Antioxidant Treatment Prevents Decreased Levels of NGF in Hippocampus of Rats Subjected to Chronic Administration of Branched Chain Amino Acids

**Streck, E.L.**; Teodorak, B.P.; Scaini, G.; Morais, M.O.S.; Jeremias, G.C; Kist, L.W.; Bogo, M.R.; Schuck, P.F.; Ferreira, G.C.

1Laboratório de Bioenergética e INCT-TM, PPGCS/UNESC, Criciúma/SC, Brazil; 2Laboratório de Biologia Genômica e Molecular e INCT-TM, PPGBCM/PUCRS, Porto Alegre/Brazil; 3Laboratório de Erros Inatos do Metabolismo, PPGCS/UNESC, Criciúma/SC, Brazil

**Introduction:** Maple syrup urine disease (MSUD) is an inherited aminoacidopathy resulting from dysfunction of the branched-chain keto acid dehydrogenase complex, leading to accumulation of the branched-chain amino acids (BCAA) leucine, isoleucine and valine. **Objectives:** Considering that patients with MSUD present neurological dysfunction and cognitive impairment, in this study we examined the effects chronic administration of BCAA on protein levels and mRNA expression of nerve growth factor (NGF). In addition, because previous observations suggest that oxidative stress may be involved in the pathophysiology of the neurological dysfunction of MSUD, we also investigated the influence of antioxidant administration (N-acetylcysteine and deferoxamine) in order to verify the influence of oxidative stress in the modulation of NGF levels. **Methods:** Wistar rats (7 days) received two subcutaneous administrations of a BCAA pool (15.8 µL/g) containing leucine (190 mmol/L), isoleucine (59 mmol/L) and valine (69 mmol/L) or saline (control group) for 21 days and were also supplemented with N-acetylcysteine (20mg/kg) twice a day and deferoxamine (20mg/kg) every two days. Twelve hours after the last injection, the animals were killed by decapitation and hippocampus, striatum and cerebral cortex were collected for NGF assays. **Results:** Our results showed decreased protein levels of NGF in hippocampus after administration of BCAA; the mRNA expression of NGF was not altered. In addition, antioxidant treatment was able to prevent the decrease in NGF levels by increasing ngf expression. **Conclusion:** In conclusion, the results suggest that BCAA may alter the regulation of NGF in developing rats. Thus, it is possible that alteration of NGF levels during brain maturation could be of pivotal importance in the impairment of cognition provoked by BCAA. Moreover, the decrease in NGF levels was prevented by antioxidant treatment, reinforcing that the hypothesis of oxidative stress can be important pathophysiological mechanism underlying the brain damage observed in MSUD.

Keywords: Antioxidants; Branched chain amino-acids; Maple syrup urine disease; Nerve growth factor.

Supported by: UNESC, CNPq and CAPES