TRAUMATIC BRAIN INJURY

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Introduction

• Two million people sustain a traumatic brain injury (TBI) each year
• Incidence: 120/100,000 population (Kraus, 2005)
• 300,000 require hospitalization
• 28% of all injury deaths involve TBI (Soshin, 1995)
• 80,000 of the survivors are affected (Krause and Sorenson, 1994)
Epidemiology

- #1 Cause of death in persons < 35 is TBI
- #2 Cause of death in persons < 35 is suicide
Traumatic Brain Injury

• 2% of all deaths

• 26% of all injury deaths

• Men ages 15-24 are at highest risk

(Sosin, 1989)
Common Causes Of Traumatic Brain Injury

- Motor Vehicle Accidents: 50%
- Falls: 20%
- Assaults and Violence: 10%
- Sports and Recreation: 5%
- Other: 5%
Economic Cost Of Traumatic Brain Injury

- $37.8 billion/year in the U.S. to treat 328,000 victims (Max, 1991)
- $48 billion/year in indirect and direct costs (Lewin, 1992)
- $325,000 is estimated lifetime treatment cost per patient for very severe, non-fatal brain injury
Children Are At High Risk

- 5 million children sustain head injuries each year
- 200,000 are hospitalized
- 50,000 children sustain head injuries from bicycles alone
- 400 die each year from bicycle accidents

Raphaely, 1980; HHS, 1989
Diffuse Axonal Injury

- Refers to mechanical or chemical damage to axons in cerebral white matter
- Axons are stretched, leading to cytoskeleton disruption and impaired axoplasm transport
- Occurs during high velocity accidents when there is twisting and turning of the brain around the brain stem
- Results in loss of consciousness and can occur in minor brain injury or concussion

Cassidy, 1994
Neurochemical Changes
Inconsistent Findings Affecting:

• Epi and Norepihinephrine: increase in circulating levels in CNS (McIntosh, 1994; Prasad, 1994)
• Serotonin: increase in circulating levels (Tsuiki, 1995)
• Cytokines: increase in immunocompetent cells in CNS (Fan, 1995)
• Excitatory Amino Acids: marked increase extracellular glutamate and aspartate (Palmer, 1993)
• Acetylcholine: decrease in the binding of cholinergic receptors (Jiang, 1994; Lyeth, 1994)
Mild Traumatic Brain Injury
One of the Following

• Any period of loss of consciousness
• Any loss of memory immediately before or after accident
• Any alteration of mental state at the time of the accident
• Transient or nontransient focal neurological deficits with:
  – Loss of consciousness 30 min or less
  – After 30 min, Glasgow Coma Scale, 13-15
  – Post traumatic amnesia <24 hrs

*Am Congress of Rehab Med, 1993*
Concussion Rating Scale During Sports

- Grade 1 - No LOC; Confusion without amnesia
- Grade 2 - No LOC: Confusion with amnesia
- Grade 3 - LOC

LOC = Loss of consciousness
# Rating Scales Commonly Used In Neuropsychiatry

<table>
<thead>
<tr>
<th>Scale</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structured Clinical Interview for DSM-IV (SCID)</td>
<td>Evaluate for psychiatric diagnosis</td>
</tr>
<tr>
<td>Neurobehavioral Rating Scale (NBRS)</td>
<td>Presence and severity of emotional and cognitive symptoms</td>
</tr>
<tr>
<td>Positive and Negative Symptom Scale (PANSS)</td>
<td>Frequency and severity of aggressive outbursts</td>
</tr>
<tr>
<td>Overt Aggression Scale (OAS)</td>
<td>Frequency and severity of agitation</td>
</tr>
<tr>
<td>Overt Agitation Severity Scale (OASS)</td>
<td></td>
</tr>
<tr>
<td>Factor</td>
<td>Comment</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Age</td>
<td>Morbidity and mortality increases with age</td>
</tr>
<tr>
<td>Psychiatric illness</td>
<td>Usually worsened</td>
</tr>
<tr>
<td>Neurological</td>
<td>If previous brain injury, recovery not as good</td>
</tr>
<tr>
<td>Behavioral pattern</td>
<td>Worsened</td>
</tr>
<tr>
<td>Social Supports</td>
<td>Better support networks are correlated with better recovery</td>
</tr>
</tbody>
</table>
## Factors Influencing Outcome Of Brain Injury

<table>
<thead>
<tr>
<th>Factor</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Injury</td>
<td>Diffuse axonal injury - problems with arousal, attention, &amp; cognitive processing</td>
</tr>
<tr>
<td>Severity</td>
<td>More severe the injury, worse the prognosis.</td>
</tr>
<tr>
<td>Anosmia*</td>
<td>Major vocational problems</td>
</tr>
</tbody>
</table>

*Loss of sense of smell*
## Factors Influencing Outcome Of Brain Injury

<table>
<thead>
<tr>
<th>Factor</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intellectual</td>
<td>Greater preinjury intelligence predicts better recovery</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td>If intoxicated at time of injury, lower level of functioning upon discharge.</td>
</tr>
<tr>
<td></td>
<td>If history of substance abuse, increased morbidity and mortality</td>
</tr>
</tbody>
</table>
Neuropsychiatric Sequelae Of Traumatic Brain Injury

Intellectual Changes

Dysfunctions in the following:

• Attention and arousal
• Concentration
• Executive functioning
• Memory impairment
Executive Functions

Dysfunctions in the following:
• Setting goals
• Assessing strengths and weaknesses
• Planning and/or directing activity
• Initiating and/or inhibiting behavior
• Monitoring current activity
• Evaluating results
Intellectual Changes

- Can be quite subtle
- Difficult to diagnose on cursory cognitive testing
Neuropsychiatric Sequelae Of Traumatic Brain Injury

- Personality changes
- Mood disorders
- Delirium
- Psychoses
- Post-traumatic Epilepsy
- Anxiety disorders
- Agitation and aggression
- Irritability
# Behavioral Syndromes Related To Specific Frontal Lobe Damage

<table>
<thead>
<tr>
<th>Frontal Lobe Location</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbitofrontal</td>
<td>Impulsivity, disinhibition, hyperactivity, distractibility, mood lability</td>
</tr>
<tr>
<td>Dorsolateral frontal cortex</td>
<td>Slowness, apathy, perseveration</td>
</tr>
<tr>
<td>Inferior orbital surface of frontal lobe (&amp; anterior temporal lobes)</td>
<td>Rage and violent behavior</td>
</tr>
</tbody>
</table>
Differential Diagnosis Of Mood Disorders

• Symptoms secondary to brain injury
  – Mood lability
  – Apathy (decreased motivation)
  – Slowness in thought and cognitive processing

• Premorbid disorders
  – Depression
  – Alcoholism
  – Personality Disorders
Prevalence Of Depression Following TBI

• 2.5 years after injury: 42% (Kreutzer, 2001)

• 8 years after injury: 61% (Hibbard, 1998)
Depression

• Incidence and severity NOT related to:
  – Duration of LOC
  – Duration of post-traumatic amnesia
  – Presence or absence of skull fractures

• IS related to:
  – Extent of neuropsychological impairment

• More common in:
  – Left anterior frontal regions

Bornstein, 1988 and 1989
Major Depressive Disorder (MDD After TBI)

- 66 hospitalized patients
- 25% diagnosed with MDD at 1, 3, 6, & 12 months following TBI
- 42% developed MDD by one year
- 4.7 months - mean duration (range 1.5-12 months)

Jorge et al. 1993
Suicide

- Occurs more frequently in people with histories of TBI (Oquendo, 2004)

Study:
- 42 patients with severe TBI
  - After 1 year
    - 10% suicidal ideation
    - 2% suicide attempts
  - After 5 years
    - 155 suicide attempts

Brooks, 1990
Delirium

- Common in patients emerging from coma
- Prominent symptoms:
  - Restlessness - Disorientation
  - Agitation - Delusions
  - Confusion - Hallucinations
- Frequently termed “post-traumatic amnesia”
- Rancho Los Amigos Scale Level IV (confused, agitated) or V (confused, inappropriate)
Frequent Causes Of Delirium In TBI Patients

- Mechanical effects
- Cerebral edema
- Hemorrhage
- Infection
- Subdural hematoma
- Seizures
- Increased intracranial pressure
Frequent Causes Of Delirium In TBI Patients, Cntd.

- Alcohol intoxication or withdrawal
- Reduced hemoperfusion related to multiple trauma
- Fat embolism
- Change pH
- Electrolyte imbalance
- Medications (sedative/hypnotics, steroids, opioids, etc.)

Trzepacz, 1994
Psychotic Disorders

- No standard definition of psychosis in the literature (Andreasen, 2000)
- May occur immediately following brain injury or after a long latency period
- Symptoms may persist despite cognitive improvement
- DSM-IV-TR Diagnosis: Psychotic disorder due to a general medical condition (2000)

Smeltzer, 1994; Nasrallah, 1981
Prevalence Of Psychotic Disorders

- 3.4% of 530 head injury patients followed up to 10 years after injury
- 5.9 year mean latency from TBI to psychosis (Fujii, 1996)
- 26% of 2907 Finnish war veterans developed psychosis (Violon and DeMoi, 1987)
  - 14% developed paranoid schizophrenia
    - All had left temporal lobe abnormalities (Buckley, 1993)
- 1-15% of inpatients with schizophrenia reviewed between 1917-1964 had histories of brain injury (Davison and Bagley, 1969)
Post-traumatic Epilepsy
Risk Factors

- Skull fractures
- Penetrating wounds
- History of chronic alcohol use
- Intracranial hemorrhage
- Increased severity of the injury
Prevalence Of Post-Traumatic Epilepsy

- 12% of severe injury
- 2% of moderate injury
- 1% of mild injury

Annegees, 1980
Delayed Onset Of Seizures

- 53% of 421 Vietnam veterans had post-traumatic epilepsy
  - 18% had first seizure after 5 years
  - 7% had first seizure after 10 years

Salazar, 1985
Post-traumatic Epilepsy and Psychosis

- 7-8% of TBI patients with epilepsy have persistent psychoses
- Difficult to distinguish from schizophrenia
- DSM-IV diagnosis - Delusional disorder due to traumatic injury
Adverse Effects Of Anticonvulsant Medications

- Phenytoin and carbamazepine may produce negative effects on cognitive performance, esp. motor and speed performance (R/O folate deficiency with phenytoin)

  Smith, 1983

- Treatment with more than one anticonvulsant is associated with increased adverse neuropsychiatric reactions.

  Reynolds & Trimble, 1986
Adverse Effects Of Anticonvulsant Medications

- Phenytoin and carbamazepine have no prophylactic effect on seizures during the first week following TBI
- May be a role for valproate

Temkin, 1990; Yablons, 1993
Anxiety Disorders Prevalence

- 24% of TBI patients have generalized anxiety disorder after TBI (Fann, 2000); However, many of these had anxiety prior to their injury.

- 29% of 1199 patients evaluated between 1942-1990 developed clinical anxiety (Epstein, 1994).
Post-concussion Syndrome

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Specific Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic</td>
<td>Headache, dizziness, fatigue, insomnia</td>
</tr>
<tr>
<td>Cognitive</td>
<td>Memory difficulties, impaired concentration</td>
</tr>
<tr>
<td>Perceptual</td>
<td>Tinnitus, sensitivity to noise and light</td>
</tr>
<tr>
<td>Emotional</td>
<td>Depression, anxiety, irritability</td>
</tr>
</tbody>
</table>

*Lishman, 1988; Silver, 1990*
Post-concussion Syndrome

Neuropsychological Testing Results

- Poorer performance on tests of reasoning, information processing, verbal learning
- Abnormal SPECT, computerized EEG, and brainstem auditory evoked potentials

Leininger, 1990; Hugenholtz, 1988
Post-concussion Syndrome

Laboratory Results

• Normal MRI and CT

• May occur many months after injury

Leininger, 1990; Hugenholtz, 1988
Post-Concussion Syndrome

Other Residual Symptoms

- 22% Decreased energy
- 22% Dizziness
- 47% Headaches
- 47% Memory loss
- 54% Irritability
Characteristics of Patients Who Develop Prolonged Post-Concussive Syndrome

- More likely to have been under stress at the time of the injury
- Develop depression or anxiety within a short period
- Experience extensive social disruption
- Exhibit physical symptoms (esp. headaches and dizziness)

*Alexander, 1995*
PTSD vs Post-concussive Syndrome

- Sometimes difficult to differentiate between the two (Warden, 2005)
- Post-concussion symptoms usually decrease within 3 months; PTSD persists, untreated
- Patients with amnesia secondary to TBI can develop PTSD (McMillen, 1991)
Agitation And Aggression Following Severe TBI

- 34-96% Exhibit Agitation or Aggression (Levin, 1978; Tateno, 2003)
- 40% Exhibit Restlessness (van der Naalt, 2000)
- 34% Exhibit Irritability (Hibbard, 1998)
Characteristic Features of Neuroaggressive Disorder

- **Reactive**
  - Triggered by modest or trivial stimuli
- **Nonreflective**
  - Usually does not involve premeditation or planning
- **Nonpurposeful**
  - Aggression serves no obvious long-term aims or goals

*Yudofsky et al, 1990*
Characteristic Features of Neuroaggressive Disorder

- **Explosive**
  - Buildup is NOT gradual

- **Periodic**
  - Brief outbursts of rage and aggression; punctuated by long periods of relative calm

- **Ego-dystonic**
  - After outbursts patients are upset, concerned, embarrassed: as opposed to blaming others or justifying behavior

*Yudofsky et al, 1990*
Other Common Neuropsychiatric Causes Of Agitation and Aggression

• Chronic neurological disorders (Huntington’s disease, Wilson’s disease, Parkinson’s disease, multiple sclerosis, systemic lupus erythematosus)
• Brain tumors
• Infectious disease (encephalitis, meningitis, AIDS)
Other Common Neuropsychiatric Causes of Agitation and Aggression, Cntd.

• Epilepsy (ictal, post-ictal, and inter-ictal)
• Metabolic disorders (hyperthyroidism or hypothyroidism, hypoglycemia, vitamin deficiencies, porphyria)
<table>
<thead>
<tr>
<th>Medication</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedative-hypnotic agents (including EtOH)</td>
<td>Intoxication and withdrawal</td>
</tr>
<tr>
<td>Stimulants (amphetamines, cocaine, caffeine)</td>
<td>Manic-like excitement</td>
</tr>
<tr>
<td>Steroids (including anabolic)</td>
<td>Therapeutic doses and withdrawal</td>
</tr>
</tbody>
</table>
General Principles Of Psychopharmacologic Treatment

- TBI patients are more sensitive to medication side effects
- Doses must be raised and lowered in small increments over longer periods of time
- Therapeutic doses may be the same as the non-brain injured patient
- Frequent reassessment to determine medication efficacy is important
Pharmacologic Treatment of Impairments of Attention and/or Memory after TBI

- Dextroamphetamine
  - Dose: Initial 2.5 mg bid; Maximum 30 mg bid
- Methylphenidate
  - Dose: Initial 5 mg bid; Maximum 30 mg bid
- Side effects for both
  - Paranoia, agitation, irritability, depression
  - Probably no decrease in seizure threshold
- Comments for both
  - Both agents may improve memory and learning attention and behavior
Pharmacologic Treatment of Impairments of Attention and/or Memory after TBI

Sinemet (L-DOPA/CARBIDOPA)

- Dosage range - 10/100 - 25/250 mg qid
- Side effects - sedation, nausea, psychosis, HAs, delirium
- Benefits - improved alertness and concentration; increased energy; increased memory, speech, mobility
Pharmacologic Treatment of Impairments of Attention and/or Memory after TBI

Bromocriptine (Parlodel)

- Dosage range - 2.5 mg/d up to 10 mg/d
- Side effects - sedation, nausea, psychosis, HAs, delirium
- Benefits - improved alertness and concentration; increased energy; increased memory, speech, mobility, improvement in nonfluent aphasia, akinetic mutism, and apathy.

? Anticholinergic properties
Pharmacologic Treatment of Impairments of Attention and/or Memory after TBI, Cntd.

Amantadine

- Initial dose - 50 mg bid
- Maximum dose - 200 mg bid
- Side effects - confusion, hallucinations, edema, hypotension
- Benefits - Treatment of anergy, abulia (passivity and indifference), mutism, anhedonia
Pharmacologic Treatment of Depression after TBI

- Heterocyclic and SSRI Antidepressants are effective in treating depression associated with TBI
- Post-TBI patients are highly sensitive to anticholinergic and parkinsonian side effects of heterocyclics
- All Antidepressants May Increase the Frequency of Seizures in patients after TBI, with: Bupropion and heterocyclics >> SSRIs, Venlafaxine
Somatic Treatment of Major Depression after TBI: ECT

- Underutilized
- Safe and effective
- Nondominant, unilateral preferred
- Fewer treatments (4-6) recommended
- Increased spacing between treatments (2-5 days)
- Use of lowest possible energy for seizure elicitation (at least 20 sec in duration)
# Pharmacologic Treatment of Mood Liability in Patients After TBI

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>40-80 mg</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>100-200 mg</td>
</tr>
<tr>
<td>Nortriptyline (Pamelor)</td>
<td>100-150 mg</td>
</tr>
</tbody>
</table>
Pharmacologic Treatment of Psychosis in Patients Following TBI: First-Generation Antipsychotic Medications

- High rates of dystonia, akathisia, Parkinsonian side effects
- TBI may make patients more vulnerable to tardive dyskinesia (Kane, 1982)
- May produce hypotension, sedation and confusion
- May impede neuronal recovery
- Should be used sparingly and at low doses
- Start with 33% to 50% of usual dose (McAllister, 1998)
- May have a delayed onset of action (Stanislav, 1997)
Pharmacologic Treatment of Psychosis in Patients Following TBI: Second-Generation (Atypical) Antipsychotic Medications

- First-line medication for treatment of psychosis associated with TBI (Corcoran, 2005)
- Well-tolerated for psychoses following TBI
- Far fewer Parkinsonian side effects and less emergence of tardive dyskinesia
- In treatment of chronic psychosis associated with TBI, be alert for emergence of metabolic syndrome
Clozapine

• Initial dose 50-100 mg

• Benefits
  – No EPS
  – Positive effect on negative symptoms

• Comments
  – 1% risk of agranulocytosis
  – Weekly blood draws
  – Highly anticholinergic
  – Sedation, hypotension
  – Lowers seizure threshold
    – 1-2% risk <300 mg
    – 5% risk 600-900 mg

Lieberman, 1989; Burke, 1999
Pharmacologic Treatment of Generalized Anxiety Disorder Associated with TBI

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buspirone (Buspar)</td>
<td>10-30 mg bid</td>
<td>No motor incoordination, dependence or tolerance</td>
<td>Delayed onset of action; sedation, dizziness, less effective in recent benzo. users</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>0.5-2 mg tid-qid</td>
<td>Fast onset of action, sedation</td>
<td>Motor incoordination, memory disturbance, dependence, tolerance, ataxia, sedation</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.5-2 mg bid tid</td>
<td>As above Longer half-life</td>
<td>As above More sedation</td>
</tr>
</tbody>
</table>
General Principles
Psychopharmacology Treatment of PTSD Associated with TBI

• Positive symptoms (re-experiencing the event, increased arousal) improve with medication

• Negative symptoms (avoidance and withdrawal) respond poorly to medication
Psychopharmacologic Treatment Of PTSD Associated with TBI

- Consider Zolpidem, Temazepam or Trazodone
- Add Valproate or Carbamazepine
- Add Propranolol or Clonidine
- Change to Venlafaxine, MAOI or add Lithium

Significant distress on re-exposure
Persistent anger distress on re-exposure
Sleep disturbance
Refractory depression and anger
Persistent flashbacks

SSRI
TCA

Silver, Hales & Yudoksy
Common Sleep Problems in TBI Patients

- Impaired REM
- Multiple nocturnal awakenings
- Hypersomnia is more common with missile injury (Castriotta, 2001; Masel, 2001)--usually resolves < 1 yr
- Insomnia is common following coma and diffuse CNS injury has more chronic course
- Daytime fatigue is a common problem (Rao, 2005)
Clinical Challenges of Pharmacologic Treatment of Insomnia in Patients After TBI

<table>
<thead>
<tr>
<th>Medications to Avoid</th>
<th>Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbiturates</td>
<td>Interfere with REM, sleep stages</td>
</tr>
<tr>
<td>Benzodiazepines (esp. long acting)</td>
<td>Motor incoordination, confusion decreased memory, tolerance, dependence</td>
</tr>
<tr>
<td>OTC Preparations</td>
<td>Anticholinergic side effects</td>
</tr>
</tbody>
</table>

Buysse and Reynolds, 1990
# Pharmacologic Treatment Of Insomnia In TBI Patients

<table>
<thead>
<tr>
<th>Medications to Consider</th>
<th>Problems/Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trazodone 50-100 mg</td>
<td>Hypotension, daytime sedation</td>
</tr>
<tr>
<td>Zolpidem; zalepon; 5-10 mg</td>
<td>Cost, short half-life</td>
</tr>
</tbody>
</table>

*Buysse, 1990; Rao, 2005*
Pharmacologic Treatment of Acute Agitation Or Aggression Associated with TBI: General Principles

• No FDA approved medication
• Using (mis-using) sedative side effects to treat aggression or agitation
• Patients develop tolerance to sedation from neuroleptics and benzodiazepines
• Medications may impair arousal and cognitive function
Use of Haloperidol in the Treatment of Acute Agitation or Aggression Associated with TBI

• Initiate haloperidol - 1 mg po or 0.5 mg IM or IV, q1h
• Increase dose by 0.5-1 mg q1h until agitation or aggression is controlled
• Maintain at a maximum dose of 2 mg po or 1 mg IV or IM bid-tid (i.e., 3-4 mg qd)
Use of Haloperidol in the Treatment of Acute Agitation or Aggression Associated with TBI

- When patient is not agitated or violent for a period of 48 hrs, taper daily at a rate of 25% of highest total daily dose
- If agitation reemerges upon tapering drug, reassess etiology and consider changing to a more specific medication
- Do not maintain patient on haloperidol for >6 weeks - except for agitation or aggression secondary to psychosis
Use Of Lorazepam In The Treatment Of Acute Agitation Or Aggression Associated with TBI

- Initiate lorazepam - 1-2 mg po, IM or IV
- Repeat q1h until control of agitation or aggression is achieved
- If IV dose must be given, push slowly! Do not exceed 2 mg (1 ml) per min to avoid respiratory depression and laryngospasm; may be repeated in 30 min if required
- Maintain at a max dose of 2 mg po, IM or IV tid-qid (i.e., 8 mg qd)
Use of Lorazepam in the Treatment of Acute Agitation or Aggression Associated With TBI, cntd.

- When patient is not agitated or violent for 48 hours, taper daily at 10% of highest total daily dose
- If agitation reemerges upon tapering drug, reassess etiology and consider changing to a more specific medication
- Do not maintain patient on lorazepam for >6 wks - except for agitation or aggression secondary to generalized anxiety disorder
**- Blockers in the Treatment of Chronic Aggression Associated With CNS Lesions**

- First reported in 1981 to treat chronic aggression in adults and children with organic brain syndromes and adults with Korsakoff’s psychosis (Yudofsky, 1981, 1984)
- More than 35 papers published since 1981 related to treatment of chronic aggression or agitation in patients with CNS lesions (Silver, 2005)
Key Characteristics Of Propranolol

- Peripheral beta receptors are saturated at 300-400 mg/d (i.e., no further ↓ BP or ↓ HR)
- Often a latency of 6-8 weeks
- Depression is an uncommon side effect (~9%)
- Increase plasma levels of neuroleptics
- Avoid combination with thioridazine (Mellaril) because of Mellaril’s 800 mg absolute dosage ceiling
Common Causes of Chronic Agitation and Aggression Associated with CNS Impairments

- Traumatic brain injury
- Stroke and other cerebrovascular disease
- Medications, alcohol and other abused substances, over-the-counter drugs
- Delirium (hypoxia, electrolyte imbalance, anesthesia and surgery, uremia, etc.)
- Alzheimer’s disease
### Categories of Medications Associated with Agitation and Aggression In Patients with TBI

<table>
<thead>
<tr>
<th>Medication</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics (opiates &amp; other narcotic analogs)</td>
<td>Intoxication and withdrawal</td>
</tr>
<tr>
<td>Anticholinergic agents</td>
<td>Including OCT meds</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Esp. in early stages of Rx</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Esp. high potency agents</td>
</tr>
<tr>
<td>Hallucinogens (LSD, PCP, etc.)</td>
<td>Intoxication</td>
</tr>
</tbody>
</table>