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OUTLINE

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DEFINITION

- Catatonia is a clinical syndrome characterized by striking behavioural abnormalities that may include motoric immobility or excitement, profound negativism, or echolalia (mimicry of speech) or echopraxia (mimicry of movement).
- Ludwig - Catatonia is a brain disease with a cyclic, alternating course, in which the mental symptoms are, consecutively melancholy, mania, stupor, confusion, and eventually dementia

HISTORICAL OVERVIEW

- Catatonia was discovered in 1874 by Kahlbaum, who also appreciated its neurological causes.
- Kraeplin and bleuler described its relationship to schizophrenia
- By 1913 Kirby had reported clear cases of catatonia in patients with manic depressive illness
- Abrams and Taylor re established that most catatonic patients have a mood disorder particularly mania and that 20% of patients with mania exhibit catatonic features [1970’s]
- Gelenberg identified catatonia in patients with neurotoxic syndromes secondary to the use of antipsychotic drugs in 1976

ETIOLOGY

Functional [Primary] Causes

1. Mood Disorders : Depression > Mania
2. Schizophrenia
3. PTSD

ETIOLOGY

Organic [Secondary] Causes

- Neurological - Brain stem, diencephalic lesions, lesions near 3rd ventricle, Frontal/Parietal lobe diseases, Head injury, Dementia, Atrophy, Encephalitis, Epilepsy
- Metabolic - DKA in DM, Thyroid dysfunction, Hepatic/Renal failure, Porphyrias
- Nutritional causes such thiamine, pellagra deficiency.

ETIOLOGY

Organic [Secondary] Causes

- Drug related : Neuroleptics, Alcohol, Opioids, Cannabis, Disulfiram, SSRI's and TCA's

MECHANISM

- The exact mechanism is not known, however several hypothesis have been offered.
- Northoff (2002) : Top down modulation of basal ganglia due to deficiency of cortical GABA may explain the motor symptoms and may also account for the dramatic therapeutic effects of benzodiazepines which cause increase in GABA activity.
- Osman and Khursani(1994) : Catatonia is caused by a sudden and massive blockade of dopamine. This may explain why dopamine blocking antipsychotics are not effective in catatonia

MECHANISM

- Clozapine withdrawal catatonia is postulated to be due to cholinergic and serotonergic rebound activity [Yeh et al, 2004]
- Moskowitz (2004) : Catatonia may be understood as an evolutionary fear response, originating in ancestral encounters with carnivores whose predatory instincts were triggered by movement. Catatonic stupor may represent a common ‘ end-state’ response to feelings of imminent doom.

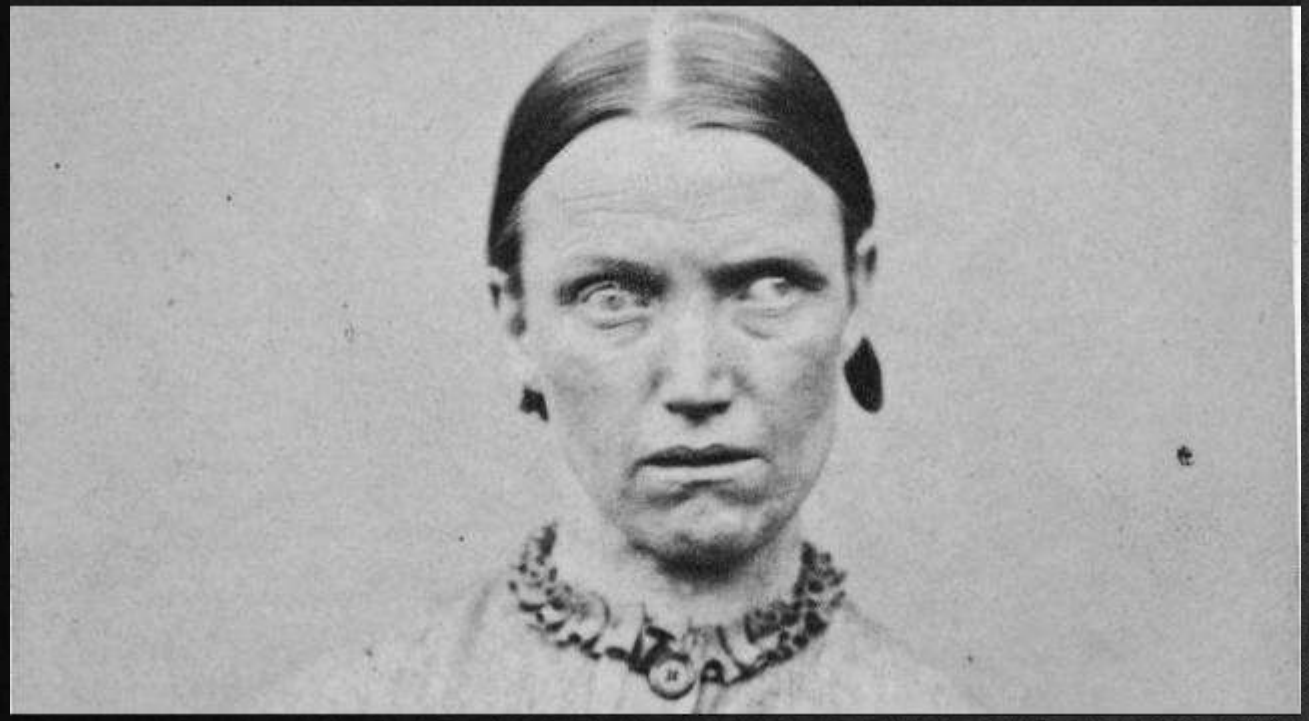
PHENOMENOLOGY

Catatonia is a syndrome that encompasses more than two dozen signs

- Stupor - it is the classic and most striking catatonic sign. It is the combination of mutism and immobility, however the two can also occur independently
- Excitement - Patient displays excessive purposeless motor activity not influenced by any external stimuli
- Posturing/Catalepsy - Spontaneous maintaining of posture including bizarre posture

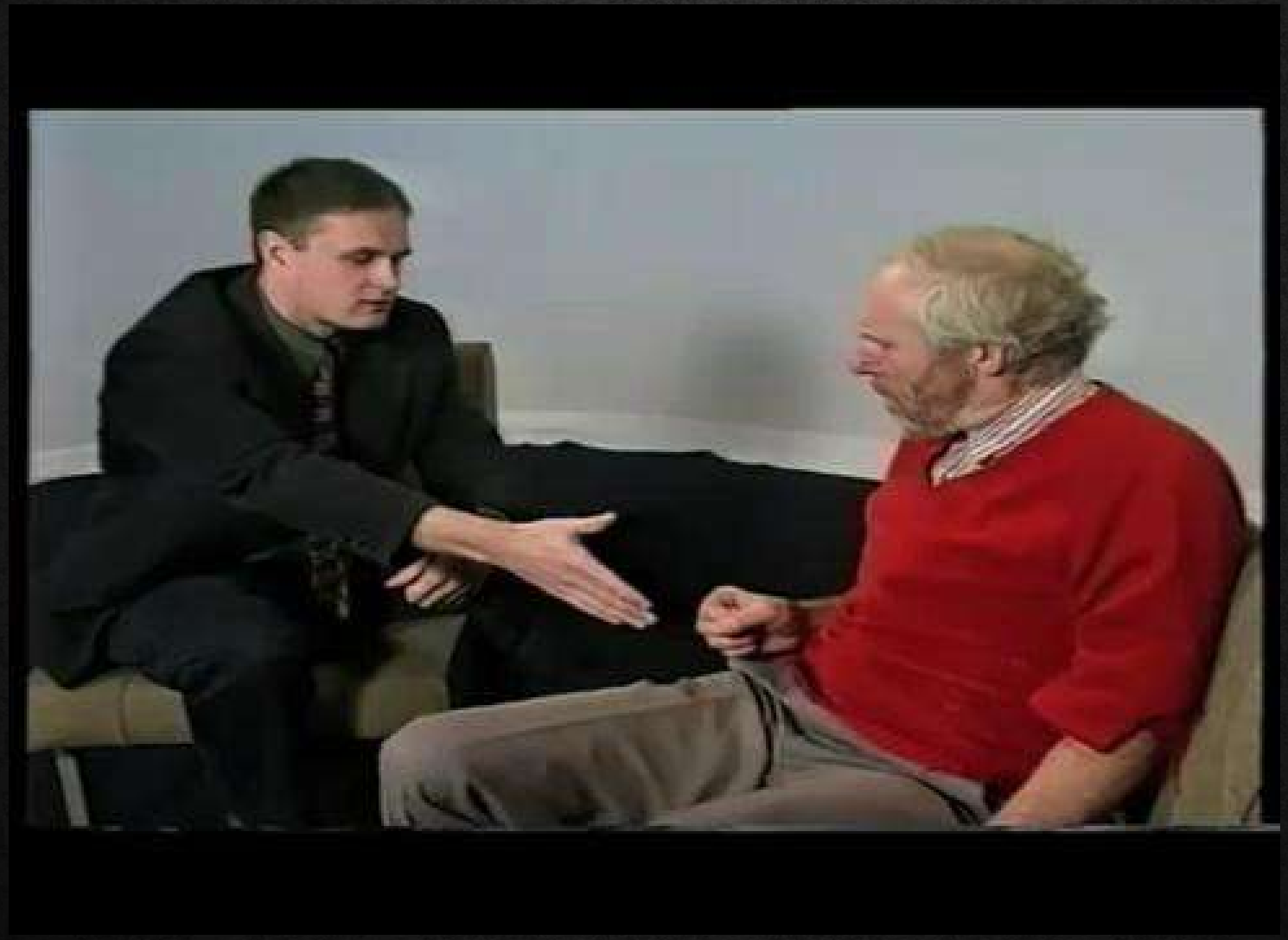
Phenomenology

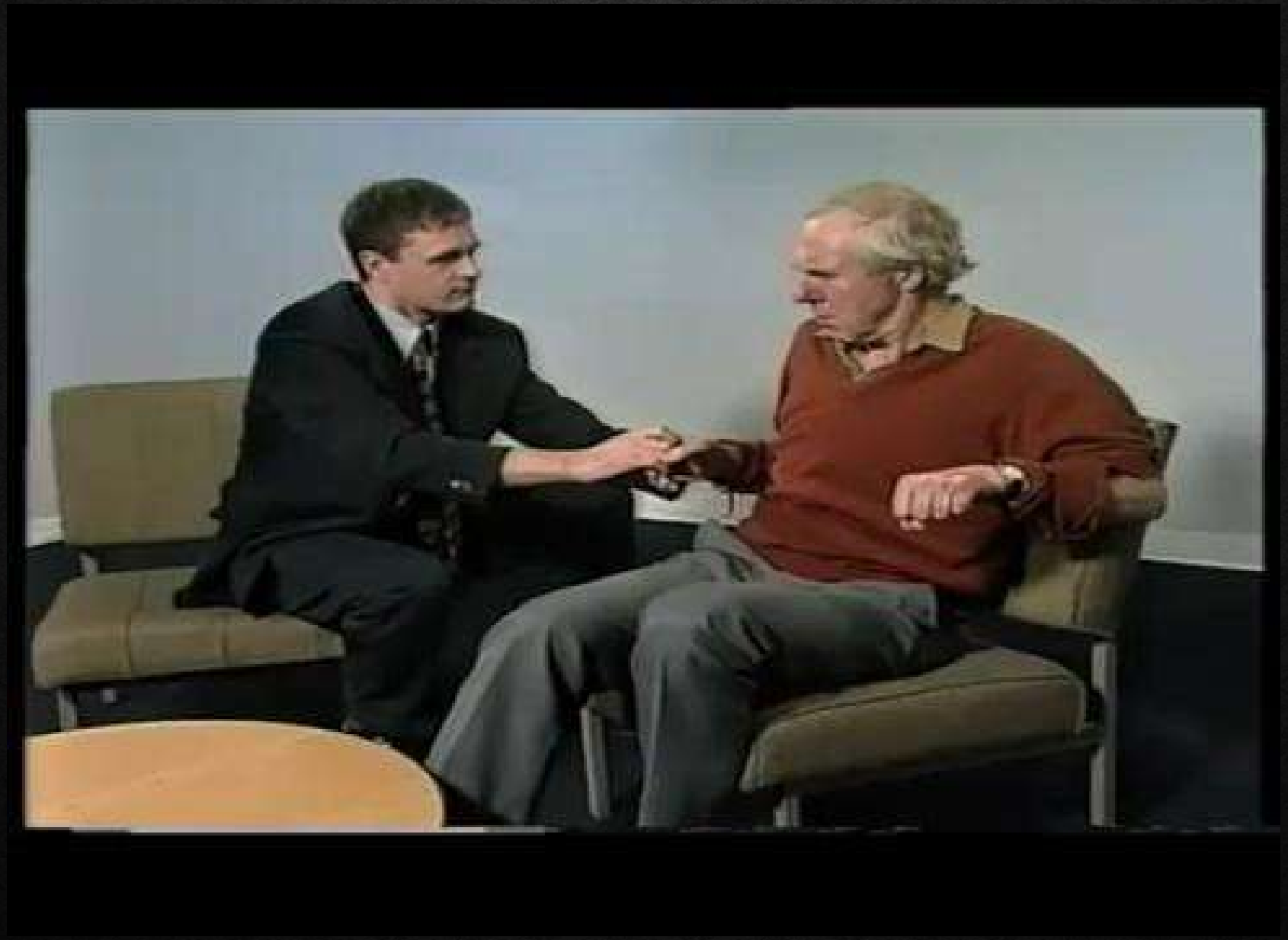
- Grimacing - Maintaining of odd facial expressions
- Echopraxia/Echolalia - Mimicking of examiner's movements/speech
- Stereotypy - Repetitive, non goal oriented action that is carried out in an uniform way
- Mannerisms - Unusual repetitive performances of goal oriented motor actions [hopping or walking tiptoe]



PHENOMENOLOGY

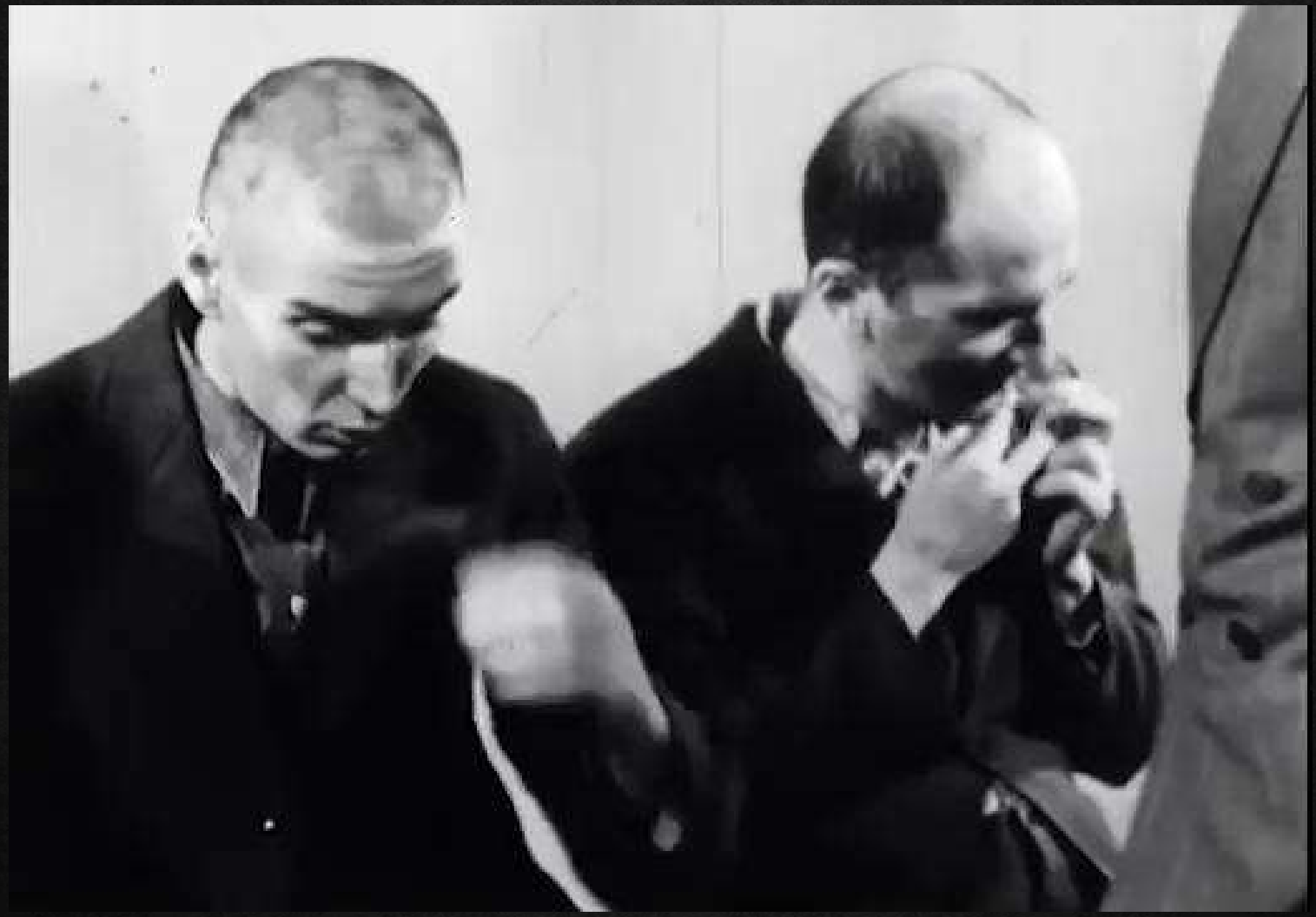
- Verbigeration : Repetition of words or phrases
- Rigidity : Maintenance of a rigid position despite efforts to be moved
- Negativism : Refusal to behave in prescribed manner and motiveless resistance to instruction or examination of pt
- Waxy flexibility : During reposturing of pt, he offers initial resistance before allowing himself to be repositioned, similar to that of a bending candle
- Withdrawal : Refusal to eat/drink or make eye contact





Phenomenology

- Impulsivity : Patient engages in sudden inappropriate behaviour. (Suddenly runs, takes off clothes, screams and later gives no answer)
- Automatic Obedience : Exaggerated co-operation with examiners request
- Mitgehen : A very extreme form of co-operation, because the patient moves their body in the direction of the slightest pressure on part of the examiner.



Phenomenology

- Gegenhalten : Resistance to passive movement which is proportional to strength of stimulus
- Ambitendency : Patient appears motorically stuck in indecisive, hesitant movement
- Perseveration : Senseless repetition of a goal directed action that has already served its purpose
- Autonomic abnormalities : Temperature, BP, Respiratory rate, Diaphoresis

Table 2.2 Catatonic spectrum behaviors

Tiptoe walking, skipping, hopping
Repeating questions instead of answering
Manneristic hand or finger movements not typically dyskinetic
Inconspicuous repetitive actions, such as making clicking sounds before or after speaking; automatically tapping or touching objects or body parts; tongue chewing, licking; lip smacking; pouting; teeth clicking; grimacing; frowning; squeezing shut or opening eyes wide
Oddities of speech, such as progressively less volume until speech is an almost inaudible mumble (prosectic speech); using a foreign accent not typical for the patient; speaking like a robot or like a child learning to read; speaking without the use of word contractions (e.g., "*I am not going to the store because I can not do it*" rather than using "I'm" and "*can't*")
Holding head in odd positions
Rocking, shoulder shrugging, sniffing and wrinkling of nose, opening eyes wide and then squeezing them shut
Rituals, such as tapping the dishes or eating utensils in a specific order before eating; tapping buttons before buttoning a shirt

CATATONIA IN ICD 10 AND DSM V

- Historically, catatonia has been more associated with schizophrenia
- When bleuler introduced concept of schizophrenia, he introduced catatonia as one of the subtypes
- This bias, giving schizophrenia an exaggerated place in the discussion of catatonia, continues to be reflected in ICD-10 and DSM-V

ICD 10

- ICD - 10 diagnosis of catatonic schizophrenia requires that the pt exhibits at least one of the following for atleast 2weeks - Stupor, excitement, waxy flexibility, posturing, negativism, rigidity and command automatism
- If pt with depression is in stupor - Severe depression with psychotic symptoms [Even w/o delusions or hallucinations]
- Patient with manic stupor - Mania with psychotic symptoms
- Catatonia due to physical causes - organic catatonic disorder

DSM V

- Diagnosis of catatonia associated with another mental disorder is made if clinical picture is dominated by atleast three or more of the following

TABLE IV.
Definition of catatonia in DSM 5 (APA, 2013). *Definizione della catatonia nel DSM 5 (APA 2013).*

Catatonia is defined by the presence of three or more of the following:
1. Catalepsy (i.e., passive induction of postures held against the gravity)
2. Waxy flexibility (i.e., slight and even resistance to repositioning by the examiner)
3. Stupor (no psychomotor activity, no reactivity to the environment)
4. Agitation, not influenced by external stimuli
5. Mutism (i.e., no or minimal verbal response- not applicable in case of established aphasia)
6. Negativism (i.e., opposing or not responding to external stimuli or instructions)
7. Posturing (i.e., spontaneous and active maintenance of posture against gravity)
8. Mannerism (i.e., odd caricatures of ordinary actions)
9. Stereotypies (i.e., repetitive, frequent, non-goal directed movements)
10. Grimacing
11. Echolalia (i.e., repeating the words spoken by the examiner)
12. Echopraxia (i.e., mimicking of movements made by the examiner)

DSM V

- The name of associated mental disorder is indicated e.g
  - catatonia associated with MDD
- If there is evidence from history, lab findings, other pathophysiological condition or delirium and the clinical picture is dominated by three or more symptoms as mentioned before, diagnosis of catatonic disorder due to other medical condition should be made [e.g catatonic disorder due to hepatic enceph]

Types of Catatonia

Taylor and Fink (2003) believe that catatonia should be classified as an independent syndrome with the following subtypes

1. Non - Malignant
2. Delirious
3. Malignant

Types of catatonia

- The non malignant type refers to the classical catatonia described by Kahlbaum
- Delirious type includes delirious mania
- Malignant type includes lethal catatonia, neuroleptic malignant syndrome, serotonin syndrome

FORMS OF CATATONIA

- Hypokinetic/Retarded catatonia (Kahlbaum syndrome) - most commonly recognised , Movement is inhibited with posturing, rigidity, mutism, and repetitive actions. Failure to respond to painful stimuli
- Excited catatonia (Delirious mania,Bell’s mania) - restless movements, talkativeness, agitation, and frenzy; disorientation and confusion is recognized as delirium
- Malignant catatonia :- Syndrome of acute onset, fever in all but elderly individuals,abnormal blood pressures, tachycardia,tachypnea of life-threatening dimensions

OTHER FORMS

- Oneirophrenia:- Patients are in a clouded state akin to dissociative anesthesia + other catatonic features
- Periodic catatonia :- Likely to occur during a mixed mood state / period of rapid cycling
- Primary akinetic mutism
- Catatonia can also be a feature in autism

OTHER FORMS

Lethal Catatonia : A severe form of Catatonia

Early Signs :

- Increasing mental and physical agitation.
- Progresses to wild agitation
- Chorea which can alternate rigidity
- Stupor, mutism and refusal of food/fluids.

OTHERS:

Fever, hypotension and diaphoresis (~NMS)

SEVERE END STAGE CASES

OTHER FORMS

Systematic Catatonia

- Insidous onset
- Progressive chronic course without remission
- Poor response to antipsychotics
- Relatives of pt are at greater risk of developing schizophrenia

OTHER FORMS

Periodic Catatonia

- Recurrent
- Typical bipolar course
- Prominent grimacing, stereotypes, impulsive actions, aggressivity and negativism alternating with stupor, posturing, mutism and waxy flexibility
- Managed by BZDs, if unsuccessful ,then by ECT

OTHER FORMS

- Dabholkar P et al [1988] reported a case of hysterical catatonia
- Pt developed coarse trembling of hands, difficulty in phonation, excessive sleep and refusal to eat. Weakness in one side of the body was developed and physician noted no neurological deficit [occurred a week after death of father]
- Motionless, mute and frequent violent shaking of body
- Recovered with 4 ect and oral diazepam, however after 4 months again developed same symptoms after a quarrel with villagers and was given the same treatment and became

CLINICAL DIFFERENCES IN CATATONIA TYPES

In primary catatonia

- Patient responds to painful stimuli
- Patient keeps eyes open most of the time
- Patient's reflexes are normal
- No focal neurological deficits
- Patient avoids self injury (arm test)
- Incontinence is of retention over flow
- EEG pattern is that of awake test
- Improves with lorazepam or continues to be same

CLINICAL DIFFERENCES IN CATATONIA TYPES

Depressive Catatonia

- Depressive face
- Athanassio's sign [Omega]
- Eye movements
- PMA retardation
- Past History

Schizophrenic catatonia

- Vigilant face
- Catatonic excitement
- Snout spasm [Schnauzkrampf]
- Scanning

CATATONIA RATING SCALES

- Bush-Francis Catatonia Rating Scale
- Braunig Catatonia Rating Scale
- Modified Roger's scale
- Lohr and Wisniewski scale (1987)
- Northoff catatonia scale

BIZARRE

1. Excitement:
2. Immobility/stupor
3. Mutism
4. Staring
5. Posturing/catalepsy
6. Grimacing
7. Echopraxia/echolalia:
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

BI SCALE

- Use the presence or absence of items 1 - 14 for screening.

- Use the 0 - 3 scale for items 1 -23 to rate severity

management

INITIAL MEASURES

- Measures to prevent medical complications such as Anticoagulant therapy, urinary catheterization, adequate nursing care
- Monitor oral intake, Urine I/O charting and Vitals
- Adequate pareneteral hydration or feeding using N-G tube if necessary

TREATMENT OPTIONS

- Strong evidence based options such as Benziodiazepines and ECT

Other options for BZD resistant catatonia such as

- Mood stabilizers, especially Carbamazapine
- Antipsychotics
- NMDA antagonists [mementine amantidine]
- Skeletal muscle relaxants [Especially dantrolene if NMS suspected]
- Transcranial Magnetic stimulation

BZD's and Barbiturates

- Since 1930, amibarbital and other barbituarates have been used for temporary improvement in catatonia
- Helped in ameliorating functional catatonic stupor for feeding the patient
- BZD's have now replaced barbituarates for diagnosis and acute management of catatonia [DOC]
- Lorazepam [IV or IM] initially for every 4 to 10 hours then increase to 4 - 8 mg/day for 3 - 5 days upto 24 mg/day
- Organic catatonia also responds well to BZD's

BZD

In a prospective, open study (Ungvari *et al, 1994a)*,

- 18 patients with catatonia were treated with eitheroral lorazepam or intramuscular diazepam
- 16 showed significant clinical improvement within 48 h, with two showing complete remission after just one dose.

BZD's correct the deficit in GABAergic neurotransmission in the orbitofrontal cortex that has been associated with motor and affective catatonic symptoms

It is necessary to continue therapy until complete clinical remission to prevent recurrence

ECT

- APA guidelines indicate that ECT is the most effective treatment for catatonic syndrome, regardless of its aetiology
- Rohland et al [1993] reported its effectiveness in organic catatonia
- Benegal et al [1993] good response to ECT in their sample of 65 patients with catatonia, which included 30 with idiopathic presentation, 19 with schizophrenia and 16 with depression
- In patients treated with ECT, better response seen in younger age group, longer seizure duration early initiation of therapy

ECT

- Even if rapid response to the first session of ECT is achieved, clinical evidence has shown that a cycle of 6 sessions should still be completed to prevent the risk of recurrence

- Rapid interruption of BZD before the first session of ECT can lead to exacerbation of catatonic manifestations ,thus some have suggested that their administration should be continued before & during ECT

Benzodiazepine/ECT approach

Advantages

- Benzodiazepines are easier to use and are safer than the alternative drugs
- If ECT is given, treatment of the primary condition (e.g., mood disorder) in most patients need not be interrupted
- Treatments can be continued into the maintenance period to prevent relapse
- Mortality rate may be lower if ECT used as the initial treatment, particularly within 5 days of the onset of the illness

Disadvantages

- ECT requires specialized equipment and trained personnel to administer ECT
- Signed consent needed[a]
- Effects on cognition in this patient group is unknown

ANTIPSYCHOTICS

- Generally not recommended during a catatonic phase even if there is an underlying psychotic illness such as schizophrenia, as the risk of precipitating NMS is considerably increased.
- However, they may be effective in treatment-resistant catatonia
- Hesslinger *et al* (2001) reported that a patient with catatonia unresponsive to benzodiazepines showed dramatic and persistent improvement on risperidone
- Hypothesized that efficacy of atypical antipsychotics was due to a direct effect on psychotic disturbance at the basis of the catatonic manifestation, which regressed after correct treatment of underlying pathology

RELAPSE PREVENTION

Less likely to relapse	More likely to relapse
Rapid dramatic response to benzodiazepine challenge	High doses of benzodiazepines needed to ameliorate catatonia
Episodic course of illness with high functioning between episodes	Catatonia associated with oneiroid state[a]
Catatonia as part of primary mood disorder	Chronic manic patient with signs of limbic sensitization[b]
ECT easily induced and ictal EEG changes meet criteria for adequate seizures	Co-morbid alcoholism, substance-induced mood disorder with catatonia, or coarse neurologic disease

RELAPSE PREVENTION

- To prevent relapse, continuation treatment is necessary for most psychiatric conditions
- Depression - ct antidepressant. Broad spectrum non specific or partially specific reuptake inhibitor like desipramine may be used
- Sertraline is also proven to be effective
- preference for broader spectrum antidepressants is due to their clear efficacy in the severely depressed patient, their tendency toward sedation rather than the arousal that occurs with a pure SSRI, their lesser effects on sexual function, and their lesser expense

RELAPSE PREVENTION

- Schizophrenia - Antipyschotic drug use is not preferred until all signs of catatonia have been resolved
- The aim is to sustain the improvement of the catatonic type of schizophrenia by relying on the antipsychotic activity of ECT
- When ECT and lorazepam have failed or produced a partial response, an antipsychotic medicine may be added during the continuation treatment
- In open clinical trials at University Hospital at Stony Brook, New York and at the Long Island Jewish Hillside Medical Center for more than a decade, the augmentation of clozapine by ECT in clozapine-resistant patients has been

RELAPSE PREVENTION

Catatonia in other conditions

- When a patient exhibits a neurotoxic reaction, we should not prescribe the precipitating agent again
- For patients who developed catatonia as a manifestation of their general medical illness, continue lorazepam in doses of 3–8 mg daily for six months or longer after the acute episode has been successfully treated.

DIFFERENTIAL DIAGNOSIS

- NEUROLEPTIC MALIGNANT SYNDROME
- MALIGNANT HYPERTHERMIA
- SERATONIN SYNDROME
- ANTICHOLINERGIC SYNDROME
- ELECTIVE MUTISM
- LOCKED IN STATE
- STIFF MAN SYNDROME
- PARKINSONS DISEASE
- METABOLIC INDUCED STUPOR

nms

- Idiopathic reaction to dopamine antagonists
- Develops rapidly over a few hours to days
- No prodrome phase
- Tremors and dyskinesias are early signs
- Leadpipe muscular rigidity, hyperthermia, fluctuating consciousness, and autonomic instability
- Severe complications, i.e., rhabdomyolysis with elevated creatine phosphokinase, myoglobinuria, renal failure and intravasular thrombosis with pulmonary embolism and respiratory failure
- Possible 20%-30% mortality with full syndrome.

SEROTONIN SYNDROME

- Use of proserotonergic drugs
- Mild cases have tachycardia, shivering, diaphoresis, or mydriasis.
- Neurological examination reveals intermittent tremor or myoclonus, as well as hyperreflexia.
- Moderate cases tachycardia, hyperthermia, and hypertension. Physical examination reveals mydriasis, hyperactive bowel sounds, diaphoresis and normal skin color, hyprereflexia greater in lower extremities
- Mental status includes mild agitation or hyper vigilance, slightly pressured speech.
- Peculiar head turning behavior characterized by repetitive

MALIGNANT HYPERTHERMIA

- Autosomal dominant condition
- Occurs within minutes after exposure to inhalation anesthetics and depolarizing muscle relaxants
- Clinically cynotic areas contrasting with patches of bright red flushing, hypretonicity, hyporeflexia, increasing concentration of end tidal CO2
- Confirmed by muscle biopsy

ELECTIVE MUTISM

- Preexisting personality disorder
- Identifiable stressor
- No other catatonic feature
- Does not respond to lorazepam challenge
- Neurological causes to be ruled out as mutism is seen in number of neurological condition

Locked In Syndrome : Total immobility except for vertical eye movements and blinking. Patient tries to communicate with this movement. No other symptom of Catatonia is present. Associated with ventral pons cerebellar peduncle lesions

Stiff man syndrome : Associated with painful spasms that are precipitated by touch, noise or emotional stimuli. Benefits from therapy with Baclofen, a gabaergic type B agonist,which can worsen some motor symptoms of catatonia.

PARKINSONS DISEASE

- Akinetic parkinsonism may resemble catatonia
- May be mute and immobile and may show posturing
- Occurs year after illness with parkinsonian symptoms and dementia.
- Anticholinergic drugs may provide some benefit

OCD GDLT

- Gilles de la Tourette syndrome and obsessive-compulsive disorder (OCD) can manifest with hyperkinetic alterations in motoricity similar to catatonia.

PROGNOSIS

- Although the overall prognosis was excellent, a high incidence of recurrent catatonic episodes was reported for idiopathic catatonia and catatonia due to affective disorders (Barnes *et al, 1986).*
- Continuation ECT is an efficacious treatment for maintaining response for those who relapse after initially responding to ECT
- Prognosis for the acute catatonic phase seems to be good, but the long-term prognosis probably depends on the underlying cause of the catatonia.

INDIAN STUDIES

- Seethalaxmi et al - Reported a lower incidence of catatonia in an IP setting. (catatonic syndrome in 11% patients).
- Chalassani et al : cross-cultural study reported an incidence of 13.5% in consecutively admitted patients in India
- Thakur et al →only study which evaluated incidence of catatonia in children and adolescents → incidence of 5.5% in the entire study sample + 17.7% in patients with affective and nonaffective psychotic disorders.
- Seethalaksmi et al reported mutism (87.5% incidence) to be most common
- Significant proportion (93%) of patients with catatonia showed a marked immediate response to lorazepam, with 75%

CONCLUSION

- > 135 years after its birth, catatonia is now recognized as an identifiable and treatable syndrome.
- Characteristics are well defined, a simple test verifies the diagnosis and the treatments of high-dose benzodiazepines and ECT are remarkably effective and safe.
- The labels of “not otherwise specified” and “secondary to a medical disorder” and the suggested use as a specifier add unnecessary redundancy and confusion.
- Thus ,Catatonia warrants the proposed separation from schizophrenia and establishment as an independent syndrome in the classification of psychiatric illnesses with a single numeric code.

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Thank you