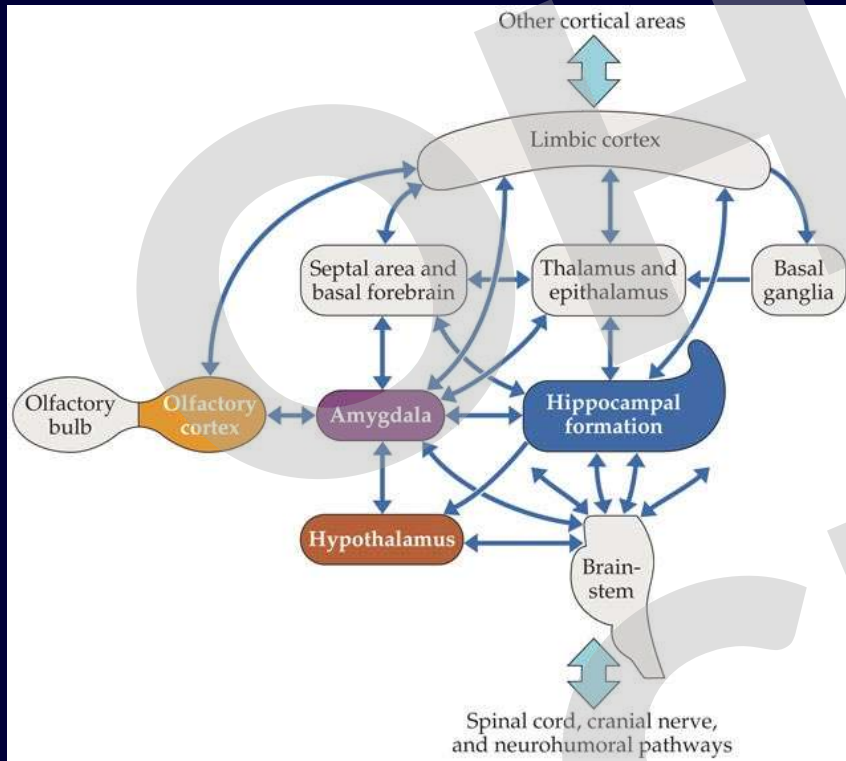


TABLE 18.2 Simplification of Limbic Functions and Corresponding Key Structures

LIMBIC FUNCTION	KEY STRUCTURE
Olfaction	Olfactory cortex
Memory	Hippocampal formation
Emotions and drives	Amygdala
Homeostasis; autonomic and neuroendocrine control	Hypothalamus

Pathophysiology of Agitation

- Anatomy
 - Hypothalamus
 - Periaqueductal gray
 - Limbic structures
 - Diffuse Axonal Injury
- Neurochemical
 - Increased glutamate
 - Decreased serotonin
 - Dysregulated dopamine
- Neuroendocrine
 - Cortisol
 - Thyroid hormone
 - Sodium imbalance

Management can be Guided by Neuroanatomy of Injury

More Activated	Less Activated
Left	Right
Orbitofrontal	Dorsal
Midline	Lateral
Anterior/Medial Temporal Lobe	

ASSESSMENT

What do we mean by agitation?

- Agitation can mean many things.
- It's important to differentiate types to help guide treatment.
- Are they minimally conscious and pulling at lines?
- Are they behaving aggressively towards staff?
- Are they angry, disoriented, restless, and/or confused?

Agitated Behavior Scale

AGITATED BEHAVIOR SCALE

Patient _____

Period of Observation: _____

From: _____ a.m. _____ p.m. _____

To: _____ a.m. _____ p.m. _____

Obsv. Environ. _____

Rater/Disc. _____

At the end of the observation period indicate whether the behavior described in each item was present and, if so, to what degree: slight, moderate or extreme. Use the following numerical values and criteria for your ratings.

1 = **absent**: the behavior is not present.

2 = **present to a slight degree**: the behavior is present but does not prevent the conduct of other, contextually appropriate behavior. (The individual may redirect spontaneously, or the continuation of the agitated behavior does not disrupt appropriate behavior.)

3 = **present to a moderate degree**: the individual needs to be redirected from an agitated to an appropriate behavior, but benefits from such cueing.

4 = **present to an extreme degree**: the individual is not able to engage in appropriate behavior due to the interference of the agitated behavior, even when external cueing or redirection is provided.

DO NOT LEAVE BLANKS.

____ 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.

____ **Total Score**

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_____ **Total Score**

Rancho Los Amigos Scale of Cognitive Functioning

I: Coma

II: Vegetative State

III: Minimally conscious state

IV: Confused and agitated

V: Confused and inappropriate

VI: Confused and appropriate

VII: Automatic and appropriate

VIII: Purposeful and appropriate

What is the underlying cause?

- Severity/location of brain injury
- Disrupted sleep/wake cycle
- Pain
- Hypoxia
- Subclinical seizures
- Communication deficits
- Psychiatric history
- Invasive lines
- Restraints
- Inconsistency of staff
- Medication side effects
- Infection
- Electrolyte disturbance



MANAGEMENT

Goals of management

- Promote the safety of patients and caregivers.
- Promote recovery of cognition.
- Minimize sedation.
- Promote healthy sleep-wake cycle.
- Promote patient comfort and psychological well-being.
- Allow patient to participate in rehabilitation.

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Regulatory Requirements

- The Joint Commission requires:
 - Plan to ensure the security of patients, staff, and visitors.
 - Plan to respond to violence.
 - Staff are trained in the appropriate use of restraints.
- Commission for Accreditation of Rehab Facilities (CARF)
 - requires facilities to have a plan for responding to violent behaviors, and under which circumstances restraints will be used.

Regulatory Requirements

- Code of Federal Regulation (CFR):
 - 42 C.F.R. §482.13(e) Standard: Restraint or seclusion. All patients have the right to be free from physical or mental abuse, and corporal punishment. All patients have the right to be free from restraint or seclusion, of any form, imposed as a means of coercion, discipline, convenience, or retaliation by staff. Restraint or seclusion may only be imposed to ensure the immediate physical safety of the patient, a staff member, or others and must be discontinued at the earliest possible time.²⁵

PeaceHealth Policy

- It is the policy of PeaceHealth that use of restraint and seclusion is in accordance with federal, state, and accreditation requirements. All patients have the right to be free from physical or mental abuse, and corporal punishment. All patients have the right to be free from restraint or seclusion, of any form, imposed as a means of coercion, discipline, convenience, or retaliation by staff. Restraint or seclusion may only be imposed to ensure the immediate physical safety of the patient, a staff member, or others and must be discontinued at the earliest possible time.

Non-pharmacologic Interventions

- De-escalation training programs for staff
 - Can improve staff confidence in responding to agitation.
 - Can reduce the rate of violent incidents.
- Use a calm voice
- Avoid argument or confrontation
- Set realistic expectations and goals
- Use the least restrictive restraints

Reduce Triggers

- Minimize overstimulation
 - Reduce brightness of lights
 - Minimize hallway noise
 - Turn off the TV
- Provide frequent redirection and reorientation
- Put up personal items in room
- Have family and friends present
- Provide consistency of staffing.
- Minimize invasive lines.
- Minimize use of physical restraints.

Restraints

- Intervention of last resort.
- Can worsen agitation.
- Only use when the safety of the patient and/or staff is at risk and all other means to redirect the patient have failed.
- Use the least restrictive form possible.
- Reassess the need for restraints frequently.

Restraints

- Net bed
- Waist roll belt
- Mits
- Soft restraints
- Hard restraints
- # of restrained parts



Normalize Sleep-Wake Cycle

- Allow natural light into the room during the day.
- Encourage wakefulness during the day, including providing therapeutic activity when able.
- Provide a dark and quiet environment at night.

Promote Sleep

- Melatonin to reset circadian rhythm
- Trazodone:
 - promotes good sleep with minimal side effects
 - 50-100mg nightly.
- Zolpidem:
 - Selective GABA agonist
 - 5-10mg nightly
 - Can sometimes cause delirium.
 - Promotes recovery of consciousness in select population.
- Atypical antipsychotics if above options ineffective (i.e. quetiapine, olanzapine, risperidone).

Promote Wakefulness

Promote Wakefulness

- Modafinil:
 - Mechanism not well understood. Weak dopamine reuptake inhibitor.
 - 100mg x 3 days, then 200mg every morning.
- Methylphenidate:
 - Norepi & dopamine reuptake inhibitor
 - initial 5mg twice daily morning and midday.

Promote Wakefulness

- Amantadine:
 - Most often used to promote recovery of consciousness.
 - Not effective for aggression.
 - Can help with apathy.
 - Weak NMDA antagonist, incr dopamine release, and inhibits reuptake.
 - 100mg bid in the morning and midday.
- Amphetamine derivatives (i.e. Adderall, Vyvanse)
 - Increases synaptic norepi & dopamine

Behavioral Dysregulation

Review

Drugs for behavior disorders after traumatic brain injury: Systematic review and expert consensus leading to French recommendations for good practice

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Table 1

Grade recommendations.

Level of scientific evidence provided by the literature (treatment studies)	Grade recommendation
Level 1 High power randomized comparative trials Meta-analysis of randomized controlled trials Decision analysis based on well-conducted studies	Established scientific evidence A
Level 2 Low-power randomized comparative trials Non-randomized comparative studies well-conducted Cohort studies	Scientific presumption B
Level 3 Case-control Studies	Low level of evidence C
Level 4 (NP4) Comparative studies with considerable bias Retrospective studies Case series	

Promote Calm

- Propranolol (best evidence; L1-2, GB):
 - beta blocker, sympatholytic, non-cardioselective, crosses BBB
 - 10mg tid. Can increase by 10mg every 1-3 days.
 - Alternative: Pindolol (L4,GC)
- Valproate (L2, GB):
 - Anticonvulsant. Blocks voltage gate sodium channels, GABAergic.
 - Initial 250mg bid. Incr every 3-4 days.
 - Alternatives: Carbamazepine, Oxcarbazepine, Lamotrigine
- Atypical antipsychotics (i.e. olanzapine, quetiapine; L3, GC):
 - Use with caution since there can be extrapyramidal and cognitive side effects.
 - Reserve for emergency situations.
 - Use minimal effective dose for agitation that is not redirectable.

Promote Calm

- Dextromethorphan-quinidine (Nuedexta):
 - Approved for pseudobulbar affect.
- Buspirone (L4, GC):
 - Serotonin 5-HT_{1A} agonist.
 - Initial 5mg 2-3 times daily.

Improve Mood

- TCA's (i.e. amitriptyline, nortriptyline; L2, GB):
 - Inhibits serotonin and norepi transporters. Also inhibits histamine and acetylcholine.
 - Can help with mood, pain, and sleep.
- SNRI's (i.e. duloxetine, venlafaxine):
 - Serotonin & norepi reuptake inhibitors.
 - Can improve mood, arousal, and pain.
- SSRI's (i.e. citalopram, escitalopram, sertraline (L1, GA), fluoxetine, paroxetine):
 - Serotonin reuptake inhibitors.
 - Can take several weeks to take full effect.
 - Useful for post-traumatic mood disorders.
 - Weak evidence to promote motor and language recovery after stroke.

Pharmacologic Considerations

- NO HALDOL!!
 - Can impede neuronal healing and functional recovery.
 - Prolongs post-traumatic amnesia.
- NO BENZOS!!
 - These can worsen confusion, cause paradoxical agitation, and increase fall risk.

Summary

- Agitation can mean many things.
- Associated with dysregulation of the limbic system.
- Important to assess for underlying irritants.
- Both medication and non-pharmacologic interventions are important.
- Normalize sleep-wake cycle.
- Minimize use of restraints.
- Avoid Haldol and benzos!

Sources

!Electronic Code of Federal Regulations. 2021. <http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=%2Findex.tpl>

Rao N, Jellinek HM, Woolston DC. Agitation in closed head injury: Haloperidol effects on rehabilitation outcome *Arch Phys Med Rehabil* 1985; 66: 30-34

Plantier D, Luauté J; SOFMER group. Drugs for behavior disorders after traumatic brain injury: Systematic review and expert consensus leading to French recommendations for good practice. *Ann Phys Rehabil Med*. 2016 Feb;59(1):42-57. doi: 10.1016/j.rehab.2015.10.003. Epub 2016 Jan 18. PMID: 26797170.

Wiat L, Luauté J, Stefan A, Plantier D, Hamonet J. Non pharmacological treatments for psychological and behavioural disorders following traumatic brain injury (TBI). A systematic literature review and expert opinion leading to recommendations. *Ann Phys Rehabil Med*. 2016 Feb;59(1):31-41. doi: 10.1016/j.rehab.2015.12.001. Epub 2016 Jan 6. PMID: 26776320.

Luauté J, Plantier D, Wiat L, Tell L; SOFMER group. Care management of the agitation or aggressiveness crisis in patients with TBI. Systematic review of the literature and practice recommendations. *Ann Phys Rehabil Med*. 2016 Feb;59(1):58-67. doi: 10.1016/j.rehab.2015.11.001. Epub 2015 Dec 14. PMID: 26700025.

Zasler, N. (2021). *Brain Injury Medicine* (3rd edition), Springer.

Lombard LA, Zafonte RD. Agitation after traumatic brain injury: considerations and treatment options. *Am J Phys Med Rehabil*. 2005 Oct;84(10):797-812. doi: 10.1097/01.phm.0000179438.22235.08. PMID: 16205436.

Questions?

