Brain Injury Psychopharmacology: Understanding Symptoms, Syndromes and Medication Interventions

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Learning Objectives

- Participants will learn about brain injury dynamics and neuroanatomy of brain injury.
- Participants will learn about syndromes specific to brain anatomy.
- Participants will learn about medication interventions for differing syndromes related to brain injury deficits and dysfunction throughout the recovery process.
Disclosures and Disclaimers

- I am **not** a physician and **I do not prescribe** medications. I am a neuropsychologist with 23 years experience in brain injury rehabilitation and treatment and will be describing treatments based upon experience and education in Brain Injury Rehabilitation.

- Many medications described in this presentation will be “off label” with regard to FDA approval for primary use. I do not personally or professionally recommend that anyone who is present today (or reads this presentation at some other time) make decisions regarding prescription of **ANY** medications based solely upon this presentation.

- Always use good clinical judgment, the counsel of educated and well trained professionals, and published information when deciding on use of medications.
Trauma to the head generates many injuries

- Direct Impact to the Skull
- Coup-Contracoup Injuries
- Shear and Strain Injuries
- Brain-Blood vessel Injuries
- Swelling of Bruised Tissue
Coup-Contra Coup Damage

- Damage Occurs in a direct line from impact through the brain
- When forces rotate, extra force stretches and shears the underlying white matter
Skull and White Matter: Brain Support that Matters

- Base of the Skull is Bony and Rough
- Brain Physically moves on top of the Skull Surface during acceleration/deceleration.
- Rubbing Causes Irritated tissue and tissue death

- White matter consists of bundles of axonal “wires” that transmit Neuron signals to other parts of the Cortex.
- Trauma causes compression, stretching, rotational twisting and shearing
- Axonal damage doesn’t always involve cell death, but injury fundamentally changes the axon’s ability to transmit a signal
• **Cell Membrane Injuries**
  - Changes in Molecular Permeability (Calcium overload and Free Radical Exposure)
  - Anoxic Trauma
  - Autodestructive and Neuroprotective Responses

• **Necrosis Occurs via Complex Processes**
  - Rapid influx of Calcium into the cell via damaged plasma membrane
  - Acute swelling of the Endoplasmic Reticulum
  -Activation of Ca-dependent degradative enzymes (lipases, proteases, nucleases)
  -Membrane lipid metabolites are generated (prostaglandins, thromboxanes, leukotrienes)
  -Platelet Activating Factor produced
• **Frontal lobes**
  – Inferior Frontal lobe damage
  – Associated with disinhibition, irritability, impulsivity, poor judgment

• **Superior frontal lobe damage**
  – Associated with apathy, poor motivation, lack of organization, initiative, perseveration, inattention.
• Temporal lobe damage
  – Memory induced behavior disorder-poor execution of behavior, deficits in range of behavior, frustration related to deficits, language disorder
  – Limbic system induced behavior disorder-aggression (both predatory and agitated) hyper or hyposexuality, hyperreligiosity.
Limbic System: Structure by Structure

- **Thalamus**
  Gateway of sensory Information
  Almost all input to brain travels through this structure

- **Hippocampus**
  Essential for the formation of new memories

- **Amygdala**
  Powerful “animal” passion center
  Sexuality, Aggression, Strongest of emotional experiences

- **Fornix**
  Connects the hippocampus and septal bodies

- **Mammillary Body**
  Receives information from Hippocampus, visual system
  Outputs to the Reticular System (activation of motor response)

- **Dentate Gyrus**
  Part of Hippocampal Formation
  Involved in regulation of affect and physical activity/motivation

- **Septum**
  Involved with Sexuality and Pleasure

- **Cingulate Gyrus**
  Involved in memory and motivational control

- **Olfactory Bulb**
Parietal/Occipital lobe damage
- Neglect syndromes-visual neglect, body neglect, inattention syndromes (specific to sensory input)
- Anosognosia (neglect of deficits)- can produce the most intractable behavioral problems, resistance to treatment, unsafe behavior
- Perceptual/Sensory distortions-field cuts, visual distortion
Early Interventions Common for CHI Patients

- Recovery follows a predictable path-
  Ranchos Los Amigos Scales Ratings
  - **LEVEL ONE-NO RESPONSE**
    - No behavior to monitor
  - **LEVEL TWO-GENERALIZED RESPONSE**
    - Responsiveness to pain, still no consistent behavior
  - **LEVEL THREE-LOCALIZED RESPONSE**
    - Responds to strong stimuli, begins to exhibit behavior, but disorganized, confused and easily agitated. Can become violent, disinhibited and aggressive
  - **LEVEL FOUR-CONFUSED/AGITATED**
    - Alert, often ambulatory. Easily overstimulated by the environment, resulting in agitation/aggression, behavior lacks purpose or goal and may appear strange to the untrained eye

- Levels 1-2 usually only in ER/ICU settings
  - Memantine
  - Mannitol/resectisol
  - Dilantin

- Level 3-4 require multiple levels of environmental and medical interventions
  - Low stimulation
  - Environmental control and structure
  - Medications that address behavior excesses and deficits
Frontal Lobe Pathologies and Medications

• **Concept of “Frontal Tone”**
  – Generalized Hyper-responsivity
  – Easily agitated
  – Pressured Speech (without manic features)

_Propanolol (Inderal) has been used as both effective and benign intervention (BP checks must be conducted to avoid hypotension)_

• **Orbital-Frontal Syndromes**
  – Aggressive, hyperactive, impulsive, euphoric, sexually disinhibited, poor judgment
  – Clinically, may present as manic
  – Often related to frontotemporal Injuries (with temporal lobe involvement)

_Medications have been used including Depakote, Topomax, Stimulants, Tenex (Guanfacine), Major Tranquilizers (Risperdol, Seroquel, Zyprexa etc.)_

• **Superior Frontal Syndromes (Mesial Frontal)**
  – Apathy, paucity of responding
  – Poor initiation
  – Flat affect, aprosodic speech

_Stimulants can be quite helpful_
Temporal Lobe and Affect
- Limbic System Damage can generate both aggression, hypersexuality, uncontrollable anger, uncontrollable depression symptoms, “manic” features, general emotional lability
- Mood stabilizing medications including Depakote, Lamictal, Trileptal
- Antipsychotics including Abilify, Seroquel, Zyprexa, Thorazine (generally only when agitation is also present)
- Be Cautious about using antidepressants as serotonergic medications can exacerbate lability and agitation.

Temporal Lobe and Memory
- Amnestic Syndromes
- Deficits in Learning and carryover

Stimulants
- Ritalin, Focalin, Adderall, Vyvance, Strattera

Non-stimulant Cognitive Enhancing Drugs
- Amantadine
Posterior Syndromes Involving Parietal/Occipital Lobes

Neglect Syndromes and Anosognosia
• These are difficult to address from a medication standpoint.
• Anosognosia can rise to a delusional level (not unlike paranoid delusions)
• Stimulants can be helpful for simpler neglect/hemi-neglect (along with therapies targeting attention to the neglected field)
• Antipsychotic medications may be necessary to limit the agitation that results from a complete denial of disability and agitation
Sleep

- Very important to obtain good data on sleep patterns
- Onset, maintenance, sleep during the day, history
- Trazadone, Ambien, Amitriptyline, Clonazepam
- Avoid Xanax, Ativan, Valium, if possible; generates disinhibitory effects
Depression is a process and a result of resources that have overwhelmed a problem.

- Attempts to solve problem fail
- Attempts are repeated without modifying the solution (no new resources)
- Failure leads to helplessness, frustration, despair, negativity etc.
Basic Depression Symptoms

- Sleep-Hypersomnia, insomnia, sleep onset, sleep maintenance
- Appetite- either extreme
- Weight-gain or loss
- Subjective depression
- Crying
- Uncontrolled anger
- Helplessness
- Hopelessness
- Worthlessness

SIGNS YOU MAY BE SUFFERING FROM DEPRESSION

- You've got enough Prozac in your purse to tranquilize King Kong.
- You really lose it whenever someone says, "Good morning."
- You keep your house so dark that mushrooms are growing in the carpet.
- Given a choice, you'd have no preference between sex or a root canal.
More Symptoms of Depression

- Guilt
- Withdrawal
- Loss of Interest
- Inertia
- Sexuality
- Suicide
- Homicide
MORE SIGNS YOU MAY BE SUFFERING FROM DEPRESSION

- On a really bad day, you wouldn't come to the door if it was Publishers Clearing House.
- You list Dr. Kevorkian as a character reference.
- Alcohol gives you strength and food settles your nerves.
- Your hands shake so badly that you can brush your teeth without any voluntary movement.
- You've cried so much that your contacts have rusted to your eyeballs

- Clinical Depression has an 8% lifetime Prevalence
- Brain Injured Patients have lifetime prevalence as high as 80%
- TBI related depression has impact on
  - Rehabilitation failure
  - Inability to live independently
  - Inability to Work
  - Divorce rate
  - Social Isolation
  - Loss of support
TBI Changes the way the patient interacts with the environment

- Negative Feedback Perseveration Escalation
- Negative Feedback Withdrawal Multiple Loss
- Negative feedback Agitation Problem Behavior
- Disrupted Economics Loss Negative Feedback
- Disrupted Relationship Loss Negative Feedback
MANY ANTIDEPRESSANT MEDICATIONS ARE NOW AVAILABLE

- Effexor
- Pristiq
- Cymbalta
- Wellbutrin
- Prozac
- Paxil
- Zoloft
- Luvox
- Celexa
- Lexapro
- Remeron
Wonder Drugs or “Wonder?” Drugs

**Aricept**
- Acetylcholinesterase Inhibitor
- Approved for the treatment of Mild to Moderate Alzheimer’s Disease
- Has modest effects on cognitive functioning for DAT patients.
- Conflicting evidence with studies that have demonstrated both efficacy and non-efficacy

**Ambien**
- Mild Hypnotic used for sleep onset difficulties
- Several Case studies published on Anoxic Brain Injured pt’s with dramatic results.
- Effects are dependent on continued use, but at least one study revealed continued effect after long-term use.

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Cholinergic augmentation with donepezil enhances recovery in short-term memory and sustained attention after traumatic brain injury1, 2


Increased Arousal in a Patient with Anoxic Brain Injury After Administration of Zolpidem Cohen, Sara I. MD; Duong, Thao T. MD. American Journal of Physical Medicine & Rehabilitation: March 2008 - Volume 87 - Issue 3 - pp 229-231
Case Studies

D. R. Sleep Data

- Start Trazadone
- Last increase of Trazadone

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Legend:
- Sleep
24 year old female, 6 months s/p chi with severe frontal lobe injury, prefrontal indications of impulsivity, poor judgment, decreased tolerance to stimuli.

**D. A. Attempts to Leave Area**

![Graph showing cumulative record over time with specific dates marked for when Topamax started and Point Sheet started.]
29 year old male with severe TBI, subdural hematoma with uncal herniation, rib fracture. Seen 3 months post injury. Acute care meds were Zyprexa, 2.5mg, TID, Morphine, 30mg, BID, Amantadine, 100mg, BID. (pt did not T/F with the morphine prescription) Pt was initially inattentive, sedate and inconsistently cooperative during sessions. Not able to voice needs consistently. Started by D/C Amantadine, reduce Zyprexa to BID, then to HS only. Pt became more alert and interactive, but also more impulsive, aggressive. Looked at behavior architecture, suggesting continued pain and started Ultram, 50mg, BID.
14 year old male with TBI admitted 6 months s/p injury. TBI included frontal contusion, evidence of diffuse axonal injury, multiple facial fractures. Admit medications were Depakote, Levothyroxine, Trazadone and Zyprexa. Pt. presented with classic “frontal tone” symptoms of agitation, pressured responses, aggression, hyper-responsiveness to his environment.

C. M. Added Propanolol
Questions & Comments