CATATONIA

[FROM GREEK: KATA=DOWN+TONOS=TENSION]

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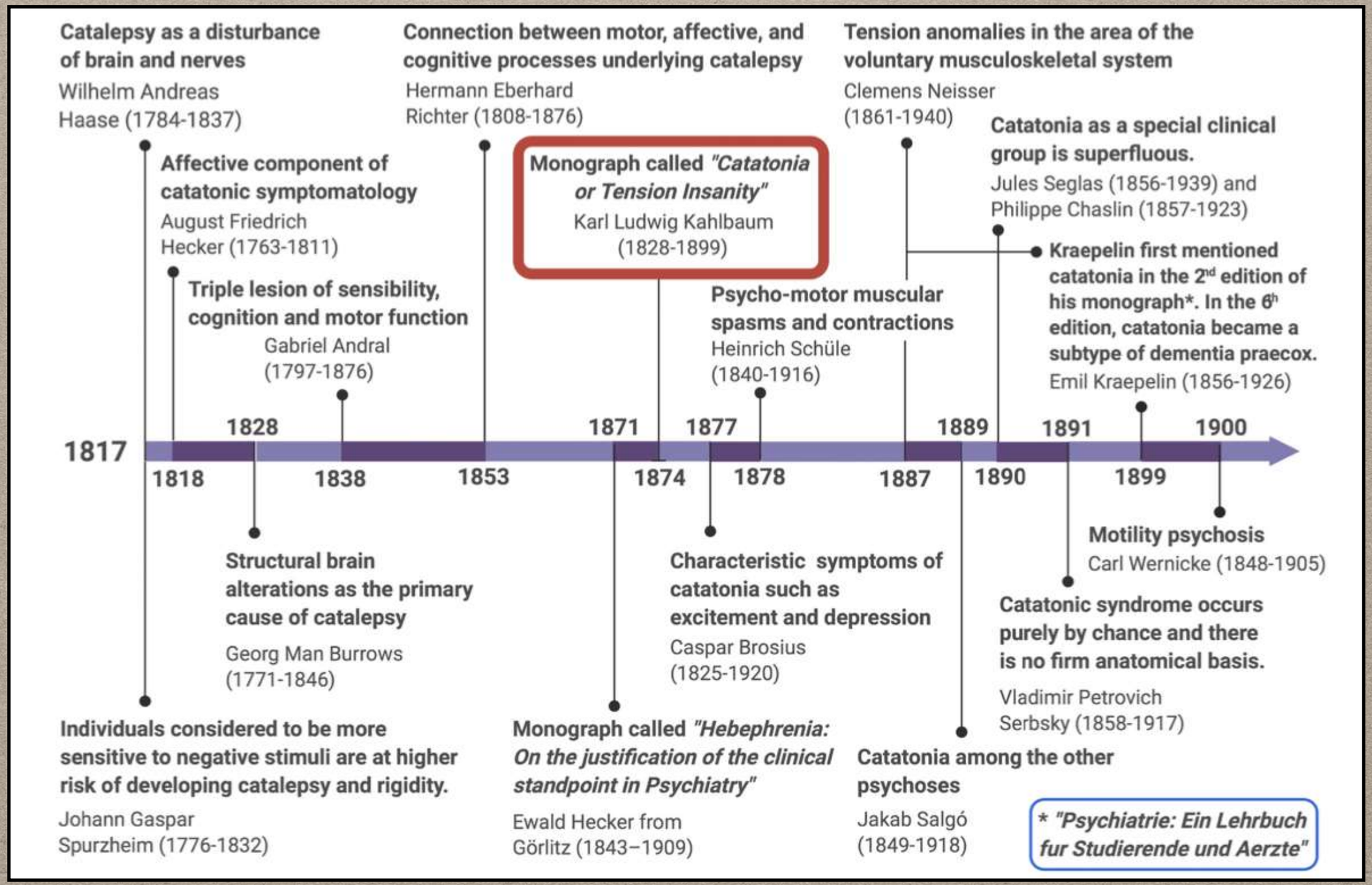
HISTORY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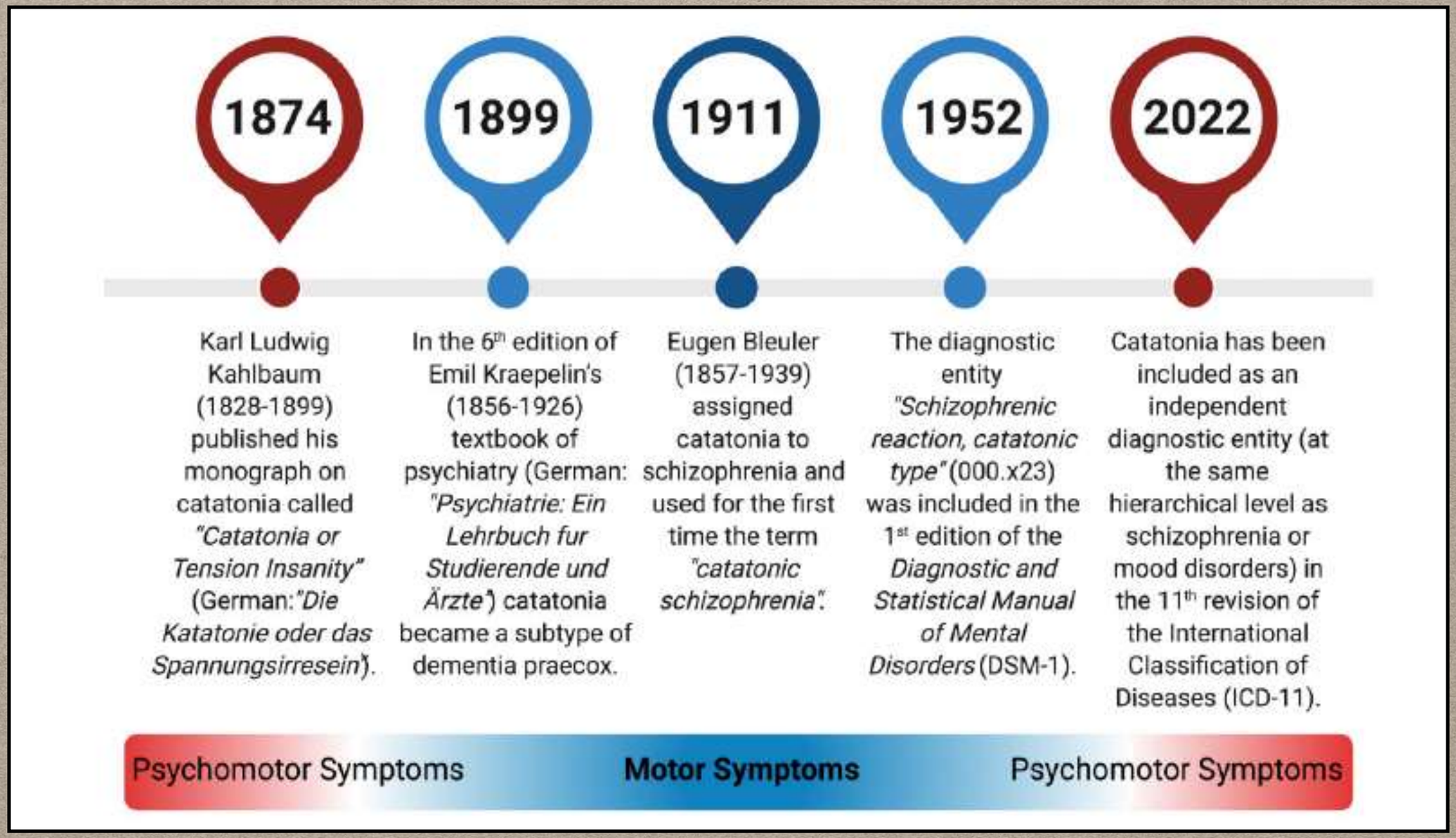
1900
Catalepsy as a disturbance of brain and nerves
Wilhelm Andreas Haase (1784-1837)
Affective component of catatonic symptomatology
August Friedrich Hecker (1763-1811)
Triple lesion of sensibility, cognition and motor function
Gabriel Andral (1797-1876)
Connection between motor, affective, and cognitive processes underlying catalepsy
Hermann Eberhard Richter (1808-1876)
Monograph called "Catatonia or Tension Insanity"
Karl Ludwig Kahlbaum (1828-1899)
Psycho-motor muscular spasms and contractions
Heinrich Schüle (1840-1916)
Tension anomalies in the area of the voluntary musculoskeletal system
Clemens Neisser (1861-1940)
Catatonia as a special clinical group is superfluous.
Jules Seglas (1856-1939) and Philippe Chaslin (1857-1923)
Kraepelin first mentioned catatonia in the 2nd edition of his monograph*. In the 6th edition, catatonia became a subtype of dementia praecox.
Emil Kraepelin (1856-1926)
Motility psychosis
Carl Wernicke (1848-1905)
Structural brain alterations as the primary cause of catalepsy
Georg Man Burrows (1771-1846)
Characteristic symptoms of catatonia such as excitement and depression
Caspar Brosius (1825-1920)
Catatonic syndrome occurs purely by chance and there is no firm anatomical basis.
Vladimir Petrovich Serbsky (1858-1917)
Individuals considered to be more sensitive to negative stimuli are at higher risk of developing catalepsy and rigidity.
Johann Gaspar Spurzheim (1776-1832)
Monograph called "Hebephrenia: On the justification of the clinical standpoint in Psychiatry"
Ewald Hecker from Görlitz (1843–1909)
Catatonia among the other psychoses
Jakab Salgó (1849-1918)
* "Psychiatrie: Ein Lehrbuch fur Studierende und Aerzte"

HISTORY


1874
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Karl Ludwig Kahlbaum (1828-1899) published his monograph on catatonia called *"Catatonia or Tension Insanity"* (German:*"Die Katatonie oder das Spannungsirresein"*).
In the 6th edition of Emil Kraepelin's (1856-1926) textbook of psychiatry (German: *"Psychiatrie: Ein Lehrbuch fur Studierende und Ärzte"*) catatonia became a subtype of dementia praecox.
Eugen Bleuler (1857-1939) assigned catatonia to schizophrenia and used for the first time the term *"catatonic schizophrenia"*.
The diagnostic entity *"Schizophrenic reaction, catatonic type"* (000.x23) was included in the 1st edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-1).
Catatonia has been included as an independent diagnostic entity (at the same hierarchical level as schizophrenia or mood disorders) in the 11th revision of the International Classification of Diseases (ICD-11).
Psychomotor Symptoms
Motor Symptoms
Psychomotor Symptoms

INTRODUCTION

- A unique syndrome: diagnosis exclusively on objective findings rather than subjective history.
- Presentation: too little (hypokinetic) OR too much (hyperkinetic) OR abnormal (parakinetic) movement.
- Underlying cause: primary mental illness OR secondary to the physiological effects of a medical condition or psychoactive substance.

INTRODUCTION

- Prevalence ~5%–18% (inpatient psychiatric units) ; ~3.3 % (neurology inpatient units).
- Incidence of catatonia is increasing in recent years.
- Heterogeneity of presentation: a reason catatonia is under-diagnosed.
- Risk of life-threatening complications. Early recognition is crucial => favourable outcome.

INTRODUCTION

- Characterized by:
  - Motor phenomena = stupor, posturing, catalepsy, waxy flexibility, stereotypies, akinesia.
  - Affective signs = fear, aggression, anxiety, flat affect, affect incontinence, impulsivity.
  - Cognitive-behavioral disturbances = mutism, autism, negativism, echolalia, echopraxia, grimacing, mannerism, rituals, automatic obedience.

ABNORMAL PSYCHOMOTOR ACTIVITY:

1. Motor and muscle tone.

posturing, catalepsy, and waxy flexibility

2. Mannerism, stereotypy, grimacing.
3. Echophenomena (echolalia and echopraxia), mitgehen/mitmachen, and gegengreifen.
4. Verbigeration and perseveration.
5. Other signs of abnormal psychomotor activity.

DECREASED PSYCHOMOTOR ACTIVITY:

1. Stupor.
2. Akinesia.
3. Mutism.
4. Negativism.
5. Withdrawal/Autism.
6. Staring.
7. Ambitendency.
8. Flat affect.
9. Affective latency.

INCREASED PSYCHOMOTOR ACTIVITY:

1. Agitation.
2. Impulsivity.
3. Combativeness.
4. Automatic obedience.

AUTONOMIC ABNORMALITY:

1. Temperature.
2. Blood pressure.
3. Pulse.
4. Respiratory rate.
5. Diaphoresis.

DIAGNOSTIC CRITERIA

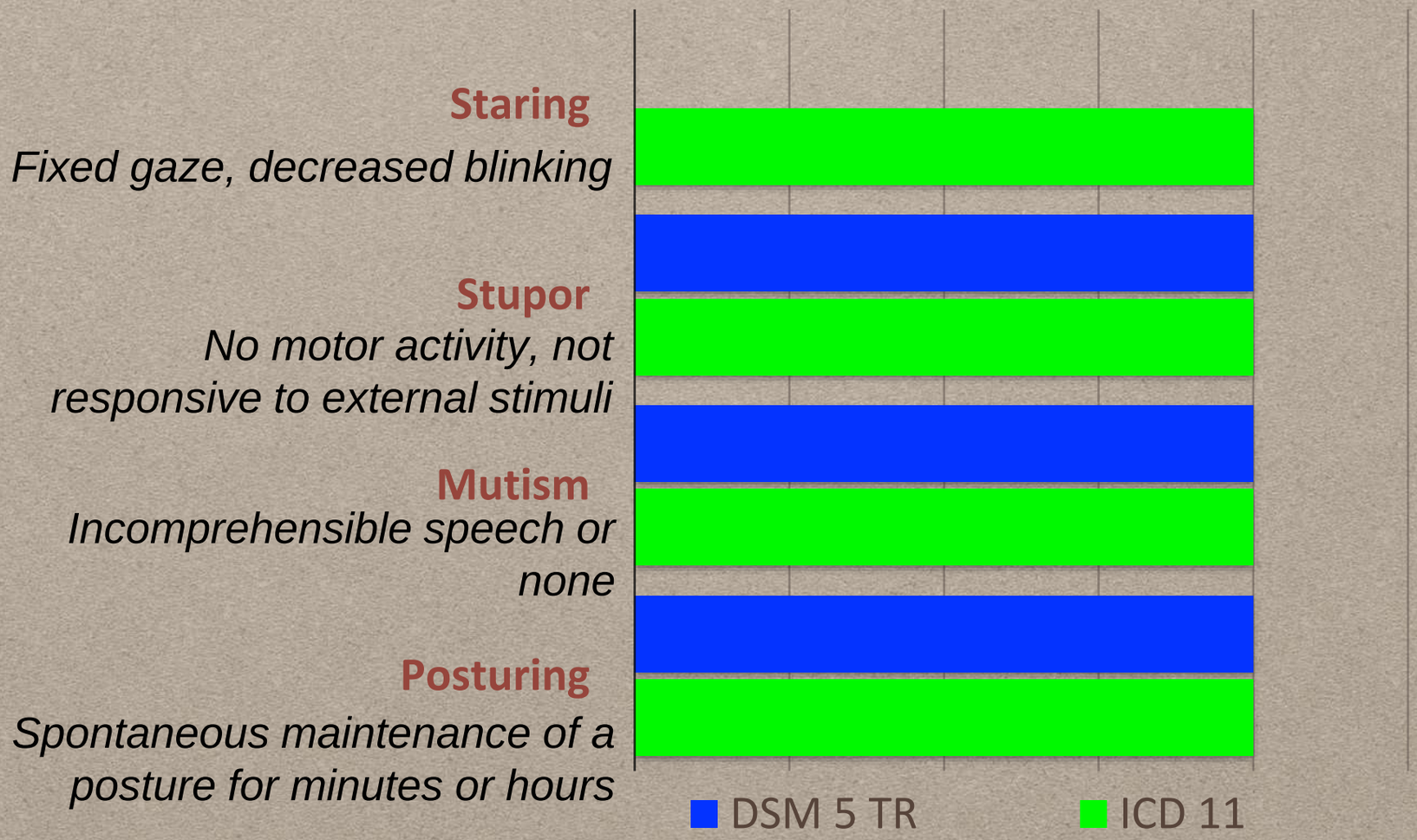
- Among several signs of catatonia, 12 are recognised as diagnostic criteria in the DSM-5, text revision.
- All 12, plus 4 additional signs, are recognised as diagnostic criteria in ICD-11.
- Any 3 of the 12 signs are sufficient for the DSM diagnosis of catatonia.
- Some signs are found in most patients: staring, stupor, mutism, and posturing.
- Some signs are almost pathognomonic, found in less than 20% of patients: echophenomena, waxy flexibility, and catalepsy.

DIAGNOSTIC CRITERIA

- Catatonic signs may emerge rapidly, reaching a maximum level within hours (in acute catatonia), or may develop slowly, over a period of days or weeks.
- Catatonic episodes may recur periodically, or they may persist for years, as seen in some patients with schizophrenia spectrum disorders or neurodevelopmental disorders, including autism spectrum disorder.
- The course of catatonia due to intoxication or to other medical conditions depends on the course of the underlying condition.
- Several clinician-administered rating scales have been validated for catatonia.
- The 23-item Bush–Francis Catatonia Rating Scale (BFCRS) is widely accepted, and teaching modules for its implementation are available at: https://www.urmc.rochester.edu/psychiatry/divisions/collaborative-care-and-wellness/bush-francis-catatonia-rating-scale.aspx

DIAGNOSTIC CRITERIA

Signs: High Frequency



DIAGNOSTIC CRITERIA

Signs: Moderate Frequency

Ambitendency
Indecisive, hesitant movements due to conflicting goals; patient appears to be stuck

Negativism
Contrary behaviour to that requested

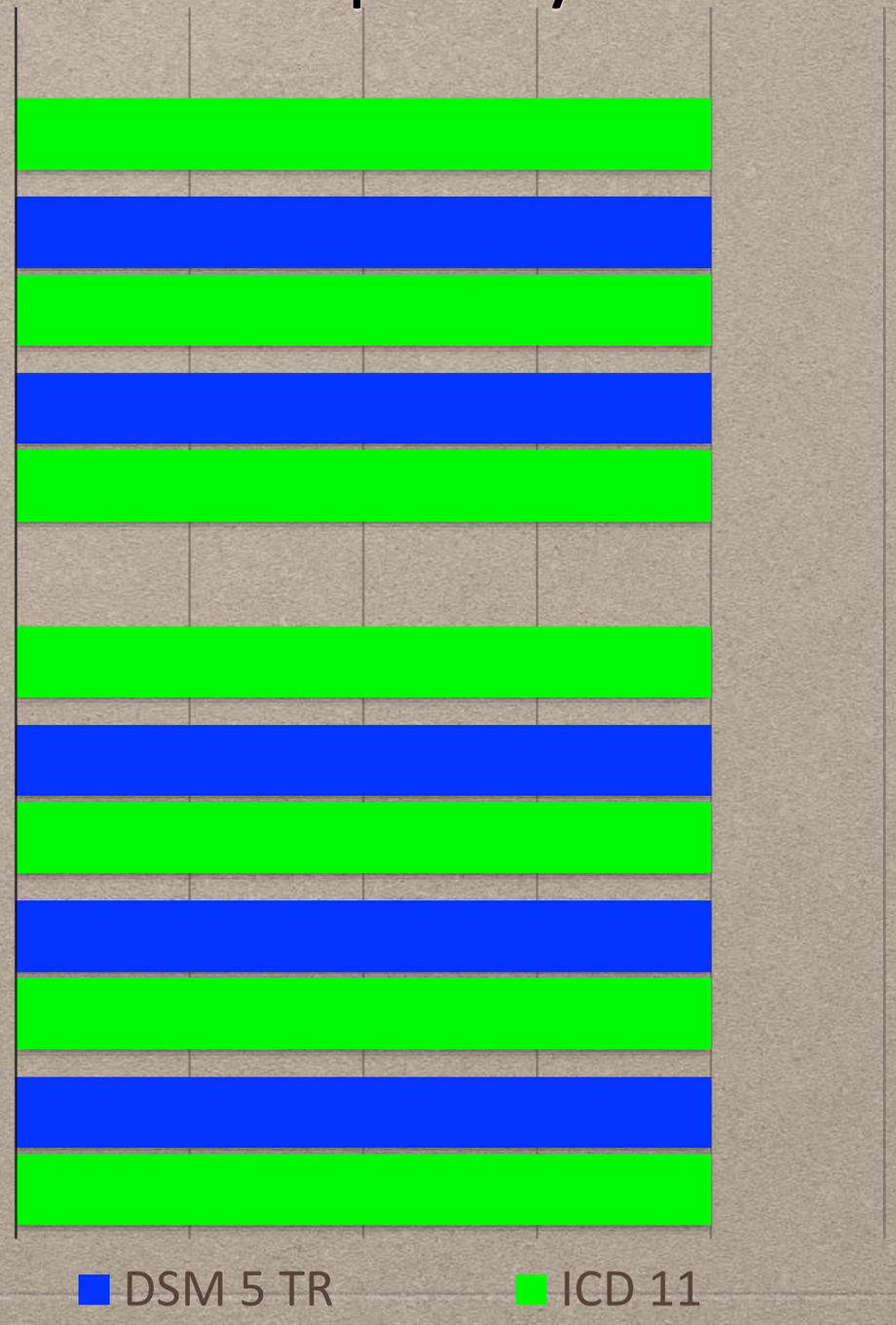
Stereotypy
Repetitive, non–goal-directed motor behavior

Rigidity
Resistance through increased muscle tone, from mild resistance to lead-pipe rigidity

Agitation
Non-purposeful movements, hyperactivity, or uncontrollable emotional reactions

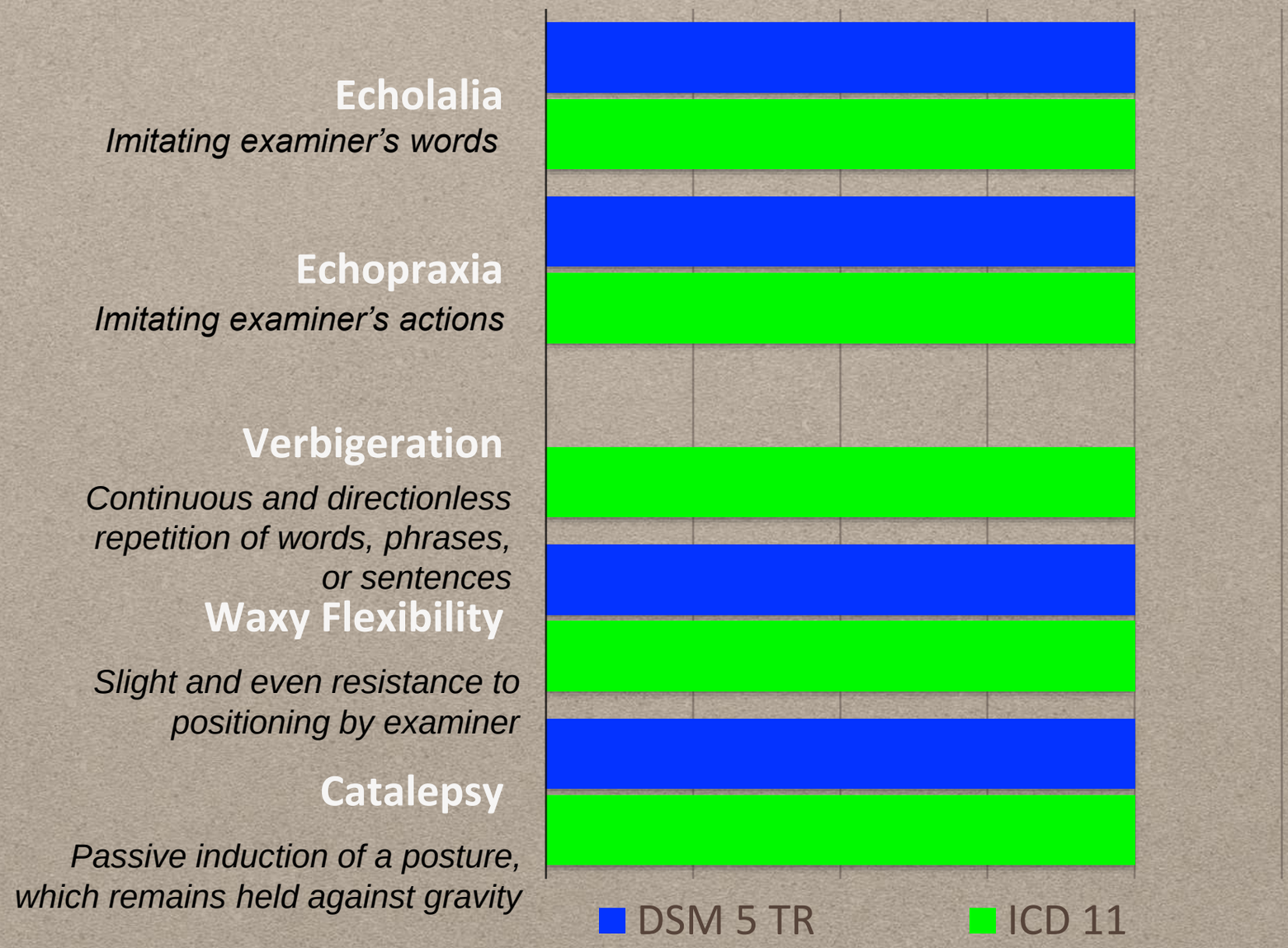
Grimacing
Distorted facial expressions, inappropriate and irrelevant to the situation

Mannerisms
Odd, purposeful movements, inappropriate to the patient's cultural context

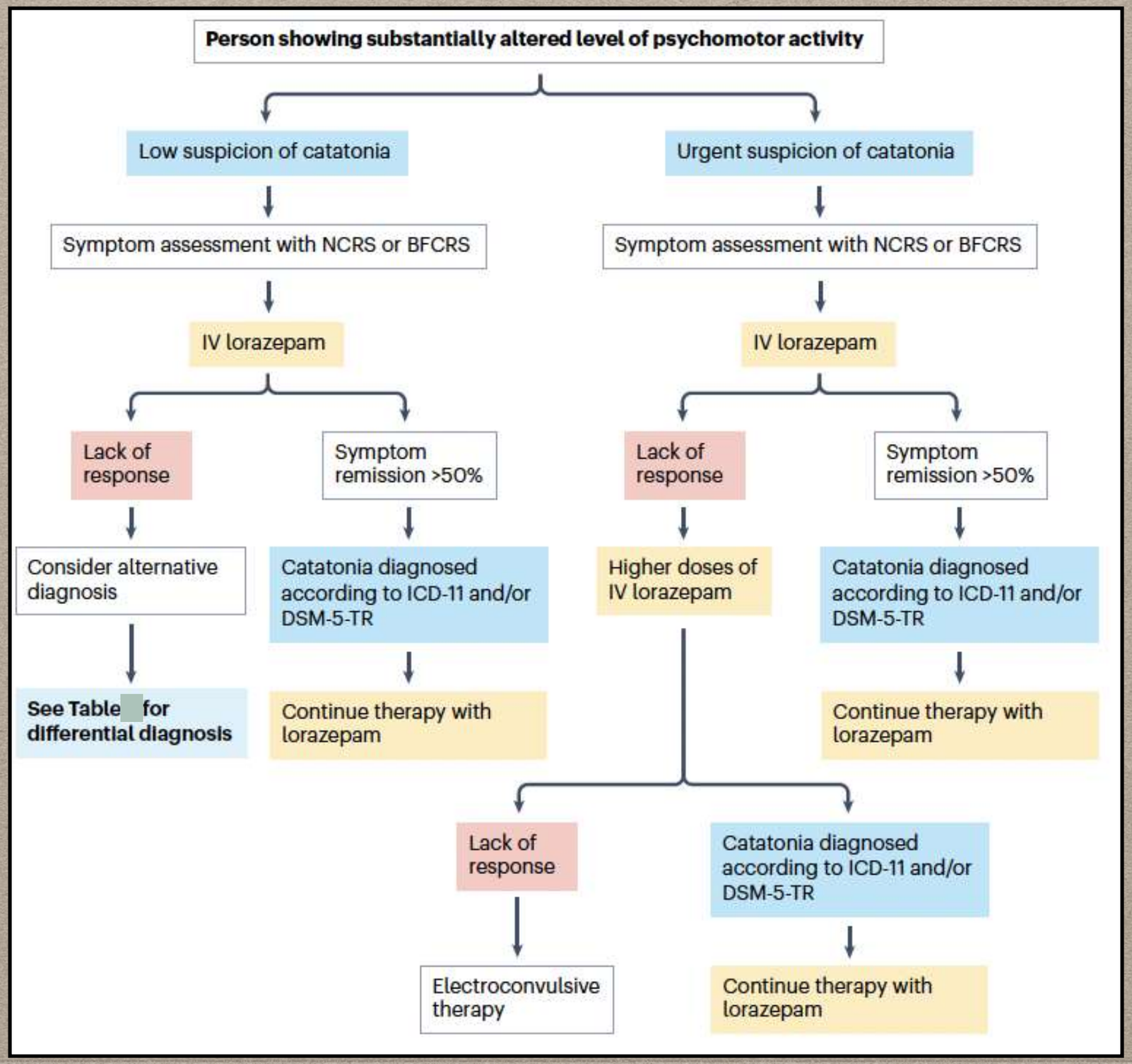


DIAGNOSTIC CRITERIA

Signs: Low Frequency



LORAZEPAM CHALLENGE TEST (LCT) ALGORITHM



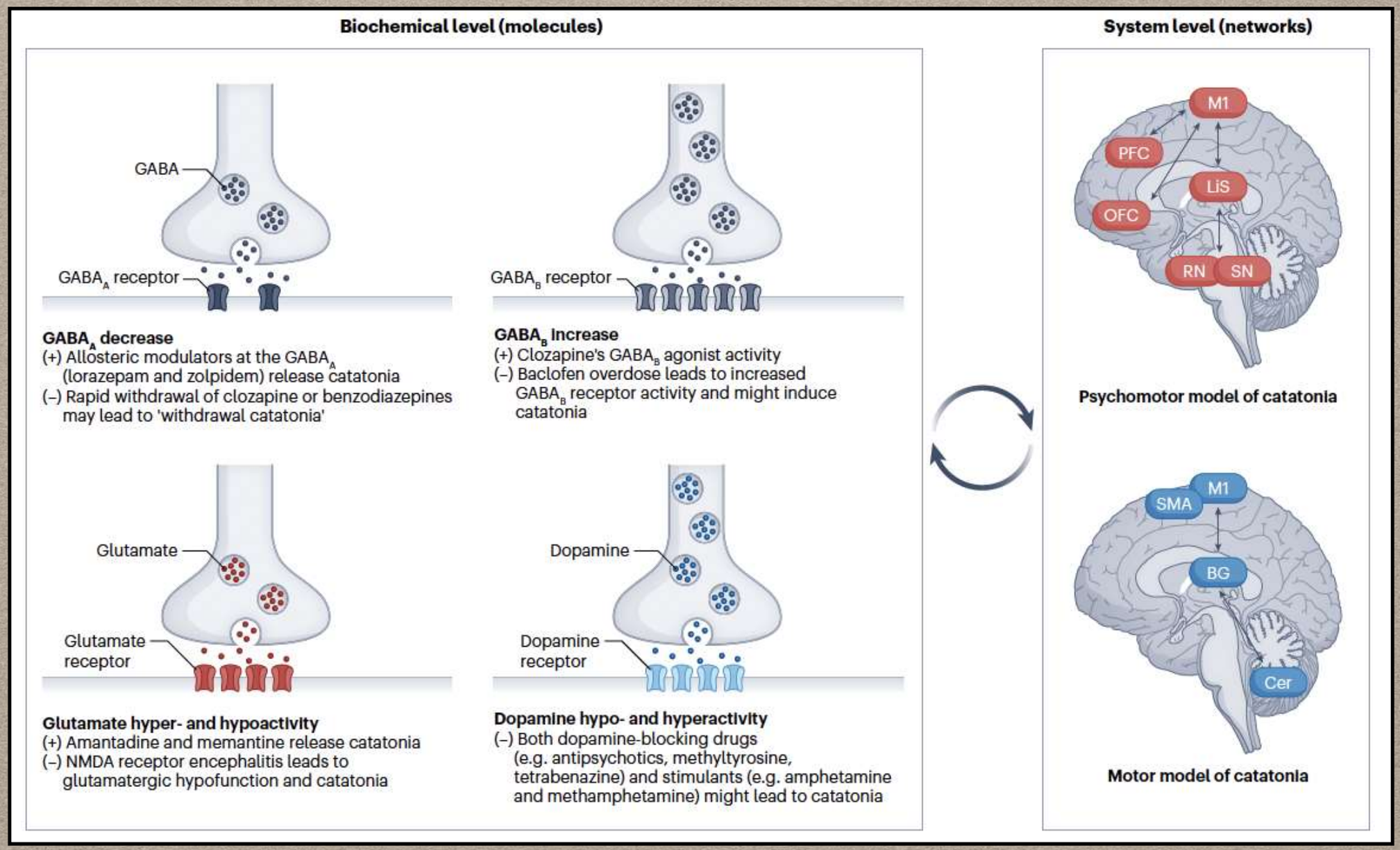
DIFFERENTIAL DIAGNOSIS

Differential diagnosis	Distinguishing features from catatonia
Stiff-person syndrome	Head retraction reflex GAD-65, glycine or DPPX antibodies usually present
Progressive encephalomyelitis with rigidity and myoclonus	
Medication-induced parkinsonism or Parkinson disease	Patients are usually interactive and cooperative Tremor usually present Insidious onset in case of Parkinson disease
Dystonia	Stupor and affective catatonic signs absent Generally good response to anticholinergics
Akathisia	Lack of other behavioural signs of catatonia (for example, echophenomena, posturing, verbigeration, mutism, staring)
Serotonergic syndrome	Triggered by serotonergic drugs; often presents with myoclonus, hyperreflexia and diarrhoea
Aphasia	Motor function intact
Anarthria (complete loss of motor speech production)	Language preserved in written form
Selective mutism	Communication completely intact in certain settings
Non-convulsive status epilepticus	Often history of epilepsy EEG usually helpful CAVE: distinguishing between the two syndromes on the basis of physical examination may be difficult
Locked-in syndrome	Individuals usually have preserved vertical gaze and blinking — generally keen to attempt to communicate using these MRI shows pontine lesions No response to benzodiazepines (for example, lorazepam challenge test) or other treatments
Delirium	Tends to resolve with reversal of underlying medical condition (though may be delayed)
Coma	No resistance to eye-opening
Vegetative state	No volitional responses and no visual tracking No resistance to eye-opening
Abulia	Intact motor functions; lack of internally generated actions, but response to external stimuli
Autoactivation deficit syndrome	
Akinetic mutism	Lack of affective and positive or active motor features (for example, catalepsy, echopraxia, mannerisms, stereotypies, gegenhalten, mitgehen)
Functional neurological disorder	Usually, progression from milder states of functional paralysis; not all symptoms of the three ICD-11 categories present

DIFFERENTIATING CATATONIA FROM DELIRIUM

Feature	Catatonia	Delirium
Clinical status	Often medically stable; however, can exhibit malignant features or have catatonia secondary to primary medical condition; may affect all ages	Due to medical illness, advanced age is a risk factor, but affects all ages
Arousal	Patients are usually awake and conscious Typically alert but may exhibit reduced or increased arousal, mixed forms of hyperkinetic and hypokinetic states in relation to motor functions and behaviour When catatonia co-occurs with delirium reduced arousal or fluctuating consciousness may occur	Most common feature is reduced level of arousal but hyperarousal and agitation may occur; fluctuating levels of consciousness a hallmark feature
Psychopathological symptoms	Usually, psychomotor signs with parakinetic movements, mostly without delusions and hallucinations but may be evident depending on the underlying psychiatric aetiology; decreased eye blinking, speech latency and negativistic response to eye and mouth opening as signals of catatonia nested in delirium	All positive symptoms possible, with hallucinations and delusions the most frequently present
Thought process	Repetitive and stereotyped thoughts, and perseveration common but the absence of thought process abnormality is not unusual	Disorganized or tangential thought process is common
Language abnormality	Mute, whispered, verbigeration or echolalia Increased volume and rate may be present in catatonic excitement	Low mumbling speech common in hypokinetic states and loud rapid speech may be present in hyperkinetic states
Orientation	Often clear but may be difficult to assess May be disoriented in comorbid delirious states	Clouded; typically disoriented
Emotional state	Usually anxious or depressed in the akinetic state; occasionally aggressive and impulsive in the hyperkinetic state, which may occur more frequently in mania	Consistent with motor subtype and the predominant psychopathological symptoms
Interpersonal	Disengaged, negativistic; occasionally automatically obedient (for example, mitgehen)	Inattentive, often sedated with limited meaningful communication possible
Response to benzodiazepines	Patients tend to become more alert and active (e.g. mutism improves) May initially become drowsy then show improvement in signs over time	Exposure to benzodiazepines may cause delirium; exposure typically leads to worsening of arousal and orientation

PATHOPHYSIOLOGY



PATHOPHYSIOLOGY

- Three distinct clinical and neurobiological views have been recognised since catatonia was described in 1874:
  - Psychomotor or affective disorder (Kahlbaum's legacy),
  - Purely motor disorder (Kraepelin's and Bleuler's legacies),
  - Neuropsychiatric perspective of the Wernicke–Kleist–Leonhard school.
- Research on pathophysiology of catatonia mirrors this conceptual distinction.

PATHOPHYSIOLOGY

- Neuroimaging studies using motor-behavioural rating scales (like BFCRS) suggest changes in dopamine-mediated cortical and subcortical motor regions as the neuronal and biochemical bases of catatonia.
- Research using NCRS (which includes affective, motor and behavioural signs i.e. a psychomotor approach) found abnormal higher-order frontoparietal networks, that are insufficiently modulated by glutamate and GABA transmission.
- Studies have shown that periodic catatonia may be associated with left premotor cortex hyperperfusion.

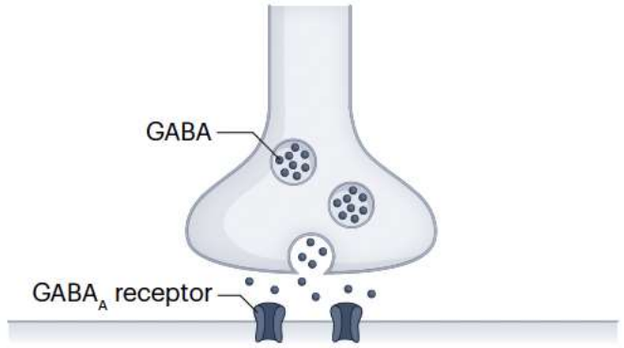
PATHOPHYSIOLOGY

- Pathophysiology of catatonia can be discussed on two specific levels irrespective of cause of catatonia (medical/psychiatric):

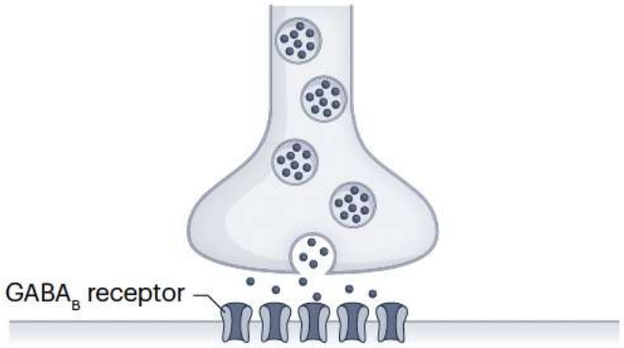
1. The biochemical (molecular).
2. The systemic (network-based).

PATHOPHYSIOLOGY

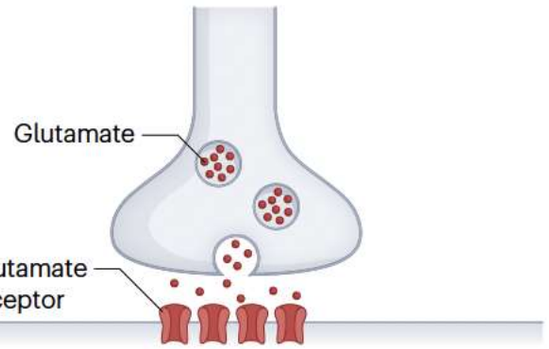
Biochemical level (molecules)



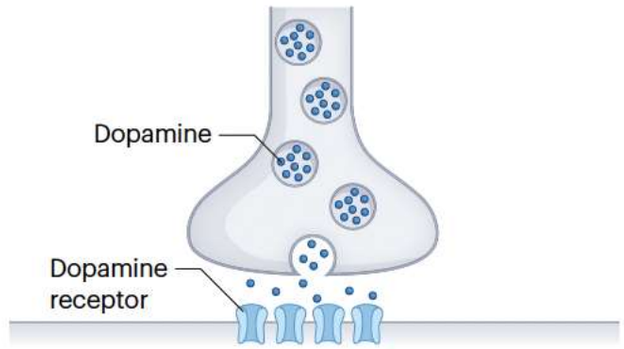
GABA$_A$ decrease
(+) Allosteric modulators at the GABA$_A$ (lorazepam and zolpidem) release catatonia
(–) Rapid withdrawal of clozapine or benzodiazepines may lead to 'withdrawal catatonia'



GABA$_B$ increase
(+) Clozapine's GABA$_B$ agonist activity
(–) Baclofen overdose leads to increased GABA$_B$ receptor activity and might induce catatonia

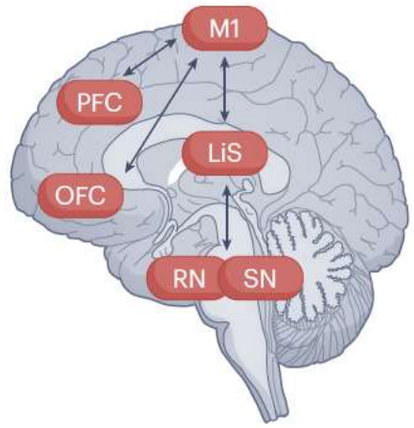


Glutamate hyper- and hypoactivity
(+) Amantadine and memantine release catatonia
(–) NMDA receptor encephalitis leads to glutamatergic hypofunction and catatonia

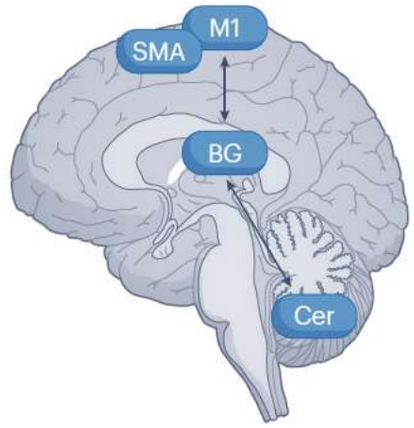


Dopamine hypo- and hyperactivity
(–) Both dopamine-blocking drugs (e.g. antipsychotics, methyltyrosine, tetrabenazine) and stimulants (e.g. amphetamine and methamphetamine) might lead to catatonia

System level (networks)



Psychomotor model of catatonia



Motor model of catatonia

PATHOPHYSIOLOGY

Risk factors of catatonia:

- **Neuroinflammatory:** inflammatory brain disorders, encephalitis, SLE, autoimmune diseases like Sjogren syndrome and antibody-mediated encephalitis, like NMDAR encephalitis, infectious encephalitis caused by HSV, HIV, COVID-19,Treponema pallidum (syphilis) and Borrelia burgdorferi (Lyme disease) infections. As a result of injury or activation of the innate immune system against infected cells, a cortico-striato-thalamocortical loop dysfunction (for example, motivation and movement systems) might develop, leading to catatonia.
- Pharmacological.
- Genetic factors.

PATHOPHYSIOLOGY

Risk factors of catatonia:

- Neuroinflammatory.
- **Pharmacological:** dopaminergic hypofunction in the mesostriatal pathway, increase in GABA-B activity by APD has been suggested to trigger APD-induced catatonia, methamphetamine use can trigger catatonia, supporting the contribution of an overactive dopaminergic system, dopamine antagonism substantially influences glutamate pathways.
- **Genetic factors.**

PATHOPHYSIOLOGY

Risk factors of catatonia:

- Neuroinflammatory.
- Pharmacological.
- **Genetic factors:** preliminary evidence shows that severe catatonic signs are associated with a loss-of-function allele of a myelin-specific gene (rs2070106), changes in the expression of a myelin-specific gene and neurochemical abnormalities (for example, low-grade inflammation or neurodegeneration).

PATHOPHYSIOLOGY

Molecular and immunological pathways:

- Dysfunction in the GABAergic, glutamatergic, dopaminergic and serotonergic neurotransmitter systems.
- Autoimmune catatonia may result from glutamatergic hypofunction.

PATHOPHYSIOLOGY

Systems perspective:

- Altered functional connectivity of the OFC to the premotor cortex and reduced GABA-A receptor density in the left sensorimotor cortex.

- Preliminary evidence shows that cortical features (cortical thickness, surface area and gyrification) across various motor and non-motor regions contribute differently to catatonia associated with SSD.

PATHOPHYSIOLOGY

Systems perspective:

- fMRI studies in catatonia associated with SSD have shown large-scale functional brain network dysconnectivity, which might result from abnormal white matter microstructure.
- Microstructural alterations within white matter tracts connecting psychomotor-related regions, like OFC, PFC, primary motor cortex, SMA and BG, can contribute to the development of catatonia.
- Studies suggest a key role for alterations such as reduced volumes of subcortical limbic structures in affect dysregulation in catatonia.

PATHOPHYSIOLOGY

Systems perspective:

- Reduced grey matter volume in the frontothalamic network may reduce intrinsic neural activity in the frontoparietal circuit.

- This results in impaired processing of negative emotional stimuli and the cessation of sensorimotor functioning, leading to affective and behavioural catatonic signs.

PATHOPHYSIOLOGY

Systems perspective:

- OFC is responsible for impulse control, affect regulation and decision making.
- Aberrant OFC–prefrontal and OFC–parietal cortical connectivity in catatonia can reflect disrupted ‘horizontal modulation’ of the corticocortical networks.
- This further leads to aberrant function of subcortical structures such as the limbic system, the raphe nucleus (serotonergic system) and the substantia nigra (dopaminergic system).
- Such alterations may be the mechanism underlying impulsive behaviour, aggression, disturbed affective and mood regulation (like fear) which are characteristic symptoms of catatonia.

PATHOPHYSIOLOGY

Systems perspective:

- Studies on subcortical and cortical motor systems found both decreased and increased structural and functional changes in MRI measures of the motor cortex or supplementary motor cortex, as well as in subcortical regions such as the basal ganglia and cerebellum.

- Abnormalities in these motor regions can still result from aberrant activity of primarily non-motor regions involved in other functions such as the OFC, PFC or raphe nucleus and default mode network regions, thus accounting for psychomotor abnormalities and not exclusively motor symptoms

PATHOPHYSIOLOGY

Systems perspective:

- A systematic review found:

1. alterations in the frontoparietal and limbic regions, the thalamus and the striatum.
2. multiple cortical and subcortical brain changes in catatonia, including diffuse atrophy and signal hyperintensities in the frontal lobe and cerebellum.
3. OFC (hypoactivation), medial PFC (hyperactivation and hypoactivation), primary motor cortices (increased connectivity), supplementary motor area (hyperactivation and hypoactivation) and cerebellum (increased connectivity).
4. mixed changes in perfusion and metabolism were observed in the motor cortex, PFC and BG regions.

MANAGEMENT

General principles of management:

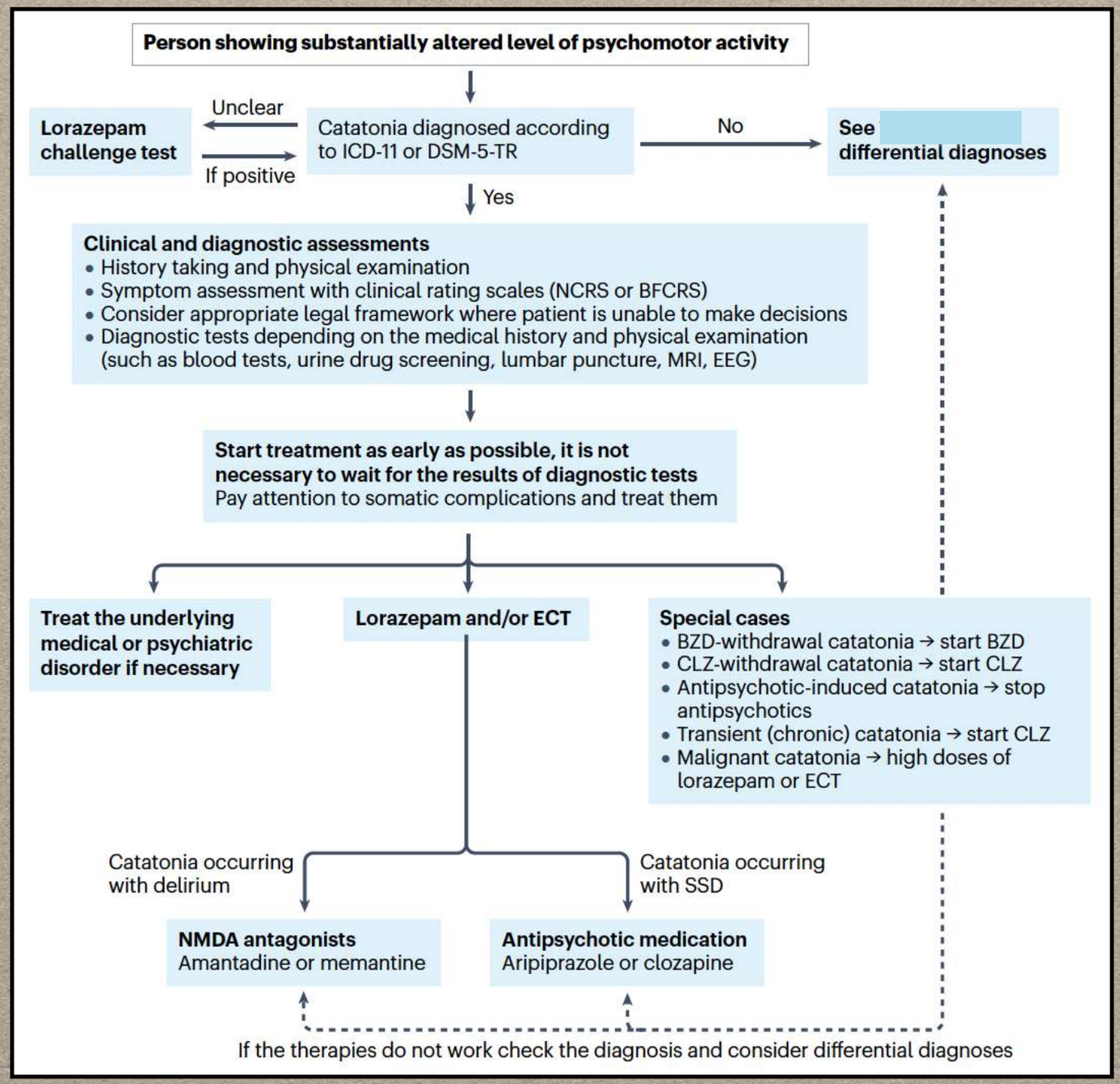
1. Direct management of the catatonic syndrome itself.

2. The treatment of any underlying conditions (medical or psychiatric diseases, or both).

3. Prevention of any medical complications that may arise as a consequence of the catatonic state.

MANAGEMENT

An algorithm for the management of catatonia



GABAergic medicines,
ECT,
NMDA antagonists,
Dopamine antagonists.

CONCLUSION

“Progress in catatonia research has the capacity to have a widespread impact in the field of psychiatry.”

REFERENCES

1. Hirjak, D., Rogers, J.P., Wolf, R.C. et al. Catatonia. Nat Rev Dis Primers 10, 49 (2024). https://doi.org/10.1038/s41572-024-00534-w

2. Heckers S, Walther S. Catatonia. N Engl J Med. 2023 Nov 9;389(19):1797-1802. doi: 10.1056/NEJMra2116304. PMID: 37937779.

3. Dusan Hirjak, Georg Northoff, Schizophrenia research, Vol. 263, January 2024, pages 1-288.