

evidence for the role of stress and opioid systems in alcohol addiction and identify novel interactions, with major importance in alcoholism treatment. Further, the actions of nalmefene and naltrexone, which may inform stress/opioid interaction in alcohol dependence, will be discussed.

Method Published articles were identified with a MEDLINE search (January 1980 to March 2012). Key terms included: opioid, hypothalamic-pituitary-adrenal (HPA) axis, alcoholism, naltrexone, nalmefene. An initial review of titles preceded a second review of abstracts to identify articles meeting inclusion criteria.

Results Alcohol addiction involves dysregulation of the EOS and stress systems, though precise abnormalities are uncertain. Normalisation of these systems in abstinence may occur, with inconsistent timings and degrees. The EOS has considerable interactions with stress at multiple levels of the HPA axis. Naltrexone, a relatively 1^{1/4}-specific opioid antagonist, paradoxically improves blunted 1²-endorphin activity in alcoholism. Naltrexone may also increase HPA responsiveness, with potential HPA normalisation, indicating an EOS-stress link. Nalmefene acts at all opioid receptors, especially K- which binds dynorphin. Dynorphin and stress interact in withdrawal, thus nalmefene may be effective in targeting relapse by negative reinforcement.

Conclusion Stress and EOS abnormalities in alcoholism, and extent of normalisation of these systems in abstinence, require further investigation. There is evidence for multifaceted interactions between opioid and stress systems in alcoholism. Since naltrexone and nalmefene have differential activity at EOS receptors, comprehensive characterisation of naltrexone and nalmefene action on stress systems is critical. Delineation of the effect of these drugs on HPA normalisation in abstinence, potentially via the EOS, is timely. This could ensure targeted and evidence-based care in those with alcohol dependency.

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A REVIEW OF STRESS AND ENDOGENOUS OPIOID INTERACTION IN ALCOHOL ADDICTION

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E Emsley,¹ R Lees,² A Lingford-Hughes,² D Nutt². ¹University of Southampton, 19 Whitehill, Bradford on Avon, Wiltshire, BA15 1SG, United Kingdom; ²Imperial College London

Objective The endogenous opioid system (EOS) is involved in hedonic processing of reward, positive reinforcement, impulsivity, and potentially craving in alcohol dependence. Stress manifests in multiple stages of addiction, including early susceptibility to alcohol abuse, progression to dependence and risk of stress-related relapse. This literature review aims to collate