Stimulation of Melanocortin Receptor-4 (MC4R) Prevents Mitochondrial Damage Induced by Binge Ethanol Protocol in Adolescent Rat Hippocampus

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Binge drinking is a common pattern of adolescent alcohol consumption characterized by a high alcohol intake within a short period of time; which may seriously affect brain function, triggering in some cases an addictive behavior. Current evidence indicates that alcohol addictive conduct is related to the impairment of the Melanocortin System (MCS). This system participates in the regulation of food intake and promotes anti-inflammatory response in the brain. However, the cellular mechanisms involved in the protective effects induced by MCS against binge-alcohol intoxication are still unknown. Here, we studied the effects of MCS activation on mitochondrial and oxidative damage induced by a binge-like protocol in the hippocampus of adolescent rats. We used a pharmacological activator of MC4R (RO27-3225) and evaluated its effects against oxidative injury, mitochondrial failure, and bioenergetics impairment induced by binge ethanol protocol in the hippocampus of adolescent's rats. Our results indicate that MC4R agonist reduces hippocampal oxidative damage promoting antioxidant (Nrf-2) and mitochondrial biogenesis (PGC1-alpha) pathways in animals subjected to the binge-like protocol. Additionally, MC4R activation prevented mitochondrial potential loss and increased mitochondrial mass that were significantly reduced by binge ethanol protocol. Finally, RO27-3225 treatment increased ATP production and mitochondrial respiratory complex expression in adolescent rats exposed to ethanol. Altogether, these findings show that activation of the MCS pathway through MC4R prevents these negative effects of binge ethanol protocol, suggesting a possible role of the MCS in the reduction of the neurotoxic effects induced by alcohol intoxication in adolescents. © 2020 IBRO

adolescence

alcohol

binge-drinking

melanocortin

mitochondria

adenosine triphosphate

alcohol

melanocortin 4 receptor

peroxisome proliferator activated receptor gamma coactivator 1alpha

protein inhibitor

ro 27 3225

transcription factor Nrf2

unclassified drug

adolescent

alcohol intoxication

animal cell

animal experiment

animal model

antiinflammatory activity

Article

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