Molecular mechanisms underlying increased PDYN and dynorphin expression in the prefrontal cortex of alcoholic men

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ABSTRACT

Alcohol dependence is a chronic relapsing disorder caused by drug x gene x environment interactions for which pharmacotherapy is but moderately effective. The prefrontal cortex is a brain region important for cognitive control / behavioral flexibility which function is impaired in alcoholics. Although the exact role of the dynorphin / κ-opioid receptor system in alcohol dependence is unknown, it has been suggested to contribute to the psychopathology of this disorder. Consistently, prodynorphin gene and dynorphin peptide expression is increased in the prefrontal cortex of alcoholic men. The aim of this thesis was to identify molecular mechanisms underlying these alterations. In line with this aim, we have shown that prodynorphin is regulated by the transcriptional control protein repressor element 1 silencing transcription factor in vitro and that repressor element 1 silencing transcription factor target gene and protein expression is altered in the prefrontal cortex of alcoholic men.