MEDICATIONS FOR TREATMENT OF ALCOHOLISM THAT DERIVE FROM THE DARK SIDE OF ADDICTION

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Drug addiction is a disorder characterized by compulsive drug intake, loss of control over intake and emergence of a negative emotional state during withdrawal. Addiction involves elements of impulsivity and compulsivity which when combined form an addiction cycle that provides a heuristic framework with which to identify the neurobiological and neuroadaptive mechanisms involved in addiction, and as a result treatments for addiction. Based on this framework 3 stages of the addiction cycle have been identified that are relevant to alcoholism. These three stages: Binge-intoxication, withdrawal-negative affect and preoccupation-anticipation (“craving”) are reflected in key neuroadaptations that drive and maintain addiction. The binge-intoxication stage includes enhanced habit (stimulus-response) activity in the dorsal striatum. The withdrawal-negative affect stage reflects reward deficits in the ventral striatum (nucleus accumbens) such as dopamine and opioid peptides, but also stress surfeit in the amygdala such as recruitment of the brain stress systems including corticotropin releasing factor, dynorphin and norepinephrine. The preoccupation-anticipation stage reflects impairments in self-regulation mediated by dysregulation of executive function in the frontal cortex. Each of these stages provides a heuristic framework for treatment and can be targeted by existing and novel pharmaceuticals. Both naltrexone and acamprosate are effective medications for the treatment of alcoholism and are approved by the Food and Drug Administration of the USA. Naltrexone acts on the binge-intoxication state to block endogenous opioids and acamprosate acts on the preoccupation-anticipation stage to block glutamatergic activation. Future medications that focus on the withdrawal-affect stage and preoccupation-anticipation stage to restore the stress surfeit dysregulation characterizing these stages of the addiction cycle may have high potential as novel approaches to medications development for alcoholism.