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Disruptions in normal circadian rhythms can increase susceptibility to alcohol and drug addiction—that much is known. What isn’t known is why this connection exists.

This elusive kinship between circadian function and addiction compelled two Geisel postdocs, Joshua Gamsby and Danielle Gulick, to explore how two key genes involved in regulating circadian rhythms affect alcohol consumption.

Working in the lab of Jay Dunlap and Jennifer Loros, who are both professors of genetics and of biochemistry at Geisel, Gamsby and Gulick compared male and female mice with mutated versions of the genes Per1 and Per2 to normal mice without the mutations. They used the mice to study how these mutations affected alcohol consumption, reinforcement, and metabolism between groups.

“Per mutant mice do not mind the taste of alcohol,” Gamsby says. “Essentially, they are little binge drinkers.” Mice without Per mutations drink at significantly lower levels.

He and Gulick observed that all mice with mutations in Per1 or Per2 found alcohol more rewarding. But among males, only those with Per1 gene mutations had significantly higher blood alcohol levels than normal mice, whereas all female mice did regardless of whether the mutation was to Per1 or Per2. The female mice with the mutations also drank more at all concentrations than did males with the mutations.

“The finding that the Per mutant mice drink more than normal mice was not surprising,” Gamsby notes. “However, discovering that this phenomenon might be due to changes in alcohol reward and in part to changes in how alcohol is metabolized was surprising.”

From a basic science perspective, this is an exciting development. Physiologically, the circadian clock governs the timing of metabolism, body temperature, and the sleep-wake cycle. Disruptions in these functions are associated with a wide variety of physical, mental, and emotional disorders, including substance abuse and dependence. Gamsby points out, however, that the question remains whether the effects on alcohol consumption are due to changes in the circadian clock generally or specifically to mutations in the Per genes.

The temptation to apply findings such as these to human behavior is difficult to resist, but while there are implications for further understanding alcoholism, Gamsby cautions that there is much more to learn. “This study is a starting point for how Per genes are related to alcohol reinforcement” he says. “Before we can develop treatments targeting this connection, we must have a better understanding of the biology behind it.”

Now adjunct faculty at the University of South Florida Morsani College of Medicine, Gamsby and Gulick are continuing their research into the relationship between alcohol consumption and changes in the circadian clock.