Pathogenic variants in GCSH encoding the H-protein cause a variant form of nonketotic hyperglycinemia

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Here we report six nonketotic hyperglycinemia (NKH) patients with variants in GCSH, encoding the H-protein involved in lipoate synthesis and the glycine cleavage enzyme. Three patients had a severe early course. Patients 1 and 2 had typical fatal neonatal presentation of severe NKH. Patient 3 presented at age 2 months with infantile spasms, hypsarrhythmia, evolving to therapy-resistant multifocal epilepsy, stagnant development and infantile death. Three patients had a late, milder course. Patient 4 presented in young childhood with epilepsy, developmental delays. Patient 5 presented at age 6 months with hypotonia and developmental regression. She has developmental delays and behavioral problems. Patient 6 presented with neonatal transient apnea. This toddler has developmental delays, hypotonia and dystonia. All patients had elevated glycine in plasma and CSF, but normal CSF lactate. Brain MRI studies were normal, except for patients 2 (changes in brainstem spinothalamic tract and colliculi), and 3 (corpus callosum hypogenes and focal abnormal subcortical white matter). Patient 5 had deficient liver