TBI TARC
Traumatic Brain Injury Technical Assistance and Resource Center

Modifying Psychopharmacologic Interventions for Traumatic Brain Injury

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Introduction & General Approach

Introduction

Alterations of mood, cognition, and behavior are common after a Traumatic Brain Injury (TBI) and are best understood in the context of a biopsychosocial model. Disruption of key brain circuitry, pre-injury personality traits, and family, sociocultural, economic, and other medical factors each play roles in determining an individual's unique symptoms.

Ideal treatment of posttraumatic neuropsychiatric symptoms involves a comprehensive, multipronged approach tailored to specific cognitive, emotional and social needs. Psychopharmacologic treatment, often a crucial component of treatment, is most effective when delivered in tandem with non-pharmacologic supportive strategies.

The goal of this brief is to provide state brain injury personnel with information to communicate with their behavioral health partners, providing them with an array of accessible approaches for modifying psychopharmacologic interventions for TBI.

General approach

Psychiatrists already possess the fundamental clinical evaluation skills needed to evaluate and treat posttraumatic neuropsychiatric symptoms effectively. Psychiatrists should feel empowered to adapt existing skill sets to meet the complex—but often highly treatment-responsive—needs of individuals with brain injury.

While symptom interpretation in TBI can be challenging and the evidence base for most interventions is relatively limited, pharmacotherapy can be a crucial component of treatment. Adherence to a systematic approach that emphasizes identification of specific psychiatric, cognitive, and behavioral target symptoms is key. These target symptoms can then be used to develop working diagnoses and guide rational pharmacotherapy. Pharmacotherapy approaches may be extrapolated from data related to the primary psychiatric disorder an individual's symptoms most resemble or informed by studies specific to TBI, if available.

Medication selection may also be driven by a hypothesis of the neurotransmitter disturbances involved based on the extent and location of structural brain injury. Because symptoms can change over time, especially early in the recovery course, ongoing monitoring for treatment response and adverse effects is essential.

Psychiatric Assessment: Modifications for TBI

Assessment begins with the standard initial psychiatric evaluation and is supplemented with additional history and examination geared toward identifying common neurocognitive and neurobehavioral sequelae of TBI that may confound psychiatric diagnosis and/or represent independently treatable target symptoms.

Please note that timing of assessment is particularly critical due to the nature of the TBI recovery process, with dramatic neurobehavioral changes expected in the first days, weeks and months following TBI.

Psychiatric interview

Cognitive impairments, especially related to self-awareness and verbal communication, may make it difficult for individuals with TBI to report symptoms accurately. Collateral information from a reliable family member or other caregiver is crucial.

In addition to the inquiries about mood, anxiety, psychosis, and other psychiatric symptoms, these domains warrant special attention in TBI: disorders of sleep and wakefulness; emotional and behavioral dyscontrol[1]; disorders of diminished motivation[2]; agitation[3]; and neurocognitive symptoms.

Medical & Neurological Review of Systems

Medical complications of TBI can contribute to neuropsychiatric symptoms, and the presence of neuropsychiatric symptoms may interfere with the injured individual's ability to seek out and participate appropriately in necessary medical care.

Neurological symptoms

Common issues include, but are not limited to:

- Headaches
- Visual disturbances and eye movement abnormalities
- Vestibular system dysfunction
- Seizures
- Dysautonomia
- Spasticity
- Chronic pain
- Neuroendocrine dysfunction
- Nausea and vomiting
- Bowel and bladder dysfunction
- Musculoskeletal pain

A full review should also include:

- Comprehensive details of injury
- Thorough pre- and post- injury functioning: personal and family
- Psychiatric history, substance use, medical, social and occupational history

Examination & Further Assessment

In addition to the psychiatric mental status exam, basic cognitive function should be evaluated with particular emphasis on attention, memory, language, and executive function.

Further neurological and medical assessment should be considered on a case-by-case basis. Neuroimaging in particular may be beneficial in demonstrating extent of injury to neural circuitry crucial for regulation of mood and behavior (especially in the frontal and temporal lobes).

Psychopharmacologic Treatment: General Principles in TBI

While identification of clear target symptoms is essential to good psychopharmacologic practice in any population, it is of the utmost importance in TBI, where the organizational structure provided by a diagnosis may not be readily available.

Absence of a clear, definitive psychiatric diagnosis need not preclude attempts at pharmacologic treatment as long as there is a solid rationale linking medication choice with target symptoms.

General Psychopharmacological Treatment Principles

Whenever Possible, Add by Subtraction First Before adding a new medication, consider whether reduction or removal of any medications might benefit target symptoms.
"Start Low, Go Slow — but Go." Individuals with TBI are sensitive to adverse effects of psychotropic medications. Initiation of any pharmacotherapy should begin with a low starting dose and be titrated gradually.
Reassess Frequently and Adjust as Needed The target symptoms, treatment response, and presence of side effects must be reassessed frequently, with therapy adjusted accordingly.
Avoid Polypharmacy — Most of the Time All efforts should be made to streamline medication regimens, but in some cases dose reduction in conjunction with addition of a low dose of a second synergistic agent may prove beneficial.

Specific Posttraumatic Neuropsychiatric Syndromes

Agitation

First-line management:

- Reduce external stimuli by minimizing light, noise and other distractions.
- Minimize use of restraints, tubes and lines.
- Staff and patient family members should frequently reorient the patient.
- Encourage proper sleep hygiene and sleep quality with a sleep schedule and bedtime routine and minimize use of electronics 30–60 minutes before bedtime.
- For restless patients, supervised ambulation may be helpful.
- Patients with aggression or behavioral issues should be managed by staff trained in de-escalation techniques.

Pharmacological Management:

- Use of beta blockers (propranolol), antiepileptic drugs (carbamazepine, valproic acid), antidepressants (selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, trazodone, lithium), antipsychotics (typical and atypical), neurostimulants (amantadine, methylphenidate) and anxiolytics (buspirone, benzodiazepines).[4,5]
- Medications should be trialed one at a time, in the lowest starting dose available and with slow increases, while monitoring for medication effectiveness and side effects. Frequent reassessment is critical.
- Be mindful that the effective dose for medications commonly used in the general population may be lower in the brain injury population due to the sensitivity of the brain after injury (although traditional therapeutic doses may ultimately be necessary). Furthermore, the need for medication and medication dosing may change during the course of brain injury recovery.
- Propranolol has the best evidence for efficacy in treating agitation in the brain injury population with no adverse effect on motor or cognitive recovery. It has been shown to improve restlessness, disinhibition, anxiety, and tremor. Consider a starting dose of 10 mg given three to four times a day with a maximum dose of 240 mg/day. Side effects include hypotension, bradycardia and lethargy. Propranolol should be considered a maintenance medication, to be given around the clock, and not on an as-needed basis for periods of acute agitation.
- For acute agitation, consider atypical antipsychotics such as quetiapine, ziprasidone, and olanzapine, again with low starting doses and given as needed. Side effects include sedation, extrapyramidal symptoms and dizziness. It is recommended to avoid use of typical antipsychotics (haloperidol) and benzodiazepines as they may hinder long-term motor and cognitive recovery, prolonged posttraumatic amnesia, and have risk of dependence and addiction.

Sleep dysfunction

Pharmacological Management:

- Use of melatonin and melatonin agonists (ramelteon), trazodone and mirtazapine.
- Medications should be trialed one at a time, in the lowest starting dose available, with slow increases, while monitoring for medication effectiveness and side effects. Frequent reassessment is critical.
- Use caution in older adults with all sedating medications, which may increase risk of nighttime falls.
- Other options used include tricyclic antidepressants (which may concurrently treat neuropathic pain and insomnia) and hypnotics (e.g., zolpidem, zopiclone, eszopiclone, zaleplon).
- Neurostimulant use for daytime arousal may facilitate nighttime sleepiness and improve sleep dysfunction. Stimulants for daytime wakefulness should typically be trialed only after attempts have been made to consolidate nighttime sleep. Modafinil, a wakefulness-promoting agent approved for the treatment of narcolepsy and excessive daytime sleepiness due to obstructive sleep apnea, may be of use.
- Non-pharmacologic interventions may also be beneficial, including bright light therapy, cognitive behavioral therapy, stimulus control, and cognitive restructuring.

Disorders of affect, mood, and anxiety

Pharmacological Management — Posttraumatic Affective Dysregulation:

- SSRIs are the first-line treatment for posttraumatic affective dysregulation and can be highly effective for this problem, typically at lower doses than are required for treatment of depression and with therapeutic benefit often seen within days of drug initiation.
- Tricyclic antidepressants (TCAs) can also be useful, though their greater side effect profile warrants some additional caution.
- Nuedexta, a combination drug comprised of dextromethorphan and quinidine, is approved for the treatment of pseudobulbar affect (pathologic laughing and crying) and can be tried if SSRIs and TCAs are unsuccessful or contraindicated.

Pharmacological Management — Posttraumatic Depression:

- SSRIs such as sertraline and fluoxetine.[6]
- Serotonin-norepinephrine reuptake inhibitors (SNRIs) and TCAs.
- Because these medications are also effective for pain, SNRIs and TCAs may be of particular utility when there are co-occurring headaches or other pain syndromes. Medications should be trialed one at a time, in the lowest starting dose available, with slow increases while monitoring for medication effectiveness and side effects.
- Cognitive behavioral therapy, problem-solving therapy, and behavioral activation training have shown favorable outcomes for treating depression in the brain injury population.

Neurocognitive Impairments

Pharmacological Management:
The most commonly used medications are amantadine, a glutamate antagonist with dopamine-modulating properties approved for treatment of Parkinson's disease and drug-induced parkinsonism; ethylphenidate, a stimulant approved for treatment of ADHD; and donepezil, an acetylcholinesterase inhibitor approved for treatment of Alzheimer's disease.

Source

Content for this brief was drawn from Section VI. Psychopharmacologic Interventions for TBI, of the Administration for Community Living. 2022. Behavioral Health Guide: Considerations for Best Practices for Children, Youth, and Adults with TBI available at: https://acl.gov/sites/default/files/programs/2022-05/TBITARC_BH_Guide_Final_May2022_Accessible.pdf. The section was written by Michael Chiou, MD, and Lindsey Gurin, MD, NYU Langone Health. The Traumatic Brain Injury Technical Assistance and Resource Center is funded by the Administration for Community Living. The Human Services Research Institute and the National Association of State Head Injury Administrators administer it.

For more information, visit https://acl.gov/programs/post-injury-support/traumatic-brain-injury-tbi.

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