Using Rat Grimace Scale to Evaluate Effect of Orexin on Opioid Withdrawal-Induced Negative Affect

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Suvorexant, an orexin antagonist, has shown potential in mitigating addictive behaviors. For example, suvorexant decreases general negative affect severity associated with opioid withdrawal while maintaining analgesia. The Rat Grimace Scale (RGS) is a well-validated technique for evaluating pain-specific affect by examining facial features. The purpose of this study was to replicate data showing that orexin antagonism decreases opioid-induced negative affect and to determine if withdrawal-related negative affect is captured by the RGS. To do so, 11 female rats were assigned to either a suvorexant (30 mg/kg) or control group and tested for mechanical allodynia and video recorded for pain-induced facial grimacing. We used the RGS to analyze facial grimacing and automated von Frey to evaluate paw withdrawal thresholds before pain induction and for 2 days after intraplantar injection of Complete Freund's Adjuvant into one of the hindpaws (i.e., main effect of pain). After the pre-pain and pain-only days, rats received daily injections (i.p.) of oxycodone (3 mg/kg) and either suvorexant or vehicle. On day 8 we performed the saccharin preference test (SPT) to assess anhedonia-like behavior. Rats in the suvorexant group had lower RGS scores compared to control rats on days 2 and 7, had higher saccharin preference and significantly higher withdrawal thresholds on the ipsilateral and contralateral paws for all days following drug administration. Because suvorexant resulted in decreased withdrawal-induced negative affect (SPT and RGS) and increased withdrawal thresholds on both the ipsi and contralateral paw, it may be that suvorexant is a useful complementary treatment for non-induced pain and related-affect such as that experienced during opioid withdrawal. Supported by NJ ACTS NIH R25TR004777 CREST Program.