The incidence of heroin use and abuse has vastly increased over the past decade in the United States, paralleling a similar trend seen in the abuse of prescription opiates. Opiate dependence is associated with depressed mood and reward function, with withdrawal-induced activation of brain stress systems, that may contribute to continued use despite efforts to stop. In order to understand and identify possible therapeutic options for such a complex brain disorder, we must first understand what characteristics make addiction different from stable drug use, and how to appropriately model them. Next, what outcomes and improvements are possible that qualify as “effective treatment”? Using an extended-access model of heroin self-administration, the findings presented in this talk will discuss two examples of potential targets for excessive opiate drug taking and dependence, kappa opioid antagonists and endogenous cannabinoid enhancers. Both operate without necessarily directly altering the rewarding or psychoactive effects of the drugs themselves, but rather affecting the counter-adaptations to the brain reward and stress systems that occur as a result of excessive drug exposure. Discussion will cover future projects exploring practical treatment with these drug classes, further identification of novel targets, and exploration of new factors that may contribute to excessive drug use.

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