Evaluation of Pro-inflammatory and Anti-inflammatory Cytokines in an Animal Model of Maple Syrup Urine Disease

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Introduction: Maple syrup urine disease (MSUD) is a rare inborn error of metabolism associated with acute and chronic brain dysfunction that is caused by a deficiency of the branched chain α-keto acid dehydrogenase complex, leading to accumulation of the branched-chain amino acids (BCAA) leucine, isoleucine and valine. Objectives: Considering that MSUD patients present neurologic deterioration often precipitated by infection, we evaluated pro- and anti-inflammatory cytokines in hippocampus and cerebral cortex of rats submitted to an animal model of MSUD. Methods: Wistar rats (10 days) received three injections of a pool of BCAA (15.8 µL/g body weight) containing leucine (190 mmol/L), isoleucine (59 mmol/L) and valine (69 mmol/L) or saline (control group), at intervals of one hour between injections, subcutaneously. One hour after the last administration the rats were killed by decapitation, the brain was removed and cerebral cortex and hippocampus were isolated; analyses of α-tumoral necrosis factor (TNFα), interleukine-1β (IL-1β), interleukine-6 (IL-6) and interleukine-10 (IL-10) levels were measured by sandwich ELISA. Results: We observed that acute administration of BCAA led to significant decrease in IL-10 and increase in IL-1β, IL-6 and TNF-α levels in cerebral cortex of rats. On the other hand, in hippocampus we only found increased levels of IL-6 and a decrease in IL-10 levels. Conclusion: Taken together, these data suggest that BCAA administration causes an imbalance between the pro- and anti-inflammatory cytokines in brain of neonate rats. Our results may help to explain, at least in part, the characteristic brain impairment observed in MSUD patients.

Keywords: Maple syrup urine disease; branched chain amino-acids; cytokines; brain

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