Intracerebroventricular Administration of α-Ketoisocaproic Acid Decreases Brain-Derived Neurotrophic Factor and Nerve Growth Factor Levels in Brain of Young Rats.

Streck, E.L.[1]; Wisniewski, M.S.[1]; Carvalho-Silva, M.[1]; Gomes, L.M.[1]; Zapelini, H.G.[2]; Scaini, G.[1]; Schuck, P.F.[2]; Ferreira, G.C.[3]

[1]Laboratório de Bioenergética, PPGCS/UNESC, Criciúma, SC, Brazil; [2]Laboratório de Erros Inatos do Metabolismo, PPGCS/UNESC, Criciúma, SC, Brazil; [3]Laboratório de Neuroquímica, IBqM-UFRJ, Rio de Janeiro, 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 leucine, isoleucine and valine as well as their corresponding transaminated branched-chain α-ketoacids. This disorder is clinically characterized by ketoacidosis, seizures, coma, psychomotor delay and mental retardation. Recent studies have shown that oxidative stress may be involved in neuropathology of MSUD. However, the effect of accumulating α-ketoacids in MSUD on neurotrophic factors has not been investigated. **OBJECTIVES:** The objective of the present study was to evaluate the effects of acute intracerebroventricular administration of α-ketoisocaproic acid (KIC) on brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) levels in the brains of young male rats. **MATERIAL AND METHODS:** The animals were divided into two groups: KIC (α-ketoisocaproic acid) and ACFs. The KIC was intracerebroventricular administered by stereotaxic into the lateral ventricle of the animal at a concentration of 0.8 μmol of KIC dissolved in 2μL ACFs and injected. The ACFs was injected in the same way. One hour after the administration the animals were killed by decapitation and cortex, hippocampus and striatum were separated. **RESULTS AND DISCUSSION:** Ours results showed that intracerebroventricular administration of KIC decreased BDNF levels in hippocampus, striatum and cerebral cortex, without induce a detectable change in pro-BDNF levels. Moreover, NGF levels in the hippocampus were reduced after intracerebroventricular administration of KIC. **CONCLUSIONS:** These data suggest that KIC on demyelination and memory processes may be mediated by reduced trophic support of BDNF and NGF. Moreover, lower levels of BDNF and NGF are consistent with the hypothesis that a deficit in this neurotrophic factor may contribute to the structural and functional alterations of brain underlying the psychopathology of MSUD, supporting the hypothesis of a neurodegenerative process in MSUD.

Keywords: Brain-derived neurotrophic fator, maple syrup urine disease, nerve growth fator.
Supported by: FAPESC, CNPq, UNESC, INCT-MT and CAPES