Hyperphenylalaninemia Increases Cytokine Levels In Brain Of Young Rats

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Introduction: Phenylketonuria (PKU) is a rare genetic disease caused by a deficiency in phenylalanine hydroxilase activity, leading to an accumulation of phenylalanine (Phe). Clinically, patients present severe intellectual disability, whose pathophysiology is still uncertain. Aim: In the present work we investigated the levels of different cytokines in cerebral cortex of rats submitted to an experimental model of PKU. Methods: Male 30-day-old Wistar rats received a single subcutaneous Phe injection (5.2 μmol/g) and/or p-chlorophenylalanine (p-Cl-Phe; 0.9 μmol/g), an inhibitor of phenylalanine hydroxilase. Control group received saline solution at the same volume. One hour after Phe administration, cerebral cortex was isolated and the levels of the cytokines interleukine-1β (IL-1β), interleukine 10 (IL-10) and α-tumoral necrosis factor (TNFα) were evaluated. Results: IL-1β and IL-10 levels were increased by the simultaneous administration of Phe and p-Cl-Phe, but not by isolated administration. On the other hand, TNFα levels increased in animals receiving Phe, p-Cl-Phe or Phe plus p-Cl-Phe, as compared to control group. Conclusion: Taken together, these data suggest that Phe administration alters cytokine homeostasis in brain of young rats. Our results may help to explain, at least in part, the characteristic brain impairment observed in PKU patients.

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