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A METABOLITE PROFILE REVEALS THE PRESENCE OF NEURODEGENERATIVE CONDITIONS ACCORDING TO SEVERITY OF HYDROCEPHALUS

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Introduction: In obstructive congenital hydrocephalus, cerebrospinal fluid accumulation is associated with high intracranial pressure (ICP), ischemia/hypoxia, metabolic impairment, neuronal damage and astrocytic reaction. The *hyh* mutant mice exhibit two different forms of hydrocephalus evolution: severe and moderate. A study was carried out in *hyh* mice to detect a metabolite profile that define the tissue response in each hydrocephalus form.

Methods: Metabolites levels in brain cortex were analyzed with ¹H High Resolution Magic Angle Spinning Nuclear Magnetic Resonance (¹H HR-MAS) spectroscopy. The study was complemented with ICP recording and histopathological analysis.

Results: Mice with severe hydrocephalus were found to have higher ICP and stronger astrocytic reaction. Several metabolites including glutamate and glutamine were found to correlate with the severity of hydrocephalus. The whole metabolite profile may be explained based in differential astrocyte reactions, neurodegenerative and ischemic conditions. The glutamate transporter EAAT2 and the metabolite taurine were found as key histopathological markers for the damaged parenchyma.

Conclusions: Spectroscopy allowed the detection of a metabolite profile related to intracranial pressure and hydrocephalus severity, and therefore can be useful to monitor the efficacy of experimental therapies.

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