PET imaging of brain opioid receptors in alcohol dependence

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Abstract:

There is strong evidence from preclinical and clinical research that the endogenous opioid system plays a key role in the modulation of alcohol drinking and dependence. The endogenous opioid peptides (beta-endorphin, enkephalin and dynorphin) bind to different subtypes of the opioid receptor (mu, delta and kappa). Naltrexone, one of the FDA-approved treatments for alcohol use disorder, is an opioid receptor antagonist. It has a higher affinity for the mu-opioid receptor subtype, but also binds to delta and kappa receptor subtypes. Randomized clinical trials have demonstrated naltrexone reduces drinking and relapse, although treatment effects are typically moderate and not all individuals benefit from naltrexone treatment. In addition, tobacco cigarette use and a functional variant of the mu-opioid receptor gene appear to influence naltrexone treatment effects. This seminar will summarize a series of studies using positron emission tomography (PET) imaging with radiotracers that selectively bind to the mu-opioid subtype (11C-Carfentanil) and the delta-opioid receptor subtype (11C-methyl naltrindole) in human subjects to examine the influence of various factors relevant to alcohol use disorder and naltrexone treatment efficacy. Topics covered will include differences in regional mu- and delta-opioid receptor availability in alcohol dependent and matched healthy volunteers, differences in the degree of receptor blockade during naltrexone treatment, and differences in naltrexone metabolism, as well as the influence of cigarette smoking and the A118G (rs1799971) single nucleotide polymorphism of the mu opioid receptor gene on opioid receptor availability under basal conditions and during naltrexone treatment.

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