RATS ANTICIPATE THE EFFECTS OF ADDICTIVE DRUGS IN A CIRCADIAN PATTERN

Andrea G. Gillman¹, Joseph K. Leffel II¹, Ann E.K. Kosobud², William Timberlake¹
¹Department of Psychological and Brain Sciences, Indiana University Bloomington
²Department of Neurology, Indiana School of Medicine

Introduction
For the past several years, evidence has been emerging that circadian timing systems may be involved in drug addiction. Circadian drug administration in rats has been shown to elicit behavior associated with drug-seeking mechanisms and was found to be influenced by circadian clocks and melatonin treatment. Recently, the mammalian circadian clock has been shown to play a role in drug addiction, particularly to psychostimulants and opioids. Thus, it was shown to alter circadian behavior in rats. This study investigated the effect of a circadian model of drug addiction on the development of drug addiction in rats.

Methods

Adult male Sprague-Dawley rats were raised individually in a controlled environment and trained to run on a 12:12 light-dark cycle. The treatment condition consisted of 24-hour alternated flooding, 0 to 4 days after injection (100 μg), 24 hours after the injection (100 μg), and 0 to 4 days after injection (100 μg). Eight rats were divided into two groups: a control group and an injection group. Injections were administered at 1230 h, 1730 h, and 2230 h. Each rat received a total of 10 injections over 24 days. The injection condition consisted of 24-hour alternated flooding, 0 to 4 days after injection (100 μg), 24 hours after the injection (100 μg), and 0 to 4 days after injection (100 μg).

Results
Nicotine, fentanyl, and haloperidol (but not amphetamine) induced all four behaviors in all animals. Previously published work has found that melatonin administration and circadian rhythms modulate drug seeking. These results indicate that circadian rhythms modulate drug seeking and that the circadian rhythm is a key factor in drug addiction.

Figure 1. Hourly wheel running behaviors of rats that received injections of nicotine, fentanyl, and haloperidol. A two-way ANOVA revealed a significant main effect of time (F(23, 105) = 3.48, p < 0.001) and a significant interaction of time by group (F(46, 210) = 2.22, p < 0.001). The injection condition significantly increased wheel running behavior compared to the control condition.

Figure 2. Wheel running behaviors of rats that received injections of nicotine, fentanyl, and haloperidol. A two-way ANOVA revealed a significant main effect of time (F(23, 105) = 3.48, p < 0.001) and a significant interaction of time by group (F(46, 210) = 2.22, p < 0.001). The injection condition significantly increased wheel running behavior compared to the control condition.

Reference