

The Effects of Orexin Antagonists on Economic Choice between Remifentanil and Milk in Squirrel Monkeys

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Opioid use disorder is prevalent, and current medications often cause undesirable side effects (e.g., sleep disturbances). Despite technological advances in neuroscience, pre-clinical substance use research often lacks translational appeal. Reverse translating models with high postdictive and ecological validity is warranted to improve treatment outcomes. As a result, our lab designed an economic choice assay with high postdictive validity to evaluate non-opioid candidate medications to treat opioid use disorder. Recently, the literature has focused on the orexin system as a possible therapeutic target for substance use disorders. Pre-clinical rodent studies suggest that high doses of both single and dual orexin receptor antagonists may attenuate opioid self-administration, decrease opioid-seeking during reinstatement, reduce opioid demand, and increase demand elasticity. The present study's primary aim is to elucidate the effects of orexin antagonists on economic choice between remifentanil and food in squirrel monkeys. Namely, we hypothesized that suvorexant and SB-334867 would dose-dependently attenuate drug choice. To this end, squirrel monkeys ($n = 7$) received daily intravenous pre-treatments of orexin antagonists before completing an economic choice assay. Indifference values (the point at which subjects displayed an equal probability of selecting drug or milk) served as our primary outcome of interest, such that shifts in the IV during the 5-day treatment period compared to a contemporaneous baseline denoted changes in drug preference. Effective treatments shift responding away from drug toward the non-drug alternative. Because suvorexant treats insomnia, we also examined sleep using actigraphy monitors. Suvorexant significantly increased sleep but had a negligible effect on choice; studies with SB-334867 are currently underway.

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