Chenodeoxycholic acid ameliorates AlCl3-induced Alzheimerôs disease neurotoxicity and cognitive deterioration via enhanced insulin signaling in rats

Hanan Salah ,Firas H. Bazzari , Dalaal M. Abdallah

Abstract

Insulin resistance is a major risk factor for Alzheimerôs disease (AD). Chenodeoxycholic acid (CDCA) and synthetic Farnesoid X receptor (FXR) ligands have shown promising outcomes in ameliorating insulin resistance associated with various medical conditions. This study aimed to investigate whether CDCA treatment has any potential in AD management through improving insulin signaling. Adult male Wistar rats were randomly allocated into three groups and treated for six consecutive weeks; control (vehicle), AD-model (AlCl3 50 mg/kg/day i.p) and CDCA-treated group (AlCl3 + CDCA 90 mg/kg/day p.o from day 15). CDCA improved cognition as assessed by Morris Water Maze and Y-maze tests and preserved normal histological features. Moreover, CDCA lowered hippocampal beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) and amyloid-beta 42 (Aϐ42). Although no significant difference was observed in hippocampal insulin level, CDCA reduced insulin receptor substrate-1 phosphorylation at serine-307 (pSer307-IRS1), while increased protein kinase B (Akt) activation, glucose transporter type 4 (GLUT4), peroxisome proliferator-activated receptor gamma (PPARↄ) and glucagon-like peptide-1 (GLP-1). Additionally, CDCA activated cAMP response element-binding protein (CREB) and enhanced brain-derived neurotrophic factor (BDNF). Ultimately, CDCA was able to improve insulin sensitivity in the hippocampi of AlCl3-treated rats, which highlights its potential in AD managemen

Molecules 2019, May