

Amino acids and autism

Autosomal recessive hereditary autism with epilepsy may be due to a recently described defect in amino acid metabolism. Dietary treatment is effective in mice with this defect.

Dysfunctional amino acid metabolism, resulting in either a deficiency – or pathologically high levels, may cause neurological disease. By means of genetic studies of three consanguineous families, US researchers identified a new biochemical mechanism that causes autism and epilepsy (1). All the patients had low levels of the three essential amino acids valine, leucine and isoleucine in their blood.

These amino acids are normally broken down into ketoacids, which are in turn

degraded by the enzyme BCKDH (branched chain ketoacid dehydrogenase). A mutation in the gene for this enzyme causes a neurological disease: maple syrup urine disease. However, in the patients in the study, the BCKDH enzyme was more *active* than normal, resulting in increased degradation of the three amino acids.

The researchers found by means of whole exome sequencing that the explanation for the increased activity was mutations in the gene *BCKDK* (*branched chain ketoacid dehydrogenase kinase*). The BCKDK protein inhibits the BCKDH enzyme and thus controls the normal degradation of the three amino acids.

Like the human patients, a mouse model for the disease, the BCKDH knock-out mouse, had low plasma and brain amino acid levels and developed severe neurological symptoms. Adding valine, leucine and isoleucine to their feed caused the neurological

symptoms of the mice, including convulsions, to vanish. The study raises exciting questions, such as whether the disease can be detected by means of our expanded newborn screening programme, and whether dietary treatment can be used for these patients.

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References

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