Neuropsychiatric issues in Phelan McDermid syndrome

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Phelan-McDermid Syndrome is a rare genetic syndrome

- Deletion affecting SHANK3 or a pathogenic variant of SHANK3
- Developmental delay
- Moderate to profound intellectual disability
- Marked speech impairment
- Variable clinical presentations: wide range of comorbidities and behaviors

The big questions

1) How common is neuropsychiatric illness in PMS?

2) What does it look like and what triggers it?

3) How can we prevent it?

Symptoms that could be considered psychiatric are part of the baseline for some people with PMS

- Disrupted sleep
- Restlessness, climbing, roaming, jumping
- Trouble focusing
- Agression
- Echolalia
- Shouting or yelping
- Repeating or compulsive behaviors
- Pica
- Head-banging and other forms of self-injury

Any behavioral problem should always be considered within the context

- Context of family and environment
- Context of the individual's level of cognitive, social and emotional development

Developmental delay ranges from moderate to profound

- Mouthing or chewing of objects
- Decreased pain perception
- Difficulties attaining adaptive and daily living skills

Language delay and/or absent speech are among the most common characteristics

- Both expressive and receptive communicative abilities affected
- Impairments inexpressive language are highly likely to contribute to challenging behaviors

Diagnosing ASD in PMS can be challenging

- Establish whether frequency and intensity of autism symptoms go beyond what would be expected given the individual's developmental level
- Presentation of autism symptoms in PMS may be different to that of autistic individuals without PMS

Sensory dysfunction occurs in several domains for patients with PMS

- Reduced pain perception, heat regulation disorder, changed sensitivity, hearing and vision impairment
- Aggressive behavior may be linked to sensory dysfunction, as well as agitation (but underlying mood cycling can also be cause)

Regression is defined as a prolonged loss of skills previously acquired

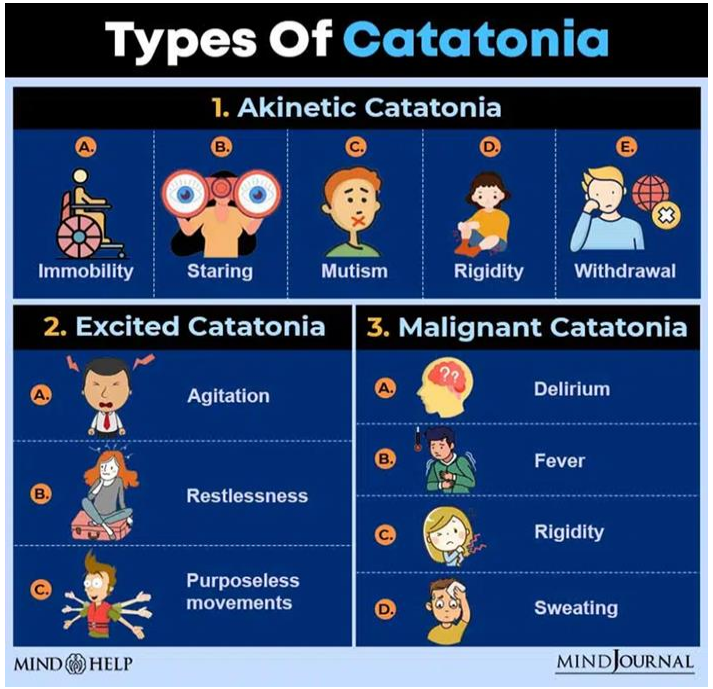
- Progressive loss of skills often seen in adolescence/early adulthood
- Loss of speech, motor, communicative, and social interaction skills
- Regressive episodes have sometimes been reported in co-occurrence with bipolar disorder or mood cycling symptoms

Behaviors suggestive of hyperactivity and attention deficit are commonly reported

- Motor restlessness, impulsivity and distraction
- Changes in behavior should be monitored overtime with a mind to what is typical and within a routine
- Restlessness or agitated behavior may be caused by underlying mood disorder

Catatonia is characterized by behavioral, affective and motor disturbances

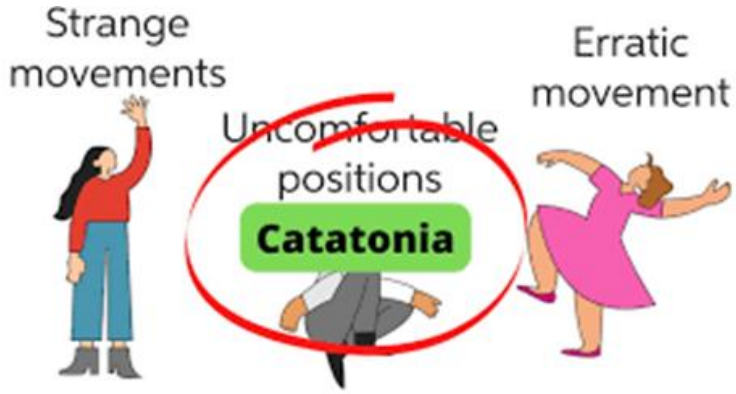
- Treatment is important to avoid life-threatening complications
- Without timely treatment a patient may develop autonomic instability with hyperthermia, intense excitement, rigidity and delirium
- Catatonia can be triggered, e.g. after moving residence, after physical illness



Excited/hypermotoric catatonia

Many doctors will never have heard of it or seen it, can be hard to distinguish from severe mania. Often begins during mania, with:

- Restlessness, pacing and new oppositional behavior
- Unclear speech, trouble managing saliva, drooling, holding food in mouth or refusing food
- Behavioral and physical rigidity
- New repeating of words & phrases (own or other people's)
- Frequent brief and unproductive trips to bathroom
- Tremor
- Flushing: red blotches on chest, face and neck, and white/purple mottling of hands
- Can include psychotic symptoms

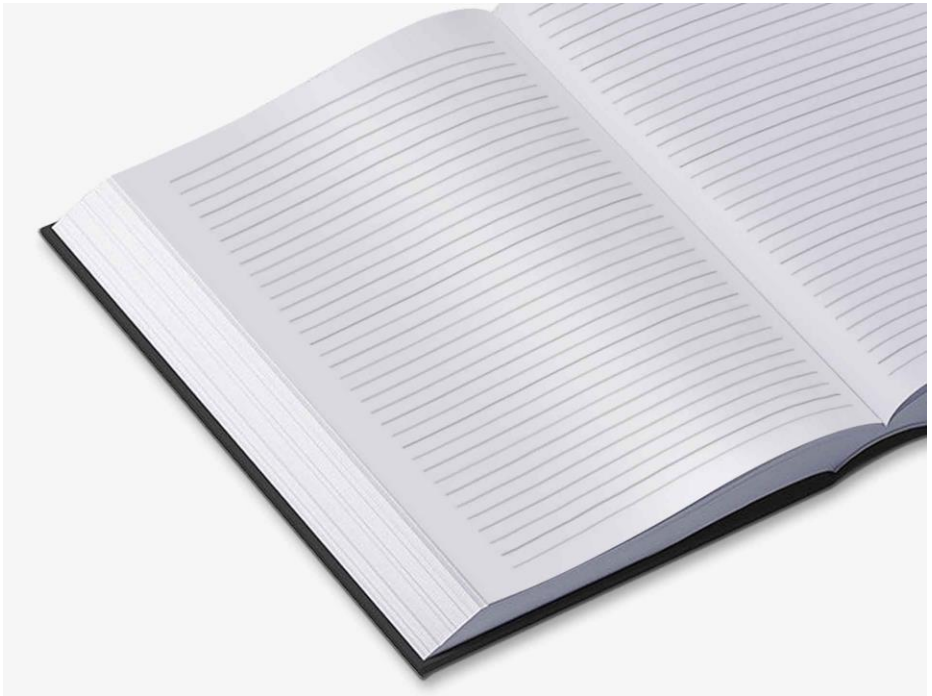


Mental health, development and behavior not only impact the individual

- Also affect their immediate context of family, living arrangement, and caregivers
- Parental stress, especially stress concerning the future
- Understanding discrepancy between developmental level and chronological age, and how this may impact worrying behaviors is important

A comprehensive diagnostic formulation is needed

- Consider factors that influence mental health
- Understand the individual within their context
- Ensure appropriate assessments and ongoing monitoring



Rule out any underlying medical issues for psychiatric or behavioral presentations

- Periodic physical assessments

Important principles and considerations

1. A comprehensive diagnostic formulation is needed
2. Rule out any underlying medical issues for psychiatric or behavioral presentations
3. For individuals with limited communicative language a Functional Behavioural Assessment (FBA) is useful
4. Understand the typical behavior/affect/routine: BASELINE!
5. Phenotype may change with aging
6. Promoting the wellbeing of support systems around the individual is crucial

Faces of Catatonia in Phelan-McDermid Syndrome

Videos and narratives shared by families, who hope these will improve recognition and treatment of this disorder.

Collected by

Teresa M. Kohlenberg, MD

PMS Neuropsychiatric Consultation Group-ECHO

PMSF Medical Advisory Committee

PMS Parent

Max at baseline in his teens, skiing (in red parka)

Max developed mania in 2020, treated with *escalating* doses of quetiapine.
At the time of this video he was not responding to Seroquel anymore; something new was happening.
Agitation, sleeplessness, trouble urinating.

Given his agitation and sleeplessness his worried family took him to the ER.
He was in ER for 3 days, given Haldol & Zyprexa. Came home almost unable to walk.

Admitted to ICU the following day catatonic with diagnosis Neuroleptic Malignant Syndrome, unable to urinate, blood pressure & temp fluctuating.

In hospital for 10 weeks.

Max was treated with IVIG (five days) and the catatonia started to lift, revealing underlying mania.

Lorazepam was initiated, improvements started
Released from hospital after 8 weeks

Lorazepam was increased further, and Max started ECT with significant improvement

Continues on ECT and multiple meds: Lithium, Depakote, Clonidine, lorazepam, sleep medication and supplement (NAC).

Here back to baseline

Chris is a 42 year old with PMS. Here he is at baseline

Chris was a talkative, social and athletic young man with moderate intellectual disability, who was able to be quite independent into his early 20's.

He could come home from high school, let himself into his own house using a keypad to shut down alarm system, make himself a snack and be safely alone for several hours.

Once he aged out of school-based services he moved into a group home, where he began to have episodes of irritability and aggression, and was started on antipsychotics for this.

Chris then steadily lost many skills over the years, including continence, a lot of his language, self-care and apparently his memory for the past.

These changes were attributed to “PMS regression”.

It seemed likely that he had been showing signs of chronic stuporous catatonia for years.

At age 40 parents learned of the possibility of catatonia, and a lorazepam trial was initiated, with modest improvements.

However, the nurse in charge of the residence was uncomfortable with higher doses and refused to have the dose increased often enough or beyond a total dose of 8 mg/day.

Chris kept habituating to his doses.

In the Fall of 2022, Chris stopped eating and drinking, and staff couldn’t get any medication into him for 2 days.

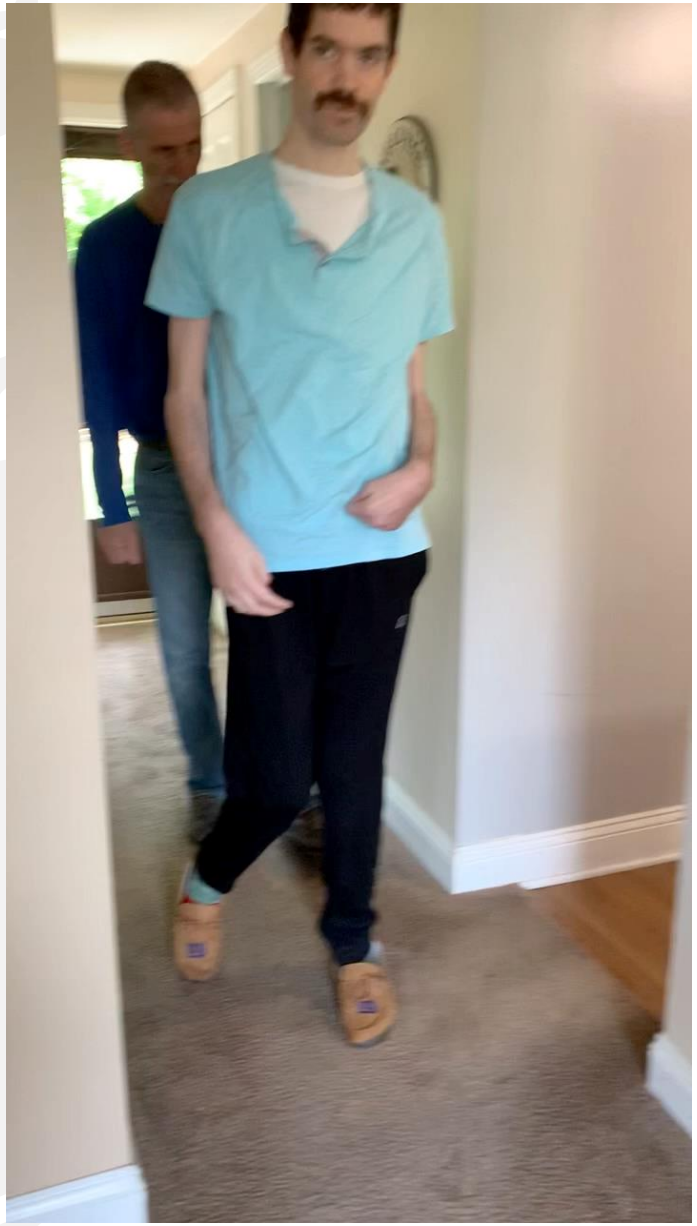
He lapsed into stupor.

This video is shortly after lorazepam was re-started, and was an improvement over the previous 3 days, when he had no voluntary movement or response.

Hospital course and recovery

- The catatonia lightened when lorazepam reached 20 mg/day, about a month into his hospital stay.
- During that month he lost a great deal of weight, had a g-tube, and developed contractures.
- Chris spent 100 days in hospital and rehab.
- Due to his group home's refusal to take him back on this dose of lorazepam, he was discharged into his parents' care without supports.
- At home he slowly regained many of his lost skills.

Regaining walking, speech, memory and humor



After 4 months, Chris had regained skills thought to be lost to “regression” for years:

- Walking easily and independently
- Speaking in full sentences
- Remembering and narrating long-past events
- Feeding himself a normal diet and regaining his lost weight
- Singing, telling jokes and laughing
- Regained his toileting skills, initiating trips to the bathroom

Chris chatting happily with parents

September 2023

A note from Chris's mother:

- Christopher's recovery is amazing! Simply amazing!
- He's back to walking fast, steady and confidently.
- Humor and personality are back. Reminding me about how I can't sing while he sings (just as badly) in a strong voice and remembers the words no matter how long it's been since he heard the song.
- He's the tour guide during any car ride, calling out in advance places that are from his past. The barber shop he hasn't visited in decades, a library he has only visited a handful of times, as well as places he's frequented numerous times.
- He's the proverbial nosy neighbor keeping track of folk's comings and goings as well as any wildlife that makes our yard their home.

Questions?