ANTIDEPRESSANT-LIKE EFFECT OF CREATINE IN MODEL BY β-AMYLOIDICATID1-40 IN MICE: IMPLICATIONS IN GSK-3β/BETA CATENIN/HO-1 PATHWAY SIGNALING

Rosa, J.M¹; Colla, A.R¹; Pazini, F.L¹; Manosso, L.M¹; Cunha, M.P¹; Prediger, R.D.S²; Rodrigues, A.L.S.¹

¹ Department of Biochemistry, Center of Biological Sciences, Universidade Federal de Santa Catarina, Florianópolis, 88040-900, SC, Brazil.
² Department of Pharmacology, Center of Biological Sciences, Universidade Federal de Santa Catarina, Florianópolis, 88040-900, SC, Brazil.

Major depression (MD) is a prevalent neuropsychiatric comorbidity in Alzheimer's Disease (AD) patients. Moreover, evidence indicates that MD increases the risk of developing AD. Molecular mechanisms underlying the MD and AD comorbidity are not well established. Creatine antidepressant-like effect has been shown by different research groups. In this context, this study investigated the effect of the acute administration of creatine on the depressive-like behavior induced by β-amyloid peptide 1-40 (Aβ1-40) administration in mice. Furthermore, the participation of GSK-3β/beta-catenin/heme-oxygenase 1 (HO-1) signaling pathway was investigated. The experimental protocols were approved by Institution Ethics Committee (PP00795 Protocol). Swiss female mice (30-40 g) received an acute intracerebroventricular administration of Aβ1-40 (400 pmol/mouse). Ten days after, mice were treated with creatine (0.01 and 10 mg/kg, p.o.), fluoxetine (10 mg/kg, p.o., positive control) or vehicle. One hour after treatments they were subjected to tail suspension test (TST), open field test (OPT) or Splash test. Subsequently, GSK-3β phosphorylation and beta-catenin, and heme oxygenase-1 (HO-1) immunocontents were determined in hippocampus by Western Blotting. Experimental groups were compared by two-way ANOVA, followed by Newman-Keuls post hoc test (significant at p<0.05). Aβ1-40 caused depressive-like behavior evidenced by the increased immobility time in the TST, increased latency to start grooming and decreased total grooming time in the splash test. These alterations were prevented by creatine or fluoxetine treatments. There was no change in locomotion in none of the groups. GSK-3β phosphorylation and HO-1 immunocontent were increased in creatine group (0.01 mg/kg) treated with Aβ1-40. Fluoxetine per se increased GSK-3β phosphorylation. No alterations in beta-catenin immunocontent were observed in any experimental group. Results indicate that creatine is effective in reversing Aβ1-40-induced depressive-like behavior associated with an inhibition of GSK-3β and an increase in HO-1, suggesting that this compound may be effective in MD and AD comorbidity.

Keywords: depressive-like, creatine, β-amyloid peptide


Financial support: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) # 308723/2013-9, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and NENASC Project (PRONEX-FAPESC/CNPq) # 1262/2012-9.