

DYSREGULATION OF THE ENDOGENOUS OPIOID SYSTEM IN THE BRAIN OF HUMAN ALCOHOLICS

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Introduction: The endogenous opioid system (EOS) plays a critical role in addictive processes. Molecular dysregulations in this system may be specific for different stages of addiction cycle and neurocircuitries involved, and therefore may differentially contribute to the initiation and maintenance of addiction.

Aims: We here evaluated whether the EOS is altered in brain areas involved in cognitive control of addiction including the dorsolateral prefrontal cortex (dl-PFC), orbitofrontal cortex (OFC), anterior insula (AI) and hippocampus, in human alcohol dependent subjects.

Methods: Levels of EOS mRNAs were measured by qRT-PCR, and levels of dynorphins by radioimmunoassay in postmortem human specimens.

Results: Prodynorphin kappa-opioid receptor mRNAs and dynorphins were upregulated or demonstrated higher dispersion in alcoholics.

Conclusions: Dysregulation in the kappa-opioid receptor / dynorphin system in alcoholics may contribute to alcohol craving and neurocognitive dysfunctions relevant for addiction and disrupted inhibitory control.

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