SSADH, or succinic semialdehyde dehydrogenase, is an enzyme that plays a critical role in the metabolism of the neurotransmitter gamma-aminobutyric acid (GABA) in the brain. GABA is a major inhibitory neurotransmitter that helps regulate neuronal activity in the brain.

SSADH catalyzes the final step in the metabolism of GABA, converting succinic semialdehyde (SSA) to succinate. Mutations in the gene that encodes for SSADH can result in a rare genetic disorder called SSADH deficiency. This disorder is characterized by a buildup of SSA in the brain and other tissues, which can lead to seizures, developmental delays, intellectual disability, and other neurological symptoms.

Research has also suggested that alterations in SSADH activity may be involved in the development of certain neurological and psychiatric disorders. For example, decreased SSADH activity has been associated with an increased risk of developing schizophrenia, and changes in SSADH expression have been observed in the brains of individuals with autism spectrum disorders.

Understanding the role of SSADH in the brain and its potential involvement in various neurological and psychiatric disorders is an active area of research. New therapies and interventions targeting SSADH activity may hold promise for the treatment of these disorders.

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four Chinese patients were diagnosed with SSADH deficiency in Tianjin Children's Hospital. We conducted a multidimensional analysis with magnetic resonance imaging (MRI) of the head, semi quantitative detection of urine organic acid using gas chromatography-mass spectrometry, and analysis of ALDH5A1 gene mutations. Two of the patients were admitted to the hospital due to convulsions, and all patients were associated with developmental delay. Cerebral MRI showed symmetrical hyperintense signal of bilateral globus pallidus and basal ganglia in patient 1; hyperintensity of bilateral frontal-parietal lobe, widened ventricle and sulci in patient 2; and widened ventricle and sulci in patient 4. Electroencephalogram (EEG) revealed the background activity of epilepsy in patient 1 and the disappearance of sleep spindle in patient 2. Urine organic acid analysis revealed elevated GHB in all the patients. Mutational analysis, which was performed by sequencing the 10 exons and flanking the intronic regions of ALDH5A1 gene for all the patients, revealed mutations at five sites. Two cases had homozygous mutations with c.1529C > T and c.800 T > G respectively, whereas the remaining two had different compound heterozygous mutations including c.527G > A/c.691G > A and c.1344-2delA/c.1529C > T. Although these four mutations have been described previously, the homozygous mutation of c.800 T > G in ALDH5A1 gene is a novel discovery.

SSADH deficiency is diagnosed based on the elevated GHB and 4, 5DHHA by urinary organic acid analysis. We describe a novel mutation p.V267G (c.800 T > G) located in the NAD binding domain, which is possibly crucial for this disease's severity. Our study expands the mutation spectrum of ALDH5A1 and highlights the importance of molecular genetic evaluation in patients with SSADH deficiency [1)]

A 12-year-old boy with succinic semialdehyde dehydrogenase (SSADH) deficiency is described. SSADH deficiency is a rare neurometabolic disorder of GABA catabolism. The clinical diagnosis is difficult and the disease is underdiagnosed. MRI showed an unusual pattern with hyperintense signal in the globus pallidus and cerebellar dentate nucleus in T2-weighted images. The remaining basal ganglia and white matter were normal. This is the second report showing this particular pattern of pallidal-dentate nucleus involvement, which might be suggestive for SSADH deficiency [2)].

1)
Wang P, Cai F, Cao L, Wang Y, Zou Q, Zhao P, Wang C, Zhang Y, Cai C, Shu J. Clinical diagnosis and mutation analysis of four Chinese families with succinic semialdehyde dehydrogenase deficiency. BMC Med Genet. 2019 May 22;20(1):88. doi: 10.1186/s12881-019-0821-z. PMID: 31117962; PMCID: PMC6532217.
2)
Ziyeh S, Berlis A, Korinthenberg R, Spreer J, Schumacher M. Selective involvement of the globus pallidus and dentate nucleus in succinic semialdehyde dehydrogenase deficiency. Pediatr Radiol. 2002 Aug;32(8):598-600. doi: 10.1007/s00247-002-0717-4. Epub 2002 May 1. PMID: 12136353.