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Reviewing the role of the orexinergic system and stressors in modulating mood and reward-related behaviors

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Highlights

- Orexins increase reward-related and anxiety-like behaviors, and stress responses.
- Orexinergic antagonists induce anti-reward effects.
- Orexinergic antagonists improve stress- or anxiety-induced psychiatric disorders.
- Orexinergic system plays inconsistent roles in modulating depression.
- Orexins have no stable pattern in modulating stress-induced reward-seeking behavior.

Abstract

In this review study, we aimed to introduce the orexinergic system as an important signaling pathway involved in a variety of cognitive functions such as memory, motivation, and reward-related behaviors. This study focused on the role of orexinergic system in modulating reward-related behavior, with or without the presence of stressors. Cross-talk between the reward system

and orexinergic signaling was also investigated, especially orexinergic signaling in the ventral tegmental area (VTA), the nucleus accumbens (NAc), and the hippocampus. Furthermore, we discussed the role of the orexinergic system in modulating mood states and mental illnesses such as depression, anxiety, panic, and posttraumatic stress disorder (PTSD). Here, we narrowed down our focus on the orexinergic signaling in three brain regions: the VTA, NAc, and the hippocampus (CA1 region and dentate gyrus) for their prominent role in reward-related behaviors and memory. It was concluded that the orexinergic system is critically involved in reward-related behavior and significantly alters stress responses and stress-related psychiatric and mood disorders.

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Abbreviations

2-AG, 2-arachidonoylglycerol; ACTH, adrenocorticotropic hormone; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; ASST, attentional set shifting task; BDNF, brain-derived neurotrophic factor; BLA, basolateral amygdala; BNST, bed nucleus of the stria terminalis; CNS, central nervous system; CPP, conditioned place preference; CRF, corticotropin-releasing factor; CSF, cerebrospinal fluid; DA, dopamine; DG, dentate gyrus; FST, forced swim test; GABA, gamma aminobutyric acid; HPA, hypothalamus-pituitary-adrenal; iNOS, inducible NO synthase; IP3, inositol trisphosphate; IL-1β, interleukin-1beta; LC, locus coeruleus; LTD, long-term depression; LH, lateral hypothalamus; mPFC, medial prefrontal cortex; MCH, melanin-concentrating hormone; NAc, nucleus accumbens; NI, nucleus incertus; OX1R, orexin 1 receptor; OX2R, orexin 2 receptor; PFC, prefrontal cortex; PTSD, posttraumatic stress disorder; PVN, paraventricular nucleus; RLN3, relaxin-3; VTA, Ventral tegmental area

Keywords

Orexin system; Reward system; Mood; Stress; Psychiatric disorder

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