

Original Article

Ghrelin alleviates depression-like behaviour in rats subjected to high-fat diet and diurnal rhythm disturbance

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Abstract: Objectives: In the era of globalization, a sedentary lifestyle is highly linked with obesity and neurobehavioral complications such as depression. While depression is associated with dopamine dysfunction in the ventral tegmental area (VTA), ghrelin enhances the dopaminergic activity in the VTA. Therefore, the present study aimed to assess the effect of ghrelin on depression-like behaviour in rats subjected to a high-fat diet (HFD) and disturbed diurnal rhythm (DDR) for 45 days. Methods: The neurobehavioral deficits resulting from HFD and DDR in rats, and the behaviour modulation by intra-VTA administration of ghrelin, alone or in combination with ghrelin receptor antagonist were confirmed by evaluation of behavioural parameters in the elevated plus-maze, forced swim test, open field test, and rotarod assessment. Further, the levels of pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β) and IL-6, oxidative stress marker malondialdehyde (MDA), and antioxidants enzymes like superoxide dismutase (SOD), reduced glutathione (GSH), and catalase (CAT) were measured. Results: The levels of TNF- α , IL-1 β , IL-6, and MDA were increased in the brain of HFD and DDR exposed rats, while that of SOD, GSH, and CAT were reduced. Intra-VTA ghrelin administration from day 41-45 to the HFD and DDR exposed rats improved cognitive behaviour and physical activity confirming the antidepressant effect. Moreover, ghrelin restored the levels of SOD, GSH and CAT efficiently, and reduced that of MDA, TNF- α , IL-1 β and IL-6, which signifies its protective effect. Conclusion: Overall, this study confirmed the ameliorative effect of ghrelin in HFD- and DDR-induced depression-like behaviour.

Keywords: High-fat diet, diurnal rhythm disturbance, ghrelin, depression, cytokines

Introduction

The rapid urbanization of the world in recent decades has significant implications for human health. In 2018, the United Nations Department of Economic and Social Affairs estimated that 55% of the global population currently lives in urban areas, and the figure is predicted to reach about 68% by 2050 [1]. Due to urbanization, the incidences of obesity, diabetes mellitus, and cardiovascular disorders have been increasing at an alarming rate, which are associated with irregular sleep habits and sedentary lifestyles. These factors also contribute

substantially to the development of depression and other mental disorders. Depression is a serious mental disorder characterized by several health problems including, but not limited to anhedonia and changes in appetite [2-4]. It carries immense psychological, functional, social and other burdens, and represents the leading cause of global disability. Chronic consumption of calorie-rich food can distinctly lead to depression-like behaviour and modifications in brain reward circuitry [5]. Moreover, crippled or abnormal diurnal rhythms in multiple body functions are associated with depressive disorders [6].



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