Diagnosis and Treatment of Catatonia

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Agenda

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  – Historical Evolution of the Diagnosis
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• Prototypes of Catatonia
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Agenda

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  – Benzodiazepines in Challenge and Maintenance Therapy
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Overview of Catatonia

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Clinical Case #1: Pt. S.

• Demographic:
  – 42y/o single white man

• Medical History:
  – diabetes, HTN, strokes (R cerebellar, R temporal, R basal ganglia)

• Psychiatric History:
  – schizophrenia, undifferentiated type

• Clinical Presentation:
  – admitted with infectious enterocolitis
  – multi-system organ failure → intubation
  – upon extubation, quetiapine 400mg po QHS
  – altered mental status and QT prolongation on EKG

• Mental Status:
  – lying in bed, eyes closed, motionless
  – resisted opening his eyelids, then kept them shut
  – no spontaneous speech
  – no rigidity, catalepsy, waxy flexibility

• Evaluation/Management:
  – initial primary diagnosis: multifactorial delirium
  – EEG: slowing, MRI: multiple infarcts, age undetermined
  – recommendations: PRN olanzapine (no improvement)
Clinical Case #1: Pt. S.

• Follow-up Visit:
  – stupor, intermittent alertness
  – mutism, intermittent repetition: “I’m scared”
  – mild rigidity and waxy flexibility
  – purposeless blanket-bunching
  – frequent head movements (side-to-side)

• Management:
  – lorazepam 1.5 mg trial
  – perked up and requested to listen to Nat King Cole
  – lorazepam 0.5 mg TID started as maintenance therapy

“I felt like I was stuck between two planes in space... Like there were pins in me everywhere holding me in place... I remember you asking questions, and I knew some answers but couldn’t say... I was scared.”

Catatonia at a Glance

• Syndrome (not a disease)
• Motor and behavioral disturbances
• Various medical and psychiatric precipitants
• Fluctuating time course

• Most common features:
  – Mutism
  – Interpersonal withdrawal
  – Negativism (resistance to instruction)
  – Stupor/Immobility
  – Staring
  – Cataplexy (posturing)
  – Rigidity
  – Stereotypy (repetitive behaviors)
  – Mannerisms (odd behaviors)
  – Excitement/combativeness
  – Echophenomena
  – Ambitendency (“stuck”)
History of Catatonia: Kahlbaum

- Coined the term catatonia
- Stages of the condition:
  - Melancholia, apathy
  - Mania, hyperactivity
  - Stupor, confusion
  - Dementia
- Credited with unifying motoric and behavioral features, outlining temporal course of catatonia.

History of Catatonia: Taking Root in Schizophrenia

- Late 1800s: Emil Kraepelin folded catatonia into dementia praecox, conceptualized catatonia as a more chronic disordered state.
- Early 1900s: Eugen Bleuler included catatonia as a (marginal) feature of schizophrenia, focused on psychodynamic theories.

History of Catatonia: Modern Progression

- 1950s – 1970s:
  - Catatonia identified in patients with mania, depression, medical and neurologic conditions
  - Up to 10% of psychiatric inpatients
  - "Lethal catatonia" identified, along with neuroleptic malignant syndrome (NMS)
- 1980s – 2010s:
  - Catatonia first treated with lorazepam
  - DSM III as subtype of schizophrenia
  - DSM IV as subtype of schizophrenia and specifier to depression or mania
  - DSM-5: Catatonia as a separate syndromal entity
Catatonia and the DSM IV-TR (APA 2000)

- Classifications
  - Schizophrenia (subtype)
  - Depressive, manic, mixed episodes (specifier)
  - Catatonia secondary to general medical condition (stand-alone diagnosis)

- Diagnostic Criteria (2+)
  - Motoric immobility
  - Excessive motor activity
  - Extreme mutism or negativism
  - Peculiar voluntary movements
  - Echolalia or echopraxia

Catatonia and the DSM-5 (APA 2013)

- Classifications
  - Catatonia associated with another mental disorder (specifier)
  - Catatonic disorder due to another medical condition
  - Unspecified catatonia
    - Distressing or functionally impairing symptoms
    - Contributing condition unclear or full criteria not met

- Diagnostic Criteria (3+)
  - Stupor
  - Catalepsy
  - Waxy Flexibility
  - Mutism
  - Negativism
  - Posturing
  - Mannerism
  - Stereotypy
  - Agitation
  - Grimacing
  - Echolalia
  - Echopraxia

Epidemiology

- General Hospital Setting
  - Prevalence: Unknown
  - Believed to be under-recognized and -treated

- Inpatient Psychiatric Setting
  - Prevalence: 7-20%
  - Due to general medical condition: 20-25%

- Sex: 1.1–1.3 : 1 (female : male)
- Age: affects all ages, rare in childhood
Bush-Francis Catatonia Rating Scale

1. Excitement
2. Immobility/Stupor
3. Mutism
4. Staring
5. Posturing/Catalepsy
6. Grimacing
7. Echophenomena
8. Stereotypy
9. Mannerisms
10. Verbigeration
11. Rigidity
12. Negativism
13. Waxy Flexibility
14. Withdrawal
15. Impulsivity
16. Automatic Obedience
17. Mitgehen
18. Gegenhalten
19. Ambitendency
20. Grasp Reflex
21. Perseveration
22. Combativeness
23. Autonomic Abnormality

• Screening: First 14 items (2+ positive)
• Monitoring: All 23 items (each measured for serial tracking)

Clinical Evaluation

• Observe patient engaging in conversation
  Look for: mutism, echolalia, verbigeration

• Scratch your head in exaggerated manner
  Look for: echopraxia

• Check chart for 24-hour oral intake, vital signs, behaviors
  Look for: autonomic instability, withdrawal

• Observe directly and indirectly at different times of the day
  Look for: fluctuations in clinical presentation

Clinical Evaluation

• Extend hand: “Do NOT shake my hand”
  Look for: ambitendence

• Reach in pocket, and say: “Show me your tongue. I want to stick a pin in it.”
  Look for: automatic obedience

• Check for grasp reflex
  Look for: frontal release signs

• Examine arms for tone
  Look for: rigidity, waxy flexibility, gegenhalten
Prototypes of Catatonia
Priya Gopalan, MD

Clinical Case #2: Pt. C.

- **Demographic:**
  - 55 y/o widowed African American female
- **Medical History:**
  - Breast cancer
- **Psychiatric History:**
  - Remote episode postpartum depression
- **Present Illness:**
  - Begins course of chemotherapy, receives one dose of intramuscular (IM) steroid, dexamethasone
  - Three days later, family notes that Ms. C is pacing around the house, “fidgety,” talking to herself, and seeing people that are not present

Clinical Case #2: Pt. C.

- **In the ED:**
  - Physical exams by emergency medicine and neurology note audiovisual hallucinations, loose associations, and echolalia, but no other abnormal findings
  - Ms. C is admitted to the general medical floor
- **During Admission:**
  - Primary team withholds chemotherapy and starts antipsychotics for delirium
  - She receives 10mg PO olanzapine and 7.5mg IV haloperidol
  - Medical work up, including: basic labs, CPK, UDS, MRI, and EEG reveal no abnormalities
Clinical Case #2: Pt. C.

- Psychiatry is consulted for evaluation of “altered mental status”
- Family confirms lack of prior psychiatric symptoms or substance abuse
- Ms. C is observed watching TV in her room, repeating the words on commercials
- She is minimally interactive with the examiner and mumbles nonsensically throughout the exam.

Clinical Case #2: Pt. C.

- No fevers, diaphoresis, or flushing
- Rigidity noted in upper extremities, but no cog-wheeling
- Catalepsy in upper extremities
- No echopraxia, automatic obedience, or ambitendency
- Positive (abnormal) grasp, glabellar, and snout reflexes
- Normal deep tendon reflexes
- No clonus or tremors

Clinical Case #2: Pt. C.

- Would you call this catatonia?
- What features of catatonia does this person exhibit?
  - Echo-phenomena
  - Verbigeration
  - Rigidity
  - Catalepsy
  - Grasp reflex
- What factors predispose this patient to catatonia?
  - History of a mood disorder
  - Medical illness
  - Steroid exposure
  - Antipsychotic exposure
Clinical Case #2: Pt. C.

- Ms. C is diagnosed with catatonia, likely due to steroids
- The psychiatry consultation service recommends stopping all anti-dopaminergic agents
- Ms. C is given 1mg IV lorazepam x 1 and re-examined one hour later.
  - At that time, she responds to questions, but is confused and gives inappropriate answers

Clinical Case #2: Pt. C.

- Psychiatry team starts lorazepam 1mg IV three times daily (TID)
  - The next day she is interactive, but still has echolalia
  - She continues to have intermittent agitation and motor exam is limited by restraints
- Lorazepam is increased to 2mg IV four times daily (QID)
  - Catatonia symptoms resolve
  - Hallucinations resolve
  - She continues to have tangential thoughts and delusions that the physicians are other people

Clinical Case #2: Pt. C.

- Aripiprazole is initiated for psychosis, and she is transferred to inpatient psychiatry for further management
- Psychiatric symptoms resolve on a regimen of aripiprazole 20mg daily and lorazepam 2mg QID, and Ms. C is discharged to home
- Aripiprazole and lorazepam are both tapered off as an outpatient with no return of symptoms
Prototypes in Psychiatry

- Carl Jung: Archetypes
- Kahana and Bibring: Personality types
- Groves: “Hateful Patient”
- Prototype models exist for numerous psychiatric conditions (e.g., bipolar disorder, personality disorders)

Prototype Models

- **Advantages:**
  - Effective
  - Practical
  - Matches natural clinical reasoning
  - Facilitates teaching and pattern-guided recognition

- **Disadvantages:**
  - Oversimplified
  - Risk of stereotyping
  - Risk of symptom exclusion
  - Associated with high false-positive rates

Retarded Catatonia (Kahlbaum Syndrome)

- **Clinical features:**
  - Stupor
  - Mutism
  - Rigidity
  - Withdrawal
  - Waxed Flexibility

- **Typical associations:**
  - Depression, psychosis, neurologic disease

A Woman Diagnosed as Suffering from Melancholia. Credit: Wellcome Library, London. Adapted with Permission.
Excited Catatonia (*Delirious Mania*)

- Clinical features:
  - Nightmarish derealization
  - Excessive activity/agitation
  - Disorganized speech
  - Confusion, disorientation
  - Stereotypy, echophenomena

- Typical associations: mania, mixed states, toxidromes

Malignant Catatonia

- Clinical features:
  - Posturing, rigidity
  - Confusion
  - Intermittent excitement
  - Fever, dysautonomia

- Course: sudden; rapid progression; fluctuation

- Mortality: 10-30%

Neuroleptic Malignant Syndrome

- Clinical features:
  - Severe rigidity
  - Altered mental status
  - Fever, dysautonomia
  - Recent neuroleptic use

- NMS and MC clinically indistinguishable

- Two sides of a coin? (Vancaster 2007)

The Distant Mute

- 57y/o man
- PMH: epilepsy, on phenytoin
- PPH: major depression, alcohol dependence
- Admission: seizures one week prior to admission, followed by dehydration and FTT

- Presentation
  - No speech
  - Averted gaze, when finally made eye contact, no blink for > 2 mins.
  - Refused to interact, engage in care, eat or drink
  - Did opposite of most commands
The Distant Mute

- **Presentation:** Abnormal eye contact, prominent mutism, uncommunicative
- **Key Point:** Mutism may be the most frequently observed sign in an acute care setting

The Waxy Stiff

- **ID:** 45y/o man
- **PMH:** none
- **PPH:** alcohol and opioid dependence
- **Admission:** found by parents kneeling in fixed position; three days of comments about being the Antichrist; two weeks of depression
- **Presentation:**
  - Minimal speech. Intermittent eye contact
  - Maintenance of unusual postures in UE, rigidity in LE

The Waxy Stiff

- **Presentation:** Sole presence of motor findings (catalepsy, waxy flexibility)
- **Key Point:** Classic catatonia presentation is not necessarily the most common
The Stubborn Grouch

- **ID:** 62y/o woman
- **PMH:** DM, kidney disease, HTN
- **PPH:** MDD, alcohol dependence
- **Admission:** intra-abdominal abscess after nephrectomy
- **Presentation:**
  - Pulled off anything placed on her (clothes, lines, tape, blankets)
  - Laying in her own urine
  - “Get out! I want you out!”
  - Doesn’t look at the interviewer
  - Later: fists clenched, eyes shut
  - Oppositional parataenia

The Stubborn Grouch

- **Presentation:** Prominent negativism
- **Key Points:** Negativism is often mistaken for volitional behavior, and may be more common in the general medical setting

The Broken Record

- **ID:** 31y/o man
- **PPH:** bipolar disorder; PCP and dextromethorphan dependence
- **Admission:** punched in the face
- **Injuries:** multiple facial fractures and head injury
- **Presentation:**
  - Intermittently pulled at lines
  - Shrugged shoulders repeatedly
  - Parroted snapping fingers, hands up, scratching head
  - “I don’t know,” “That’s okay”
  - Automatic obedience
The Broken Record

- **Presentation:** Purposeless agitation, hyperactivity, echophenomena
- **Key Points:** Challenges traditional images of catatonia, can be confused with delirium

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Catatonia and its Underpinnings

Pierre N. Azzam, MD
Differential Diagnosis

• Mutism (akinetic, elective, post-ictal)
• Parkinson’s disease-related akinesia
• Gilles de la Tourette’s disorder
• Hyperactive delirium
• Hypoactive delirium
• Locked-in syndrome
• Abulia
• Coma

Precipitating Conditions

Psychiatric Illness
  – Affective disorders *
  – Schizophrenia *
  – Autistic spectrum disorders*
  – Conversion disorder
  – Obsessive compulsive disorder (OCD)

Neurologic Insults
  – Epilepsy *
  – Encephalopathy *
  – Encephalitis*
  – Infarct (cingulate, temporal, parietal) *
  – CJD
  – Hemorrhage
  – Meningitis
  – Traumatic Brain Injury

Medical Conditions
  – Acute intermittent porphyria *
  – Systemic lupus erythematosis*
  – Addison’s disease
  – AIDS
  – Cushing’s disease
  – Hepatitis
  – Hyperparathyroidism
  – Tuberculosis
  – Uremia

Medications/Drugs
  – Corticosteroids *
  – Metoclopramide *
  – Neuroleptics *
  – Phencyclidine (PCP) *
  – Disulfiram
  – MDMA (ecstasy)
  – Stimulants
  – Withdrawal states: benzodiazepines *, dopaminergic drugs
Pathophysiologic Theories

“Similar symptomatology in neuroleptic catatonia (including NMS) and psychogenic catatonia may reflect a common pathophysiology involving dopamine and GABA neurons in mesostriatal, mesolimbic, and hypothalamic pathways.”

– Fricchione 1997

Proposed Neural Networks

- Diffuse rather than focal lesions
- Striatal-thalamocortical tracts
  - Basal Ganglia
    - motor regulation
  - Orbitofrontal Cortex
    - motivation; perseveration
- Other proposed involvement
  - Hypothalamus
    - hyperthermia, dysautonomia
  - Limbic System
    - subjective fear
  - Parietal Cortex
    - visuospatial processing

Proposed Neurochemistry

- Dopamine HYPOactivity
  - Mesolimbic
  - Nigrostriatal
  - Hypothalamic
- GABA A HYPOactivity
  - Orbitofrontal
  - Limbic connections
  - Striatal DA inhibition
- Glutamate HYPERactivity
  - Posterior parietal
  - Frontal GABA A inhibition
- 5-HT and possible link to serotonin syndrome?
Management of Catatonia
Priya Gopalan, MD

Essentials of Management

- Observe closely and monitor vital signs
- Manage precipitating conditions
- Discontinue offending medications
- Restart recently withdrawn dopaminergic agents
- Monitor for medical complications
- Involve health care proxy

Additional Workup

- Collateral Information: history of drug use or psychiatric illness, presentation course
- Vital Signs: ↑HR, BP, RR
- Serum Labs: ↑CPK, WBC ↓Na, Fe
- Head imaging
- EEG: no consistent findings; may wax and wane with frontal slowing
Potential Medical Complications

- Aspiration
- Burn
- Cardiac failure
- Dehydration
- DIC
- DVT/PE
- GI bleed/obstruction
- Pneumonia
- Renal failure

- Respiratory distress
- Rhabdomyolysis
- Seizures
- Sepsis
- Urinary retention
- Urinary tract infection

*Death: up to 25% in malignant catatonia*

Preventive Measures

- DVT precautions (anticoagulation)
- Aspiration precautions
- Hydration
- Nutrition (parenteral)
- Stretching (PT/OT)
- Wound Care
- Mobilization

Mainstays of Catatonia Treatment

- Barbiturates: historical first-line treatment
- Benzodiazepines: current first-line treatment
- Dopamine Agonists: adjunctive agents
  - Amantadine: pre-synaptic DA agonist
  - Bromocriptine: post-synaptic DA agonist
- Dantrolene: used in cases of MC (rigidity)
- Electroconvulsive Therapy: treatment in BZD non-responsive patients, malignant catatonia
Benzodiazepines in Catatonia

- **BZD Challenge**
  - Lorazepam 1-2mg IV x 1, monitor response
  - Lorazepam 1mg IV Q30min until response (up to 4-6mg)

- **BZD Maintenance**
  - Response to challenge predicts response to maintenance treatment (~90%)
  - Dosing based on response to challenge
  - Typical start dose: lorazepam 1-2mg po/IV TID
  - Daily adjustment based on response

ECT in the Treatment of Catatonia

- If inadequate response within 5 days of med trial (sooner if malignant catatonia), seek ECT or alternative treatment
- Prospective study (n=28): 4 patients who did not improve with benzodiazepines after 5 days improved with ECT treatment (Bush 1996)
- Case series: delay in ECT for malignant catatonia, by 5 days death for 14 patients; versus 16 of 19 patients who survived when they received ECT within 5 days of diagnosis (Philbrick 1994)
- Pennsylvania: Court order for ECT when patient is unable to consent

Case-Reported Treatments

- **Antiepileptic Drugs**
  - Carbamazepine
  - Topiramate
  - Valproic Acid
- **Atypical antipsychotics**
  - Aripiprazole
  - Olanzapine
- **Levodopa**
- **Lithium**
- **Methylphenidate**
- **NMDA-antagonists**
  - Memantine
  - Amantadine
- **Zolpidem**
Misconceptions in the Medical Setting

- Catatonia must be “psychiatric”
  Catatonia presents in the setting of medical and psychiatric conditions (additive effects?).
- “The patient is just playing possum”
  Many behaviors are not ones people typically choose when they are being “problematic.”
- Unresponsive = Asleep
  BZDs remain the treatment of choice.
- Response to Ativan proves it’s psychiatric
  BZDs treat catatonia, often not the precipitating condition.

Treatment Outcomes

- Non-Malignant Catatonia
  - BZD response: 70%
  - ECT response: 85%
  - AP response: 7.5%
- Malignant Catatonia
  - BZD response: 40%
  - ECT response: 89%
  - AP response: 0%

When to Maintain Treatment

- Less Likely to Relapse
  - Rapid, dramatic response to BZD
  - Episodic course
  - High inter-episode functioning
  - Primary mood disorder
  - If ECT: adequate seizures, easily induced
- More Likely to Relapse
  - High-dose BZD required
  - Coarse neurologic disease
  - Oneiroid state
  - Chronic mania
  - Alcohol dependence
  - Substance-induced mood disorder with catatonia
Summary

- Catatonia is a heterogeneous syndrome of motor and behavioral disturbances
- Various neurologic, medical, psychiatric etiologies (affective disorders, general medical conditions, psychotic disorders)
- Pathophysiology related to DA and GABA depletion
- Rapid identification, supportive measures, somatic treatments are life-saving
  - BZD – first line
  - ECT – gold standard, use if BZD ineffective/contraindicated
  - Dopaminergic agents – use adjunctively
- Prolonged and malignant cases require aggressive management

Questions?

References

References


References

Mahendra R. Where have all the catatonics gone? Psychological Medicine 11:659-671, 1981.