



Catatonia, NMS, and Serotonin Syndrome

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Catatonia: How common is it?

- 7.8-9.0% prevalence rate
 - Highest rates in non-psychiatric (i.e., medical) settings and in patients undergoing ECT.
- 1.6-5.5% of all patients seen on psychiatry consultation service
 - Prevalence higher for older patients
- Up to 46% of cases may have etiology that is not primarily psychiatric

When are you called?

- Staff reports the patient is “Playing **POSSUM**”
- **P**erseveration (speech or behavior)
- **O**ppositionality to all requests
- **S**peech that trails off or is whispered
- **S**lowed response to questions or commands
- **U**ndernourished (reports of decreased PO intake)
- **M**otionless but awake

Diagnosing Catatonia: DSM-5

DSM-5 requires 3 or more of the following:

- Catalepsy
- Waxy flexibility
- Stupor
- Agitation
- Mutism
- Negativism
- Posturing
- Mannerisms
- Stereotypies
- Grimacing
- Echolalia
- Echopraxia

Bush-Francis Rating Scale

- Excitement
- Immobility/stupor
- Combativeness
- Autonomic Abnormality
- Impulsivity
- Mutism
- Staring
- Posturing/catalepsy
- Grimacing
- Echopraxia/echolalia
- Stereotypy
- Mannerisms
- Verbigeration
- Rigidity
- Negativism
- Waxy flexibility
- Withdrawal
- Automatic Obedience
- Mitgehen
- Gegenhalten
- Ambitendency
- Grasp Reflex
- Perseveration

Challenges with Diagnosis

- Clarifying specific symptoms can be difficult
 - Rigidity vs. gegenhalten vs. negativism
- Inconsistency between scales
- Symptoms occur on a spectrum
- Wide variety of manifestations

Prototypes of Catatonia

- The Distant Mute
 - Mutism, immobility, interpersonal withdrawal
 - Team may be concerned this is volitional
- The Waxy Stiff
 - Catalepsy, waxy flexibility, rigidity
 - Often identified by physicians; may misattribute to psychiatric illness
- The Broken Record
 - Echophenomena, verbigeration, hyperactivity
 - Often misdiagnosed as delirium
- The Stubborn Grouch
 - Negativism, repetitive movements, excitement
 - Medical workup often not completed due to lack of cooperation.

Pathophysiology of Catatonia

- Disruption in the tracts connecting the basal ganglia and the cortex, leading to relative hypodopaminergia.
 - Dorsolateral prefrontal and anterior cingulate / medial orbitofrontal → akinetic mutism, dysautonomia
 - Lateral orbitofrontal → imitative and repetitive behaviors
 - Supplementary motor / motor / posterior parietal → rigidity, initiation and termination of movement
- Hyperactivity of the supplementary motor area and presupplementary motor area → motor control, initiation and inhibition of movement

Pathophysiology of Catatonia

- GABA and serotonin may be involved
 - The dopaminergic projections in the brain are modulated by GABA-ergic and serotonergic neurons.
 - Benzodiazepines (GABA-A agonists) are helpful
 - GABA-B agonists (baclofen) are harmful and can induce catatonia
 - Serotonergic medications also may induce catatonic symptoms.
- Glutamate may also play a role
 - Anti-NMDA receptor encephalitis can cause catatonia.
 - NMDA receptor antagonists have been used as treatments in some cases.

Evaluating Catatonic Patients

- Observe patient while trying to engage in conversation.
- Scratch your head in an exaggerated manner.
- Examine the patient's arms for cogwheeling. Move the arms with alternating lighter and heavier force.
- Move patient's arm into different positions and observe whether they remain in position.
- Ask the patient to extend his/her arms. Place one finger beneath each hand and try to raise it slowly after stating, "Do not let me raise your arms."

Evaluating Catatonic Patients

- Extend your hand and state, “Do not shake my hand.”
- Reach into your pocket and state, “Stick out your tongue. I want to stick a pin in it.”
- Check for grasp reflex.
- Check the chart for reports from prior 24 hours. Check for PO intake, VS, and incident.
- Observe the patient indirectly daily to observe for other catatonic symptoms.

Potential Causes of Catatonia

- Medical Illness
 - Seizures
 - CNS structural damage
 - Encephalitis (e.g., anti-NMDA) or other CNS infection
 - SLE with or without cerebritis
 - Disulfiram
 - Phencyclidine
 - Neuroleptic exposure
 - Corticosteroid exposure
 - Porphyria
 - Post-partum state
 - Iron deficiency
- Psychiatric Illness
 - MDD
 - Bipolar Disorder
 - Psychotic disorders

Workup for Catatonia

- Complete Blood Count, Comprehensive Metabolic Panel
- Creatine Kinase (to look for rhabdomyolysis)
- Iron studies
- Toxicology screens
- Other bloodwork as indicated
 - Cultures
 - HIV
 - Paraneoplastic panel
 - Autoimmune studies
- Consider head CT, brain MRI, and EEG

Catatonia vs. Delirium

- DSM-5 states that catatonia cannot be diagnosed when symptoms are present exclusively in the setting of delirium
- Clinical practice suggests that most patients with neuromedical etiology for catatonia also have delirium
- 12-37% of patients with delirium may have features of catatonia
 - More commonly associated with hypoactive delirium and more common in women
 - Common features of catatonia include excitement, immobility, mutism, negativism, staring, withdrawal

Subtypes of Catatonia

- DSM-5 specifiers:
 - Hyperactive
 - Hypoactive
 - Mixed level of activity
- Malignant Catatonia (aka Lethal Catatonia)
 - Characterized by severe muscle rigidity, hyperthermia, and autonomic instability
 - Delirious Mania
 - Neuroleptic Malignant Syndrome
 - Serotonin Syndrome

Management of Catatonia

- Identify the underlying cause.
 - Perform full psychiatric evaluation to identify mood or psychotic disorders.
 - Obtain collateral information about patient's mood and behavior prior to admission.
 - Perform medical workup, especially for those with other symptoms of medical illness.
- Frequent vital signs
- Supportive care
- Remove possible culprit medications
- Initiate treatment with medications or ECT

Treatment of Catatonia: Benzodiazepines

- Intravenous lorazepam is greatly preferred
 - Quick onset of action
 - Despite a shorter half-life than other benzos, effective clinical activity may be longer because tissue distribution is less rapid and extensive
 - Also demonstrates a higher binding affinity for GABA_A receptor
- Initial dose of 2mg
 - Follow-up dose based on response and sliding scale of suspicion
- If established efficacy or diagnosis certain, continue with standing regimen
 - 8-24mg/day is typical
 - Taper very slowly after improvement

Treatment of Catatonia: ECT

- Effective in 85-90% of cases; 60% of cases that fail medication
- Should be considered for failure to respond to lorazepam in 48-72 hours, malignant symptoms, excited subtype
- Maintenance ECT often required

Treatment of Catatonia: Alternatives

- NMDA receptor antagonists
 - Amantadine (18 cases)
 - May also have dopamine agonist activity
 - Start at 100mg daily
 - Titrate by 100mg every 3-4 days to maximum of 400mg in 2-3 divided doses
 - Memantine (9 cases)
 - Start at 5mg bid
 - Increase to 10mg bid if ineffective
- Antiepileptic medications
 - Carbamazepine (7 cases)
 - 100-1000mg daily
 - Valproic acid (5 cases)
 - 600-4000mg daily
 - Topiramate (4 cases)
 - 200mg daily

Treatment of Catatonia: Alternatives

- Antipsychotic medications
 - Hypothesized to work through 5-HT_{1A} agonism and 5-HT_{2A} antagonism, which may lead to increased dopamine in the prefrontal cortex.
 - Aripiprazole (9 cases)
 - 3-30mg daily
 - Clozapine (9 cases)
 - 150-300mg daily
 - Olanzapine (7 cases)
 - 2.5-20mg daily
 - Risperidone (2 cases)
 - 0.5-8mg daily
 - Ziprasidone (2 cases)
 - 40-160mg daily

Treatment Algorithm

Intravenous lorazepam
(initial test dose, then 6-8mg daily)

Electroconvulsive therapy
(at least 6 treatments)

Glutamate (NMDA) antagonist
(amantadine or memantine)

Anti-epileptic medication
(carbamazepine or valproic acid)

Atypical antipsychotic
(aripiprazole, olanzapine, clozapine)

Neuroleptic Malignant Syndrome (NMS)

- No DSM diagnostic criteria
- Expert panel criteria:
 - Exposure to dopamine antagonist (or removal of dopamine agonist) within past 72 hours
 - Hyperthermia
 - Rigidity
 - Mental status alteration
 - CK elevation (>4 times upper limit of normal)
 - Autonomic instability
 - Hypermetabolism
 - Exclusion of other medical or substance-induced causes

NMS: Complications and Treatment

- Complications
 - Rhabdomyolysis
 - Seizures
 - Respiratory failure
 - Acute kidney injury
 - Sepsis
 - Acute MI
 - Acute liver failure
 - Pulmonary embolism
- Mortality rate 5.6%
- Treatment
 - Remove offending agent
 - Similar treatment to catatonia

Serotonin Syndrome (SS)

- Sometimes considered a subtype of malignant catatonia
- Symptoms:
 - Spontaneous clonus
 - Inducible clonus AND agitation or diaphoresis
 - Ocular clonus AND agitation or diaphoresis
 - Tremor AND hyperreflexia
 - Hypertonia AND hyperthermia AND ocular clonus or inducible clonus
- Classically induced by combination of MAOI with serotonergic medication
- Now more commonly seen with polypharmacy or overdose
- Clues to Serotonin Syndrome
 - Look for it in patients with antidepressant overdose
 - Look for it in any patient on >4 psychiatric medications
 - Consider it in all catatonic patients

Treatment of Serotonin Syndrome

- Supportive treatment and wash-out is usually all that is needed
 - May use benzodiazepines to manage agitation or if catatonic symptoms are present
 - Short-acting antihypertensives
- If this is not working, can consider cyproheptadine (5-HT_{1A} and 5-HT_{2A} antagonist)

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