Current Research in Pharmacology and Drug Discovery 3 (2022) 100113

Contents lists available at ScienceDirect

Current Research in Pharmacology and Drug Discovery

journal homepage: www.journals.elsevier.com/current-research-in-pharmacology-and-drug-discovery

Ghrelin mediated regulation of neurosynaptic transmitters in depressive disorders

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ARTICLE INFO

Keywords:
Ghrelin
GHSR
Depression
Psychotic disorders
Neurotransmitter

ABSTRACT

Ghrelin is a peptide released by the endocrine cells of the stomach and the neurons in the arcuate nucleus of the hypothalamus. It modulates both peripheral and central functions. Although ghrelin has emerged as a potent stimulator of growth hormone release and as an orexigenic neuropeptide, the wealth of literature suggests its involvement in the pathophysiology of affective disorders including depression. Ghrelin exhibits a dual role through the advancement and reduction of depressive behavior with nervousness in the experimental animals. It modulates depression-related signals by forming neuronal networks with various neuropeptides and classical neurotransmitter systems. The present review emphasizes the integration and signaling of ghrelin with other neuromodulatory systems concerning depressive disorders. The role of ghrelin in the regulation of neurosynaptic transmission and depressive illnesses implies that the ghrelin system modulation can yield promising anti-depressive therapies.

1. Introduction

Ghrelin is an orexigenic hormone, isolated from the rat stomach (Kojima et al., 1999). It is synthesized in the body and binds with the growth hormone secretagogue receptor (GHSR). It regulates the somatotropic secretion of hormones from the pituitary gland (Andrews, 2019). GHSR is mainly found in the arcuate nucleus of the hypothalamus (ARC). Ghrelin stimulates orexigenic neuropeptide Y (NPY) in the ARC via GHSR (Delhanty and van der Lely, 2011). In fact, ghrelin enhances food intake, and thus promotes weight gain by the activation of NPY neurons in the ARC, leading to its popular tag "The Hunger Hormone" (Andrews, 2019). Majorly, ghrelin is released by the stomach and many other organs including bowels, kidneys, lungs, thyroid, hypothalamus, and pituitary gland (Kojima et al., 2005). However, it is also found in trace amounts in the various brain regions (Cabral et al., 2017). Ghrelin is prepared and synthesized endogenously from preproghrelin, which also yields obstraitin in minute quantities (Zhang et al., 2008). Obstratin produces physiological variations in the body, like the decline in pancreatic secretions and enhancement of memory and cognition (Gargantini et al., 2013). The discovery of ghrelin and its receptors is a milestone achievement that emphasizes ghrelin-related endocrine mechanisms. Ghrelin governs physiological functions such as the predominant hypothalamus nucleus, which regulates hunger, and the ARC (Marino et al., 2011). Ghrelin and its components are synthesized by many adjacent neurons in the third ventricle. These neurons of the ventricles form ghrelin to act within the brain circuitry in different regions (Cowley et al., 2003). Several studies have established the involvement of ghrelin in the regulation and metabolism of glucose (Qian et al., 2019). Few studies demonstrated that ablation of ghrelin does not affect the change in body weight as well as obesity and adiposity, though normalized glucose metabolism and homeostasis (Castaneda et al., 2010).

The significance of ghrelin in the regulation and metabolism implies that it may be useful for regulating normal blood glucose levels, and might be a therapeutic target for diabetes (Shankar et al., 2020). The role of ghrelin was studied in insulin resistance and regulation of glucose which revealed that ghrelin was effective in regulating glucose levels (Chabot

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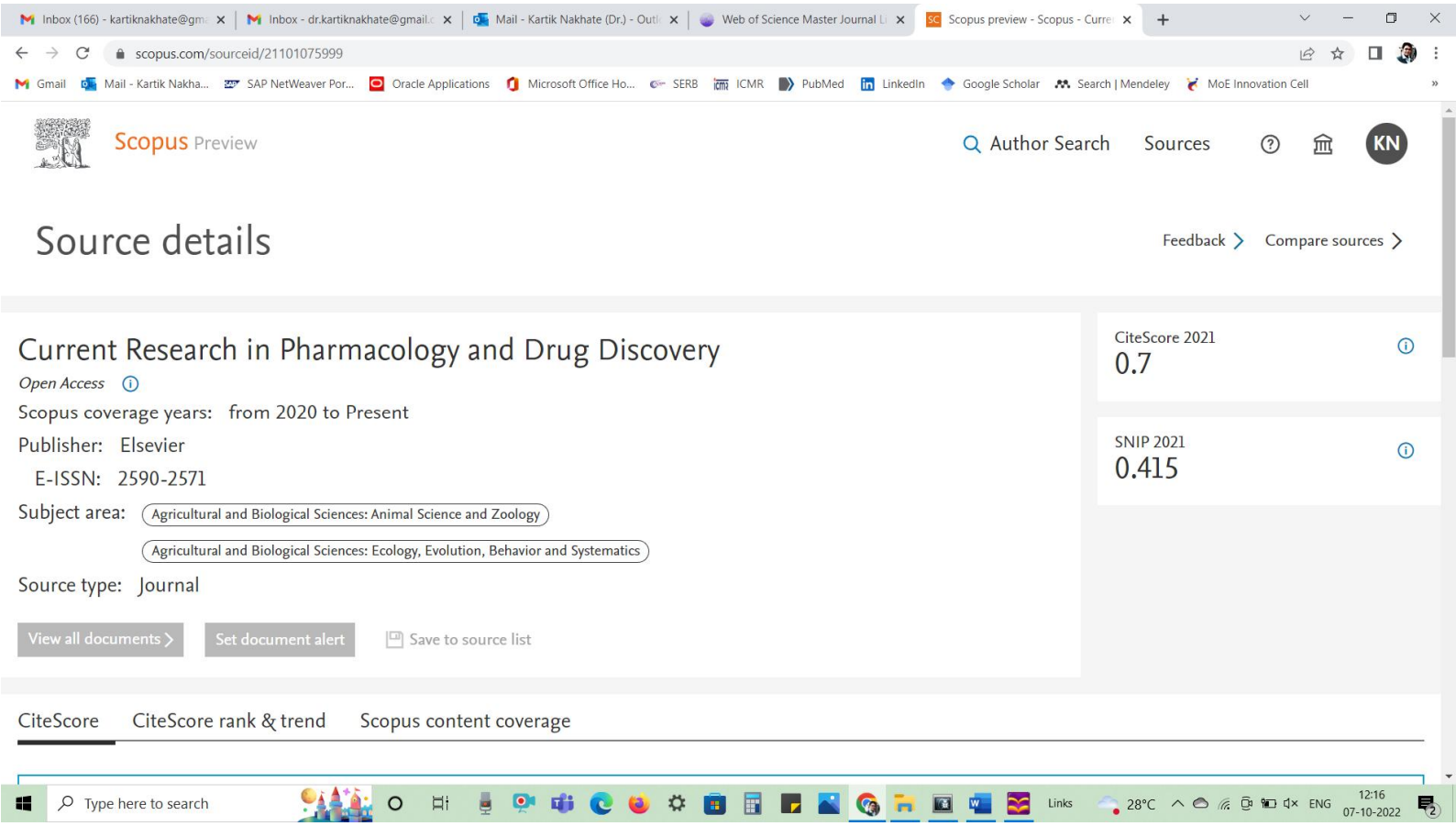
https://doi.org/10.1016/j.crphar.2022.100113
Received 3 February 2022; Received in revised form 7 June 2022; Accepted 7 June 2022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