Development of Cross-Tolerance Between Ethanol and Baclofen in C57Bl/6J Mice

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Alcohol is one of the most commonly used drugs of abuse. One criteria of alcohol abuse is the development of tolerance, meaning that more of the substance has to be ingested to produce the same pharmacological or behavioral effects. The phenomenon of cross-tolerance is when use of one substance leads to tolerance to an unused substance. Ethanol has also been shown to produce cross-tolerance to other drugs, such as benzodiazepines. The purpose of the current study was to investigate whether prior binge-like ethanol exposure in C57Bl/6J (B6) mice would produce a cross-tolerance to the locomotor sedative effects of the $GABA_B$ agonist R(+)-baclofen. We exposed 32 B6 male mice to a limited-access binge-like drinking procedure. Mice received daily access to either 0.2% saccharin or 20% ethanol for 2 hours, 3 hours into the dark cycle each day. There were four groups; 5 days of saccharin or ethanol access, and 10 days of saccharin or ethanol access. Baseline locomotor recordings were taken before ethanol drinking using Versamax activity monitors. Twenty-two hours following the last day of binge-like ethanol access, all animals received a 10mg/kg injection of R(+)-baclofen and Versamax activity was recorded for 1 hour. Sedation scores were calculated by subtracting the challenge day locomotor scores from the baseline locomotor scores. There was no effect of length of exposure (5 versus 10 days) or fluid type (ethanol versus saccharin) on total sedation scores ($p<.05$). A Length of Exposure*Fluid Type*Time-Bin ANOVA looking at sedation scores in 5 minute bins revealed a trend towards an omnibus interaction, but it did not reach significance ($p=0.64$). There was a main effect of time, with sedation scores being lower immediately following the injection ($9<.05$). These results indicate that ethanol does not produce a locomotors cross-tolerance to R(+)-baclofen.

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