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Expression of 3-hydroxyisobutyrate dehydrogenase among neural cells

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Branched-chain amino acids (BCAA) – isoleucine, leucine and valine – belong to a limited group of substances transported through the blood-brain barrier and serving as substrates for meeting brain energy demands. Previous studies have shown the ubiquitous expression of a branched-chain alpha-keto acid dehydrogenase among neural cells. This enzyme catalyzes the initial and rate-limiting step in the irreversible degradative pathway for the carbon skeleton of valine and the other two BCAA. Unlike the acyl-CoA derivates in the irreversible part of valine catabolism, 3-hydroxyisobutyrate can be released from cells by transport across the mitochondrial and plasma membranes. Therefore, to assess the ability of neural cells to make use of this valine derived carbon skeleton as a metabolic substrate, we have investigated the distribution of the enzyme processing this hydroxyl acid, 3-hydroxyisobutyrate dehydrogenase (3-HIBDH), in cultured neural cells. To achieve this, 3-HIBDH has been purified from rat liver to serve as antigen for the production of an antiserum. Affinity purified antibodies against 3-HIBDH specifically recognized the enzyme in liver and brain homogenates. Immunoblotting demonstrated the ubiquitous expression of 3-HIBDH among cultured macroglial (astroglia, oligodendroglia and ependymocytes) and neuronal cells. Furthermore, immunofluorescence double-labeling of astroglial cells with antisera against 3-HIBDH and the mitochondrial marker pyruvate dehydrogenase localized 3-HIBDH to mitochondria. The expression of 3-HIBDH in neural cells demonstrates their ability to engage in the catabolism of valine imported into the brain for generation of energy.