

Why care?

- Neurological disorders do occur in well-treated classic galactosemia
- Several groups have also reported neurological symptoms related to **movement**.
 - Direct appeal from PGC parent about tremor
 - Informal assessment indicates this may be an area of concern for the community
 - Research literature suggests movement disorders are there, but data are very limited
- We can learn more about galactosemia from movement disorders, and vice versa
 - Accurate labeling of movement abnormalities is critical for **directing treatment choices**, and for **understanding disease mechanisms** in classic galactosemia.

What are movement disorders?

- Movement disorders are **clinical diagnoses**: There is no gold standard test beyond expert clinical opinion.
 - Both published and self-reported labels like “tremor” may be highly inaccurate.
 - Can be primary or **secondary**; can be a **symptom** or a specific disease label.

Tremor

Involuntary rhythmic oscillation in a specific area: arm, leg, jaw, vocal cords, neck...
With action like writing or lifting a cup (ex: essential tremor); when limb at rest (ex: Parkinson

disease)

Shaking, nervous

Cerebellum and associated pathways; maybe elsewhere in brain too

Medications to suppress tremor; surgical options like deep brain stimulation

Dystonia

Abnormal involuntary twisting posture in any body area; fixed or variable

twisting, pulling, wry neck, scoliosis, turning, tremor

basal ganglia; maybe cerebellum

Medications to control dystonia; botulinum toxin injections into affected muscles;
non-medication symptomatic relief options; surgical options?

Ataxia

Abnormal regulation of movement speed, force, and direction.

Targeting movements; rhythmicity of movements

Clumsy, shaky, tremor, bad balance, uncoordinated

Cerebellum: different areas for limb ataxia versus gait (walking) ataxia

physical therapy, occupational therapy

Bradykinesia, rigidity: “parkinsonism”

Ability to do voluntary movements easily and quickly; movement speed

Slow, hard to do things, stiff, clumsy, uncoordinated

Basal ganglia

Treatments that help underlying associated cause like dystonia or Parkinson disease

What have we learned so far?

Pilot study at PGC 2010 meeting

45 participants, ages 5.7 to 60.1 years. 64% female.

38% self-reported hand tremors; none self-reported other movement disorders diagnoses.

Six people reported some variation of “always”, “forever” or “birth” for age of tremor onset

Otherwise reported tremor onset ranged from age 5 to 32 years.

All but one had action tremor on exam, while many also had dystonia or ataxia in addition to tremor.

Only one subject had a clear family history of tremor, in an autosomal dominant multi-generational pattern.

Most common exam findings were dystonia, tremor, and ataxia. Could be alone or in combinations.

Limb (arm) ataxia, not gait.

Dystonia limbs, neck, trunk.

Tremor arms/hands, with action and sometimes with posture.

Bradykinesia but no other indication of parkinsonism.

Rare questionable chorea, no other movement labels.

Movement disorders findings seen in both males and females, and across age groups.

Range skewed to mild findings, few moderate (from neurological viewpoint).

Using high sensitivity research definition for “affected”, 42% with movement disorders

This is a research diagnosis!

Generous inclusion may create false positives.

This means including very mild findings that might be clinically normal.

Another way to go is high specificity: only super definite findings, miss some true positives.

What next?

Better assessment of community interests and concerns, including quality of life impact.

Treatment approaches to dystonia and action tremors may be particularly applicable to galactosemia.

Re-analyze larger data set using high specificity “affected” research definitions (drop out very mild scores).

Expand on pilot study to learn more great information: symptom range; are predictors clearer in bigger group.

Note this means everybody is important: no tremor, lots of tremor, and all in between!

Adjust how we look for movement disorders based on new information from neurology side.

Pull in pediatric movement disorders expertise to expand age range.

Compare movement disorders outcomes to other long-term outcomes like ovarian function, scholastic data.

Longitudinal multi-center efforts: let’s all work together!