Catatonia in Autism Spectrum Disorders – A specifier or much more ?

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RADIANT NETWORK

Hertfordshire Partnership NHS Trust

Autism Spectrum Disorders

ASD – DSM V

A. **Persistent deficits in social communication as manifested by all >**	Social emotional reciprocity
	Nonverbal communicative behaviours
	Developing & maintaining relationships

ASD – DSM V

B.

Restricted behaviour, interests as manifested by at least two of >

- Stereotyped motor movements

- Inflexible adherence to routines/ritualised pattern

- Highly restricted/fixed interests (unusual objects)

- Hyper/hypo activity to sensory input

ASD – DSM V specifiers

- ✓ Requiring very substantial support
- ✓With or with out accompanying intellectual impairment
- ✓With out with out accompanying language impairment
- ✓Associated with known genetic medical condition
- ✓Associated with a neurodevelopmental, mental or behavioural pattern

- ✓**With catatonia – to indicate comorbid catatonia**

Autism Spectrum Disorder – ICD 11 criteria

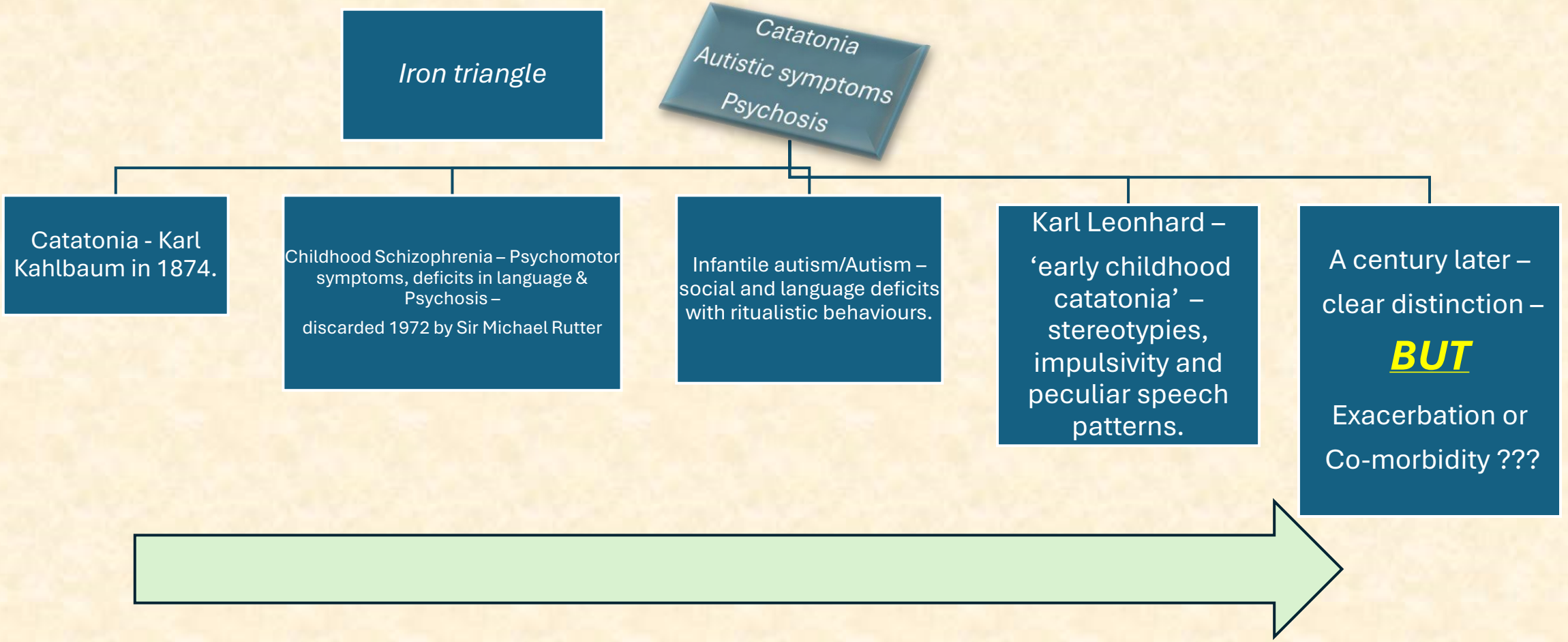
Persistent deficits in ability to initiate and sustain reciprocal social interaction and social communication

Range of restricted, repetitive and inflexible behaviour patterns and interests.

Onset during developmental period, symptoms can manifest later

Six Specifiers – Intellectual development and language function.

Historical perspectives



CATATONIA

Catatonia is a marked disturbance in voluntary control of movements characterized by:
(ICD -11)

* Extreme slowing/absence of motor activity

* Mutism

* Maintenance of rigid/bizarre postures

* Resistance to attempts to be moved
- Automatic compliance to instructions
- Specifiers - with another mental disorder, psychoactive substances & Unspecified.

Review of literature:

European Psychiatry

www.cambridge.org/epa

Catatonia in autism spectrum disorders: A systematic review and meta-analysis

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Review/Meta-analyses

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Key points

- ✓12 studies – 1,534 individuals
- ✓Later, 7 out of 12 studies (969 individuals) for meta-analysis.
- ✓Mean age – 21.25 years
- ✓70-100 % were males.
- ✓20.2 % with ASD had catatonia
- ✓Motor disturbances were common in ASD with catatonia
- ✓Four studies from US, seven from Europe and one from Asia.

Table 1. Main characteristics of the included studies regarding catatonia and ASD.

Study	Study type and design (NOS)	Type of sample	Country	Sample	Diagnostic criteria	Mean age (SD)	Gender %Males	Key findings
Billstedt et al. [37]	Longitudinal (6)	Population-based	Sweden	108 ASD 13 Catatonia	DSM-III/DSM-IV/ ICD-10/HBSS/ CARS/ABC/ Wing criteria/ DISCO	25.5	70	ASD subjects showed a poor outcome at follow-up. Childhood IQ-level was positively correlated with better adult outcome, as was the existence of some communicative phrase speech at age 6 years. Those diagnosed with catatonia had severe motor initiation problems
Breen and Hare [38]	Cross-sectional (5)	Population-based	UK	99 ASD 20 Catatonia	ABQ	15.7	79.8	Attenuated behavior indicative of catatonia was common in young people with ASD. Six catatonic core symptoms were commonly reported, with difficulty initiating movement being least reported and physical and/or verbal prompts required most reported
Ghaziuddin et al. [33]	Cross-sectional (7)	Clinic-based	US	81 ASD 18 Catatonia	Clinical criteria	13.9 (2.04)	80.2	Subjects with catatonia were older and had a lower score of global functioning. Aggression was more common among the group diagnosed with catatonia compared with the noncatatonic group. Similarly, reduced movements and loss of speech were also more common among this group
Hare et al. [45]	Cross-sectional (5)	Population-based	UK	99 ASD 20 Catatonia	ABQ	15.7	79.8	Catatonia appears to be more prevalent in both ASD and in genetic syndromes that are strongly associated with comorbid ASD than was previously thought
Hutton et al. [40]	Longitudinal (5)	Population-based	UK	135 ASD 3 Catatonia	ADI-R/ADOS/ SAPPA/ICD-10	na	77	The presence of obsessive–compulsive behavior and of catatonia, which mainly seemed to stem from obsessive–compulsive symptoms, might be particularly characteristic of ASD. Of 135 individuals with ASD, 16% reported a new psychiatric disorder, of whom three patients reported a catatonia
Ohta et al. [44]	Longitudinal (4)	Clinic-based	Japan	11 ASD 2 Catatonia	DSM-IV/ICD-10/ Wing criteria	27.6 (5.5)	100	The average age at onset of catatonia was 19 years (ranged 15–23). A total of 11.6% ASD had catatonia. Before the manifestation of a typical catatonic symptom, eight cases had prodromal symptoms, typically a gradually emerging lethargy with compulsive behaviors lasting for more than 1 year

Results

Characteristics of patients with ASD and Catatonia	
Motor disturbances	85 %
Intellectual disability	Up to 81 %
Impaired speech	29 – 100%
Negativism	69.5 – 85 %
Agitation uninfluenced by external stimuli	62 – 75 %
Aggression	62 – 73 %
Echolalia	Up to 61.3 %
Posturing	63.3 %
Stereotypies	19.4 – 61.1 %

Characteristics of ASD individuals who developed catatonic features during follow-up (2.2 – 12%)	
Agitation	18.2- 95.5 %
Stereotypies	90.1 %
Posturing	81.8%
Negativism	77.3 %
Mutism	63.6%
Echolalia	9.1 %
Self harm behaviour	27.7-90.9 %
Aggression	18.2 – 19 %

Other key points:

- Obsessive-compulsive symptoms were found in 26.6% preceding catatonia.
- 39%-83% had marked anxiety.
- 44.0%-55.6% showed hyperactivity symptoms.
- Between **60.0% and 72.7% of ASD individuals with obsessive-compulsive symptoms developed catatonic features during follow-up**.
- Treated with Benzodiazepines (95.5%), anti-psychotics (27-100%) & ECT used in 22 individuals.

REVIEW OF LITERATURE -

Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-025-06855-3

ORIGINAL ARTICLE

Check for updates

Systematic Review of Symptoms of Catatonia in Autism Spectrum Disorder

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Accepted: 18 April 2025

Key Points

- Initially included 1195 studies > 45 selected for results.
- **Six symptom clusters defined**
- Extended beyond diagnostic criteria of catatonia in ICD 11 to support improved clinical recognition in ASD population.

✓Psychomotor changes

✓Speech disturbances

✓Behavioural & functional regression

✓Affective & psychiatric symptoms

✓Physiological symptoms

✓Arousal disturbances

Summary of key symptom groups in autistic catatonia

SYMPTOM GROUP	NO. OF STUDIES REPORTING	PERCENTAGE
PSYCHOMOTOR ACTIVITY	45	100
BEHAVIORAL & FUNCTIONAL CHANGES	41	91.1
PHYSIOLOGICAL SYMPTOMS	35	77.8
AFFECTIVE & NON-AFFECTIVE	31	68.9
SPEECH DISTURBANCES	19	42.2
Arousal & awareness	7	15.6

Table 3 Psychomotor activity symptoms

Subgroup	Symptoms identified	Number of studies reporting	Percentage (%)
Abnormal psychomotor activity	Rigidity	19	42.2
	Facial grimacing	10	22.2
	Waxy flexibility	16	35.6
	Echophenomena (Echolalia and Echopraxia)	16	35.6
	Stereotypy	14	31.1
	Mannerisms	11	24.4
	Posturing	34	75.6
	Catalepsy	6	13.3
	Abnormal/repetitive movement/tone*	17	37.8
	Tics*	9	20.0
Increased psychomotor activity	Extreme hyperactivity	26	57.8
	Impulsivity	2	4.4
	Combativeness	14	31.1
Decreased psychomotor activity	Mutism	36	80.0
	Staring	14	31.1
	Ambitendency	3	6.6
	Stupor	39	86.7
	Negativism	20	44.4
	Freezing, initiation and termination of movement; & difficulties ambulating/gait abnormality*	19	42.2
Compliance	Motor compliance	14	31.1
	Automatic obedience	4	8.9

*Symptoms not included in ICD-11 diagnostic criteria

✓ **Stupor was the most found symptom among the studies included.**

✓ **Tics and gait abnormality were found to be in 20 and 42.20%, respectively.**

Speech & Behavioural function symptoms

Table 4 Speech symptoms

Symptoms identified	Number of studies reporting	Percentage (%)
Reduced content and rate of speech	13	28.9
Verbal repetition (perseverative speech)	3	6.7
Incoherent speech	4	8.9
Abnormal speech tone/prosody	2	4.4

Subgroup	Symptoms identified	Number of studies reporting	Percentage (%)
Changes in behavior/function	Behavioral change	5	11.1
	Obsessional/compulsive behaviors	10	22.2
	Behavior that challenges	11	24.4
	Self-injury	13	28.9
Regression in skills/function	Loss of motor skills	10	22.2
	Cognitive decline	9	20.0
	Social/occupational impairment	24	53.3

Affective & Non-Affective symptoms in ASD individuals with Catatonia

Table 6 Affective and non-affective mental health symptoms

Subgroup	Symptoms identified	Number of studies reporting	Percentage (%)
Affective	Low mood	10	22.2
	Mood lability	5	11.1
	Irritability	7	15.6
	Mania	2	4.4
	Suicidality	2	4.4
	Anhedonia	9	20.0
	Crying	10	22.2
	Abnormal affect	8	17.8
Non-affective	Anxiety	11	24.4
	Psychosis	6	13.3

Physiological symptoms in ASD individuals with Catatonia

Subgroup	Symptoms identified	Number of studies reporting	Percentage (%)
Oral intake/appetite changes	Reduced intake	13	28.9
	Change in appetite	9	20.0
	Weight loss and Dehydration	13	28.9
Sleep disturbances	Insomnia, hypersomnia, circadian rhythm disruptions	12	26.7
Emesis	Vomiting	3	6.7
	Regurgitation	2	4.4
Autonomic symptoms	Abnormal vital signs	7	15.6
	Excessive salivation	1	2.2
	Sweating	1	2.2
	Flushing	1	2.2
	Acrocyanosis	2	4.4
Bowel and bladder dysfunction	Incontinence	11	24.4
	Retention	1	2.2
Somatic symptoms	Diffuse aches and pains	3	6.6

BUT WHY CATATONIA ?

- Classic catatonia – straightforward to diagnose
- Challenging overlap of symptoms – motor stereotypies, mannerisms, mutism, echolalia and negativism
- Autistic catatonia ? – freezing/slow/stopping during movement
  - Risk of overdiagnosis of catatonia.
- Severe self- injury & Unremitting tics - ? Suggestive of catatonia – responds well with BZD/ECT.

- Such behaviours are separate entity or part of catatonia continuum for patients with NDD ?

Moore S, Amatya DN, Chu MM, Besterman AD. Catatonia in autism and other neurodevelopmental disabilities: a state-of-the-art review. Npj Ment Health Res. 2022 Sep 14;1(1):12. doi: 10.1038/s44184-022-00012-9. PMID: 38609506; PMCID: PMC10955936.

TRAUMATIC EXPERIENCES

- Potential risk factor for catatonia/catatonia like states
- '*Pervasive Refusal Disorder'* – neurotypical patients of asylum-seeking families – significant reduction in oral intake, communication, movement and self-care.
- Disruptions to daily routine, grief, loss of structure post environmental change, parental divorce and physical abuse – triggers for catatonia (Wing & Shah et al, 2000)

PATHOPHYSIOLOGY

- Biological convergence can occur at multiple levels:

1. Genetic
2. Neural circuits – Excitatory/Inhibitory imbalance
3. Neuroimmune interface

GENETIC

Table 2. Examples of potential convergent biological mechanisms in catatonia and NDDs.

Level	Mechanism	Catatonia	NDDs
Genetic	Noncoding single nucleotide variants	• Small nucleolar RNA mutations are hypothesized to impact downstream gene regulation & splicing in catatonia[45]	• Mouse models with small nucleolar RNA deletions recapitulate symptoms of autism[46]
	Structural variants	• 22q13.3 and 22q11.2 deletions are associated with catatonia[39]	• Disruption of 22q13.3 and 22q11.2 deletions associated with NDDs[112]

- Strong familial aggregation of catatonia
- Candidate genes like Myelin Basic Protein
- Catatonia in patients with NDD with established genetic aetiologies – Prader Willi Syndrome, 22q13.3 deletion (Phelan – McDermid syndrome), Down syndrome, late onset Tay Sachs disease
- Non-coding micro-RNA (SNORD 115) identified in Prader Willi/Angelman syndrome – known to regulate downstream effector genes ultimately affecting NMDA receptor function

Neural circuits

Neural circuits	EI imbalance	• Local glutamate overactivity and GABA underactivity is thought to play a role in catatonia[34,52]	• Mouse models support disruption in EI balance leading to ASD phenotypes. Increasing EI balance in prefrontal cortex using optogenetics leads to social deficits[61,62] • Decreased GABA receptor density and altered GAD1 and GAD2 levels. Functional imaging studies identify local hyperconnectivity and decreased long-range connections[60]

- NMDA receptor dysfunction – altered cellular excitability – catatonia risk in SHANK3 – associated disorders.
- Overlap with ASD susceptibility locus linked with catatonia, 15q15 gene – encoding GABA receptors – E/I imbalance

Neural circuits

- Low dopamine > excess Glutamate release > excitotoxicity
- GABA hypoactivity > decreased inhibitory tone (BZD)

➢ Hyperactivity in supplementary and pre-supplementary motor areas – altered GABA concentration – E/I imbalance - Hypokinetic catatonia

➢E/I in ASD – postmortem studies – NLGN3 and SHANK3 genes – rodent models – EI precipitates as ASD like social deficits – rescued by GABA agonism or NMDA antagonism.

Neuroimmune interface

Neuroimmune interface	Autoimmunity	• NMDAR encephalitis is causally linked to the development of catatonia[52] • Systemic autoimmune conditions, like SLE, increase risk for the development of catatonia[113] • Rodent models suggest that brain inflammation in catatonia is mediated by microglial activation[37] • Standard treatments for catatonia, like ECT, have been shown to have an immunomodulatory effect over chronic administration[71]	• Family history of autoimmune conditions increase the risk for ASD[65] • Gene network analysis identify immune dysregulation and microglial activation as key molecular signatures[77] • Rodent models suggest that attenuation of microglial activity can rescue ASD-like behaviors[37]

✓ Auto-antibodies on receptors of excitatory glutamatergic neurons > excitatory hypofunction > neuropsychiatric symptoms (Seizures, psychosis & catatonia) = NMDAR Encephalitis

✓ Family history of auto-immune conditions (T1 DM, Psoriasis, RA) – more likely in ASD patients. Role of gene encoding for B cell protein (complement pathway), microglial differential activation affecting synaptic transmission in ASD like traits.

✓ ASD patients more prone to acquired conditions later in life like Multiple sclerosis & Guillain Barre Syndrome

GENETIC TESTING

Table 3. Genetic testing strategies for neurodevelopmental disabilities.

Fragile X testing

Previously recommended as first-tier test for all males with NDDs, but low yield has resulted in reconsideration of this recommendation (https://www.nature.com/articles/gim2017146)

Uses polymerase chain reaction to detect CGG repeats in the *FMR1* gene

>200 repeats cause Fragile X Syndrome, while 55–200 repeats is associated with Fragile X premutation-associated conditions (https://www.futuremedicine.com/doi/full/10.2217/fnl.14.11)

Chromosomal microarray

Detects genomic deletions and duplications as seen in 22q11.2 deletion syndrome or 15q11.2 duplication

Considered a first-tier test for NDDs with diagnostic yield of 10–20% (https://www.sciencedirect.com/science/article/pii/S0002929710002089)

Gene panel testing

Varies widely depending on the specific company

Detects a limited range of genetic variants known to be associated with NDDs

Whole exome sequencing

Uses next-generation sequencing to identify single base pair changes (single nucleotide variants) in gene-coding regions (exons)

Recent recommendations to include as first- or second-tier test for NDDs with diagnostic yields up to ~50% in most severely affected patients[80].

Does not detect genomic deletions/duplications or repeat expansions

Whole genome sequencing

Uses next-generation sequencing to identify single base pair changes (single nucleotide variants) in both gene-coding regions (exons) and gene regulatory regions (introns)

Can detect genomic deletions/duplications, but not repeat expansions

Recent recommendations to include as first- or second-tier test for NDDs with diagnostic yields up to ~50% in most severely affected patients[80].

DNA methylation analysis

For a few NDDs such as Beckwith-Wiedemann, Prader-Willi, and Angelman syndromes, abnormal methylation patterns are causative (https://pubmed.ncbi.nlm.nih.gov/28818477/)

Usually only ordered when clinically suspected

Genetic testing

- Genetic testing and counselling recommended for all with NDD
- If suspicion of Auto-immune encephalitis – watch for - autonomic dysfunction, new onset seizures, new focal neurological signs
- Immunomodulatory therapies – IV immunoglobulins or systemic glucocorticoids
- Minocycline and Vitamin D – improve ASD related behaviour in animal models.
- Rituximab & Mycophenolate – research-based evidence of improvement in SHANK3 associated treatment resistant NDD

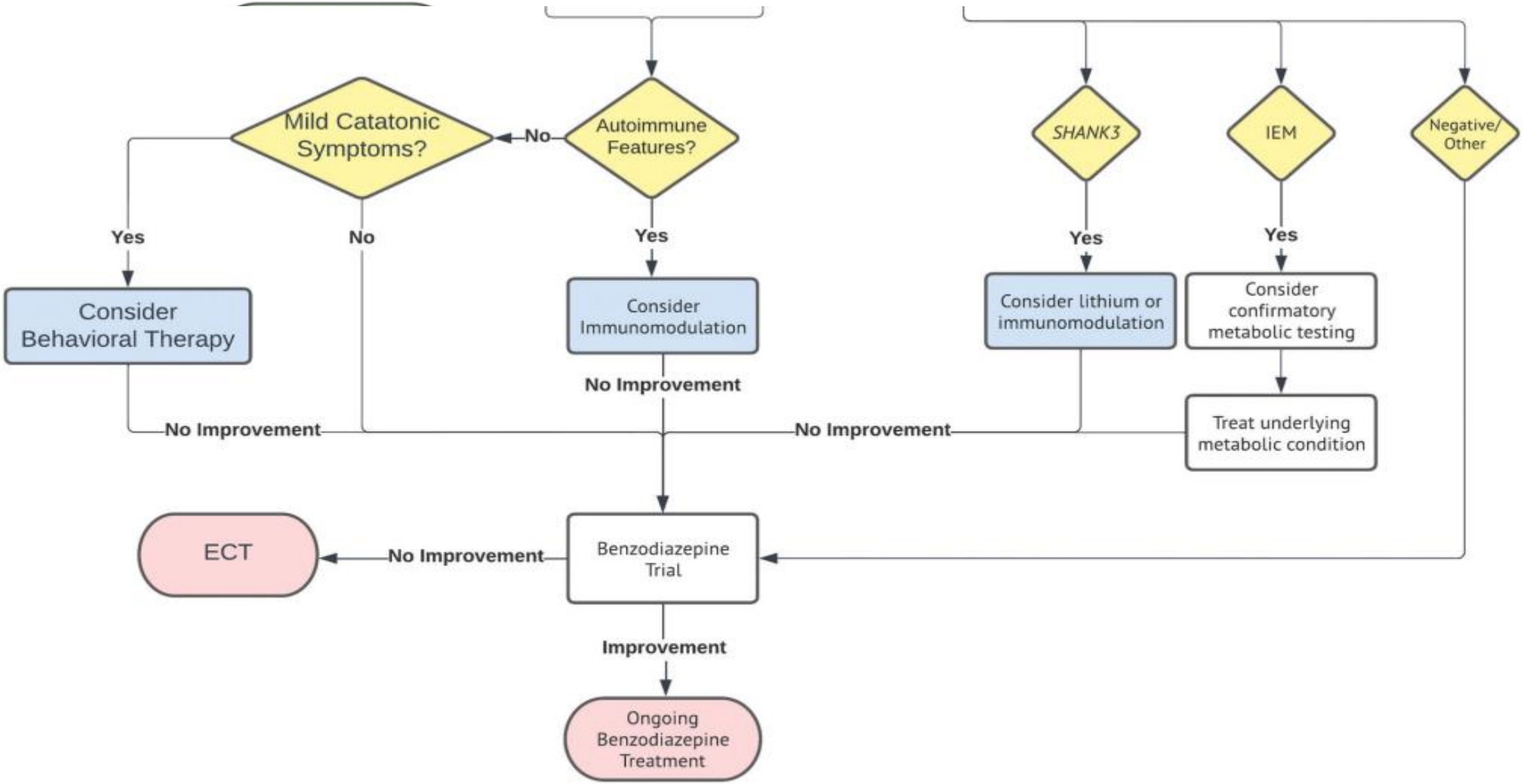

Fig. 2 Proposed evaluation and treatment of catatonia in patients with NDDs. BFCRS Bush-Francis catatonia rating scale, ECT electroconvulsive therapy, IEM inborn error of metabolism, PCRS Pediatric catatonia rating scale, Green circles represent entry points, Red circles represent exit points, Yellow diamonds represent decision points, White boxes represent established processes, Blue boxes represent processes novel to our algorithm, "?" represents a potentially informative approach to consider but without sufficient data to fully support implementation.

Catatonia – Just a specifier or more in individuals with ASD ?

- Patient review:

- 38/F, diagnosed with Mild Learning Disability, ASD, in the community presented with rigid posturing, fixated stare, unable to move, reduced speech content.
- Significant worsening from her baseline
- No recent social stressor identified
- History of emotional and sexual abuse in the past
- Duration of on-going symptoms x 10 days

Catatonia – Just a specifier or more in individuals with ASD ?

- She was in the community with no past admissions, not on any regular medications.
- The doctor was consulted via the community team through the emergency services.

- What to assess for ?
- What treatment options ?

Thank you so much

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