

## The most common GRIN symptoms described by families are:

1. Delay in cognitive development, often comparable with behaviors similar to those associated with the autism spectrum. But unlike what we see in autistic kids, GRIN children can be very social.
2. Epilepsy and absences: some seizures are difficult to control with antiepileptic drugs. Some patients who suffer from epilepsy have also been diagnosed with syndromes such as WEST or Landau-Kleffner syndrome, as well as with infantile spasms.
3. Non epileptic crisis- moments of hysteria/severe anxiety (still to be differentiated from dysautonomia and so called “neuro-storms”).
4. Movement disorders and delay in psychomotor development: including hypotonia (low muscle tone), hypertonia (high muscle tone), dyskinesia (involuntary movements), stereotypies (repetitive movements), dystonia (combination of high and low muscle tone) and difficulty with fine motor skills, and walking. Dystonia can be hard to diagnose because a child can be more hypotonic than hypertonic and can consequently be diagnosed with hypotonia only
5. Speech and communication disorder: ranging from being non-verbal to having difficulty forming words/sentences.
6. Visual or eye problems: such as cerebral or cortical visual impairment (CVI), abnormal eye movements like strabismus and nystagmus, problems with binocular vision, etc.
7. Sensory processing problems. Often associated with irritability or increased sensitivity to certain aspects of their environment such as sounds, lights and touch. Some children may experience difficulties in eating because they are unable to tolerate certain food's tastes, textures and consistencies.
8. Gastrointestinal disorders: constipation, maldigestion, gastroparesis (slow emptying of the stomach content), aerophagia (swallowing air), borborygmi (intestinal gas noises), gastric reflux, difficulty burping and vomiting. Gastrointestinal migraines can be considered in some of these patients.

9. Dysphagia: Difficulty swallowing and excessive drooling. It is usually associated with coughing during eating and drinking. In some children excessive drooling can be attributed to weakness of the muscles in the mouth.
10. Sleep disorders: difficulty falling asleep, nocturnal awakenings (crying or laughing), and seeming to need fewer hours of sleep. Best to assess sleep disruption with a 18h- or longer EEG (see section on GRIN Diagnostic tests)
11. Difficulty gaining weight / failure to thrive, low energy levels
12. Altered mental states: irritability, anxiety and/or nervousness. These states can vary rapidly and can come in suddenly without an obvious trigger.
13. Behavioral disorders: aggressive behavior including self-harm (biting hands and wrists), difficulty concentrating, being overly friendly to strangers, extreme impulsivity, no sense of danger, running away (eloping). Compulsive or repetitive behaviors have also been observed.
14. Dysautonomia: heart rhythm disturbances, excessive sweating, skin color changes in the extremities (blood circulation disturbances), blood pressure alterations, difficulty breathing and thermoregulation issues (body temperature regulation). When a group of these symptoms has a sudden onset, it is termed Paroxysmal Sympathetic Hyperactivity Storms (PHS) or neurostorms
15. Other potential symptoms associated directly or indirectly with GRIN disorders: low thyroid hormone levels, Kidney stones, high levels of ammonia and urea in the blood
16. Migraines: although difficult to prove our GRIN patients suffer from this, there is evidence that the NMDA receptors are involved in the control of migraines, and drugs, targeting the NMDA receptor, are being developed to help control migraines.  
  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5935645/>
17. Respiratory issues and recurrent respiratory infections. Important to rule out problems with dysphagia or muscle weakness that may be the cause of or can contribute to the recurrence of respiratory disease.