Expression of calpastatin, minopontin, NIPSNAP1, rabaptin-5 and neuronatin in the phenylketonuria (PKU) mouse brain: possible role on cognitive defect seen in PKU.

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Abstract

Phenylketonuria (PKU) is an inborn error of amino acid metabolism. Phenylalanine hydroxylase (PAH) deficiency results in accumulation of phenylalanine (Phe) in the brain and leads to pathophysiological abnormalities including cognitive defect, if Phe diet is not restricted. Neuronatin and 4-nitrophenylphosphatase domain and non-neuronal SNAP25-like protein homolog 1 (NIPSNAP1) reportedly have role in memory. Therefore, gene expression was examined in the brain of mouse model for PKU. Microarray expression analysis revealed reduced expression of calpastatin, NIPSNAP 1, rabaptin-5 and minopontin genes and overexpression of neuronatin gene in the PKU mouse brain. Altered expression of these genes was further confirmed by one-step real time RT-PCR analysis. Western blot analysis of the mouse brain showed reduced levels of calpastatin and rabaptin-5 and higher amount of neuronatin in PKU compared to the wild type. These observations in the PKU mouse brain suggest that altered expression of these genes resulting in abnormal proteome. These changes in the PKU mouse brain are likely to contribute cognitive impairment seen in the PKU mouse, if documented also in patients with PKU.

PMID: 15863237 [PubMed - indexed for MEDLINE]