Suvorexant, a Dual Orexin Receptor Antagonist, Normalizes Sleep Disruptions During Cocaine Abstinence and Facilitates Extinction of Cocaine Seeking

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The orexin (hypocretin) system is involved in many physiological functions, including arousal, motivation, and sleep/wakefulness patterns. Cocaine seeking is associated with increased orexin system function, resulting in sleep disruptions during withdrawal. Cocaine users report sleep disturbances as a major contributor to relapse, and thus blocking orexin signaling might ameliorate sleep disruptions and reduce relapse risk. We investigated whether suvorexant, a dual orexin receptor antagonist, could normalize sleep disruptions, and decrease cocaine craving during abstinence. Rats were trained to develop a conditioned place preference for cocaine, which was subsequently extinguished. Rats were conditioned to associate distinct environments with injections of cocaine (10 mg/kg) or saline over 4 days; they then were given free access to the same environments in the absence of cocaine/saline injections over five days and the time spent in the cocaine-paired environment was measured. During extinction training, rats were treated with suvorexant (30mg/kg; p.o.) or vehicle 1h prior to their inactive period. A subset of rats were also implanted with a transmitter to record EEG/EMG activity. After conditioning, rats showed a preference for the cocaine-paired environment. During abstinence, rats treated with suvorexant showed a faster extinction in preference for the cocaine paired compartment. EEG/EMG data revealed cocaine-induced sleep disturbances were normalized by suvorexant. Thus, suvorexant decreases cocaine craving possibly by normalizing sleep, making it a strong candidate treatment for reducing relapse in cocaine use disorder. Studies supported by grants from R0DA0045765, R25ES020721 and Busch Biomedical Grant Program to MHJ.