



Targeting synaptic mitochondria and mitochondrial biogenesis for treatment of psychiatric disorders in rat brains

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Abstract:

Mitochondria play role in depression pathogenesis through mitochondrial dynamin-related protein (Drp-1), fission 1 protein (Fis-1) and brain derived neurotrophic factor (BDNF) through tyrosine kinase B (Trk-B) receptor activation. The precise role of neurotrophins-mitochondrial interaction in depression is unclear. We aimed to study role of mitochondria in pathogenesis and treatment of depression using three different antidepressants. We established animal model of stress-induced depressive behavior named learned helplessness (LH) model. Rats with LH model were treated with fluoxetine FLX (20 mg/kg), imipramine IMP (20 mg/kg) or citalopram CTL (20 mg/kg), i.p. for 2 weeks. The order of decreasing number of LH rats was as follows: CTL>IMP>FLX. Mitochondrial enzymes of brain SDH, MDH, IDH, MAO and SOD enzymes, total antioxidant status, ATP production, BDNF, Drp-1, Trk-B and Fis-1 of depressed (DEP) rats elicited significant declines. Brain lipid peroxides was highly elevated in DEP rats. All these levels were back to normalcy after intake of antidepressants and the protein expression levels of BDNF, Drp-1, Trk-B (full length not truncated) and Fis-1 were enhanced either in prefrontal cortex (PFC) or hippocampus.

Electron microscopy of DEP rats exhibited cristae disarrangement, mitochondria with dense matrix surrounded with degenerated cells, mitochondria with increased thickness and remarkably electron dense cristae in degenerated cells. Intake of FLX, CTL or IMP improved mitochondrial damage in brain as well as PFC and hippocampus. We concluded that, use of FLX, IMP and CTL improved depression induced in rats via antioxidant mechanism and through modulation of neurotrophins family in brain PFC and hippocampus.

Biography:

Hesham A El-Beshbishy has obtained his PhD in 2001 in the field of Medical Biochemistry and Molecular Biology from Manchester University, UK. He works in the Center for Genetics and Inherited Diseases, Taibah University, Madinah, Saudi Arabia. He is also a Professor in Faculty of Pharmacy at Al-Azhar University, Cairo, Egypt. Previously, he was the Supervisor of the Medical Laboratories Technology Department, Faculty of Applied Medical Sciences at Taibah University in Saudi Arabia. He has published more than 48 papers in reputed journals and has been serving as an Editorial Board Member of several international journals.