REVIEW ARTICLE
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Psychopharmacology of Catatonia: A Tour D'horizon

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ABSTRACT *~ Since its first inception by Kahlbaum in relation to schizophrenia, Catatonia syndrome is currently believed to cut across many neuropsychiatric diagnoses. In this focussed review, authors touch briefly on prevalence of catatonia in psychiatric presentations, discuss clinical diagnosis, neurobiology, typology, and conclude with a psychopharmacological algorithm to treatment.* Psychopharmacology Bulletin. *2025;55(1):64–69.*

Definition

Catatonia, or ***tension insanity*** as coined historically by the German Psychiatrist ***Karl Ludwig Kahlbaum*** in 1874, could complicate organic or psychiatric presentations and comprises a constellation of motor/speech/behavioural and autonomic phenomena.[1]

Prevalence

Catatonia has been reported to complicate circa ***7–17%*** of psychiatric presentations.[2] Mood disorders comprise 45% of these cases, schizophrenia 20%, dementia 15%, and autism spectrum disorder 4–17%. Other psychiatric disorders with reported catatonia include, inter alia, intellectual disability (syndromic cases as well), obsessive-compulsive disorder, de la Tourette syndrome, PTSD, and conversion (functional neurological symptom) disorder. The distribution of neuropsychiatric diagnoses in series of catatonic patients supports the nonspecificity of the syndrome.

Screening

The threshold for the diagnosis of catatonia includes 3/12 criteria of DSM-5-TR or 2 or more from BFCRS (***Bush-Francis Catatonia Rating Scale***), the

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preferred rating scale with high interrater reliability, validity and ease of administration. Of note, relying solely on DSM-5-TR criteria for diagnosing catatonia can prove inadequate since for e.g. staring is not included on list where it is prevalent up to 74%. Signs of catatonic syndrome are protean[3] and include-

1. Ambitendance
2. Automatic obedience (command automatism)
3. Carus catalepsia (catalepsy)
4. Congelatio (gelatio)
5. Cerea flexibilitas
6. Cataphasia (verbegeration)
7. Detentio
8. Delirium acutum
9. Echolalia
10. Echopraxia
11. Emberyonic posture
12. Gegenhalten
13. Hyperkinesis
14. Mannerism
15. Mitmachen
16. Mitgehen
17. Obstruction
18. Psychogenic pillow
19. Stereotypy
20. Staring
21. Stupor
22. Schauzcramfe
23. Prosectic speech
24. Negativismus (active & passive)
25. Affective latence
26. Advertence
27. Westphal's pupils

Other ***scales*** for measuring catatonia on clinical grounds include Northoff Catatonia Rating Scale, Braunig Catatonia Rating Scale, Rogers Catatonia Scale, and the Kanner Scale.[4] All-in-all, it is easy to make assumptions about how catatonic phenomena are distributed, but the only concept with replicated empirical validation remains the positive/productive vs. negative/deficit dichotomy.

Typology

Sabbe and Van Den Eede classify catatonia into ***Malignant*** and ***Non-malignant*** Each is then subdivided into ***Excited*** and ***Retarded*** and hence for e.g. NMS can be subsumed under malignant retarded catatonia rubric.[5] Retarded/stuporous form is by far the most common clinically. Excited catatonia,[6] seen almost exclusively in schizophrenia, is characterized by bizarre, frenzied, and purposeless hyperactivity. Almost sealed off in their catatonic shell, patients may gesticulate, march in place, loudly declaim or engage in verbigeration with rapid, bizarre, nonsensical talk. In rare instances, these excited forms might erupt into Stauder's lethal catatonia with dysautonomia that can be ultimately fatal.

According to ***severity*** and ***prognosis***, these ***variants*** were classically described-[7]

Catatonia mitis
Catatonia gravis
Catatonia protractica

Periodic catatonia[8] is a fascinating and underrecognized clinical entity that has been widely embraced by European researchers. Its clinical hallmark is the presence of repeated catatonic phases, often occurring with regular periodicity. It has an AD genetic basis. Case reports attest to utility of lithium slowing or arresting periodicity of illness.[9]

Diagnosis capitalizes on thorough history (medical/neurological/drugs), physical/neurological examination, differential diagnosis from related disorders and an exhaustive laboratory workup to rule out/in organicity (e.g. autoimmune encephalitis with anti-NMDAR antibodies).[10] Drug-induced catatonia includes disulfiram, PCP, steroids, and neuroleptics.

It is prudent to emphasize that there is ***no*** specific diagnostic lab test for catatonia. That said, the ***triad*** of leukocytosis, hyperCPKaemia and low serum iron can be used as an adjunct in the diagnosis of malignant catatonia and NMS.

Examination for Catatonia typically involves-[11]

1. Observe the patient during normal conversation (e.g. posturing).
2. Scratch the head in an exaggerated manner while speaking with the patient to see if they will copy the movement (for echopraxia)
3. Passively move the patient's arm to examine for cogwheeling, varying the amount of force provided while telling the patient to keep their arm loose (for hypertonus).
4. Have the patient extend their arm and with one finger apply light pressure on their index finger while telling the patient, "Do not let me raise your arm." (for mitgehen)

5. Extend your hand for a handshake while telling the patient, "Do not shake my hand." (for ambitendency)
6. Reach into your pocket and state, "Stick out your tongue; I want to stick a pin in it." (for automatic obedience)
7. Position the patient in obviously uncomfortable posture for a considerable periodof time (for cerea flexibilitas)
8. Check for grasp reflex.
9. Check oral intake/vitals/agitation.

Lorazepam Challenge Test is commonly used as a diagnostic probe with a positive test validating the diagnosis of catatonia.[12] Procedure entails giving 1–2 mg lorazepam IV then re-examining the patient in 5 minutes. If no change, a second dose is given with reassessment. At least 50% reduction of catatonia on BFCRS-score constitutes ***a positive response.*** Particularly in France, ***Zolpidem Challenge Test P.O.*** is similarly used.[13] This is both diagnostic and therapeutic. Robust response to BDZs can conceptualize catatonia as a ***movement disorder,*** an expression of ***extreme anxiety***, a type of ***seizure disorder*** or a state of ***extreme inhibition***.

Differential is legion and encompasses related disorders such as neuroleptic malignant syndrome (NMS), serotonin syndrome, epilepsy, and delirium.[14]

Animal Model The opossum, ***Didelphis virginiana***, spontaneously manifest catatenoid features (e.g. posturing) after being stressed.

Evolutionary-based fear response Moskowitz[15] posited that catatonia can be better understood as a fear response, akin to the animal defence strategy of ***tonic immobility.*** Association of catatonia with anxiety/agitated depression and robust response to benzodiazepines (BDZs) give some kudos to this contention. Together with dysautonomia, this gives credit to ***novel vagal theory of catatonia***.[16]

Neurobiological underpinngs include-[17]

$GABA_A$ ***hypoactivity***

$GABA_B$ hyperactivity

Glutamate NMDA ***hyperactivity***

Dopamine-2 ***hypoactivity***

Serotonin-2 hyperactivity

Cholinergic hyperactivity

Prognosis Since catatonia is readily treatable, prognostication is generally considered to be good in nearly half the cases especially in the short-term and when treated with ECT.[18] Association with mood disorders predicts a better outlook than schizophrenia. Organic cases vary in outcome based on the underlying causation.

Treatment of catatonia should be instituted quickly even pending lab workup. This should consist of specific treatment for the catatonia, treatment of any underlying disorder and prevention and management of complications of catatonia (e.g. prolonged recumbency).

Benzodiazepines (BDZs) and electro-convulsive therapy (ECT) are the treatment modalities of choice in catatonia irrespective of underlying causation.[19]

It is always advisable to revisit the diagnosis in cases of catatonia unresponsive to first-line treatments.

A stepwise approach is proposed. A starting point is a trial of lorazepam (preferably IV) for at least 2–3 days at doses of at least 6–8 mg daily. Higher doses up to 24 mg/d can be used based on clinical response/tolerability. During this time, workup for ECT should begin. Lorazepam is usually the agent of choice (although other BDZs can also be used) because of higher affinity to $GABA_A$ receptors and effective in 85% of cases. For BDZs-responsive catatonia, BDZs should be tapered down slowly whilst treatment of primary disorder is ongoing. There seems a subset of patients who would relapse whenever BDZs are discontinued. These patients might require long-term maintenance treatment with BDZs.

Bilateral ECT, 6–10 sessions, is then recommended, at least twice a week. If ECT is not immediately available, adding of either amantadine 100 mg daily or memantine 10 mg daily to BDZs.[20–21] It is recommended to titrate up over three to four days to a maximum dose of amantadine 600 mg daily or memantine 20 mg daily. This is followed by adjunctive carbamazepine 300–600 mg/d, or valproate 500–1500 mg/d. Lastly, adding either aripiprazole 10–30 mg, olanzapine 2.5–10 mg or clozapine with each dose given in combination with lorazepam. We recommend checking iron studies at this step since use of antipsychotics with low iron can risk conversion to NMS and better to avoid altogether in case of malignant catatonia or conceivably where no underlying psychotic-level disorders are entertained. Caution should also be exercised where there is a prior history of NMS. Interestingly, low serum iron portends a poor response to BDZs.

Also, of note, catatonia due to schizophrenia (vs. mood disorders) is less responsive to benzodiazepines, hence ECT should be deployed earlier on.

If the catatonia co-occurs with delirium (e.g. with COVID-19),[22] amantadine or memantine should be used as a first line treatment strategy while also considering the use of atypical antipsychotics in combination with lorazepam earlier in the process.

Clozapine-withdrawal catatonia has been reported and mandates clozapine reintroduction as first-line. In the same vein, catatonia secondary to BDZs withdrawal respond to BDZs reinstitution. ✤

Disclosure

Authors has nothing to declare.

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