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OREXINS: LOOKING BACK IN STRESS AND FORWARD TO ADDICTION

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Introduction: The hypothalamus plays an important role in regulating stress, reward and motivated behaviours. Central to this is the orexin (hypocretin) system, which is a key player in regulating these processes. The orexin system reflects an established functional dichotomy, where reward-mediated pathways are regulated by the anatomically distinct lateral hypothalamic orexin neurons; and stress is regulated by the orexin neurons located in the perifornical area.

Objectives: To analyse current experimental literature on the role of orexin in the regulation of both stress and addiction

Methods: PubMed - searched with MeSH term "orexin" or "hypocretin", with additional terms; "addiction", "stress", "relapse".

Results: The orexin neurons of the lateral hypothalamus act on the mesolimbic dopamine pathway, activating it directly, to produce its reward-seeking behavioural effects. The orexin neurons of perifornical area however mediate the response to stress, by increasing arousal, locomotor activity, and cardiovascular responses. But, via the activation of the hypothalamic-pituitary axis (HPA), it can also mediate effects on the mesolimbic dopamine pathway, in particular the ventral tegmental area (VTA), and cause reward-seeking behaviour as well. Additionally neurons containing corticotrophin-releasing factor connect the HPA reciprocally with lateral hypothalamic orexin neurons.

Conclusions: The pathways by which they work through are now understood reasonably well, but there is still new evidence emerging all the time which is increasing our understanding of the whole system, and this will have major implications in how we can approach addiction and diseases where the reward pathways are continuously activated.