Oral Presentation of Food and Ethanol or Quinine Under a Multiple Schedule

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Introduction

This study builds on previous work showing that rats will reliably press a lever (respond) to receive food or ethanol when this opportunity occurs multiple times in the same behavioral session. In this procedure, rats were initially trained to respond for food and ethanol (18% v/v) or food and oral oxycodone (0.1-3.2 mg/ml); however, subjects were also willing to respond for water (dH2O) at levels nearing those for ethanol, which raised concerns over the effectiveness of ethanol as a positive reinforcer in this procedure. To better understand the effectiveness of ethanol as a reinforcer in this procedure, we directly compared responding for ethanol with responding for dH2O and responding for 0.05% quinine, a bitter tasting substance. This serves as a valuable tool for investigating alcohol's reinforcing effects (McCane, et al., 2021).

Methods

Rats were trained under a multiple schedule, in which periods/components of responding for food presentation alternated with components of responding for ethanol (n=8) or oxycodone (n=4). During the respective components, subjects had to respond on the lever 10 times to receive one food pellet or 0.1 ml of either drug solution. Further, different concentrations of ethanol or doses of oxycodone were presented to the subjects until they met one of two stability criterion: (1) 3 days in which the level of responding did not differ from the mean level by more than ±20%, or (2) a maximum of 8 days. The dependent variables for these components were the response rate in responses per second, the amount of pausing before each reinforcer (i.e., pre-ratio pausing or PRP), the number of drug presentations per session, and total drug intake. In the second part of this experiment, both dH2O and quinine availability were interspersed with ethanol (18%) availability until the same stability criteria were met. Blood ethanol concentrations (BECs) were collected during stable responding for ethanol, dH2O, quinine, or following naltrexone treatment.

Results

Response rate for food remained consistently high, while response rates for ethanol and oxycodone were lower overall. When both ethanol- and oxycodone-trained subjects were able to respond for increasing doses of oxycodone, overall response rate and completed fixed ratios decreased, while PRP was non-significantly increased and total intake was significantly increased (Figure 1). These effects occurred regardless of their training history (i.e., ethanol or oxycodone). Naltrexone had little impact on food-maintained behavior, but led to small reductions in ethanol-maintained responding and significant decreases in BECs (Figure 2). In contrast, naltrexone produced non-significant increases in oxycodone-maintained responding and significant increases in total intake (Figures 3). Importantly, quinine presentation decreased response rate and increased PRP to a greater extent than those for both ethanol and dH2O (Figure 4).

Results

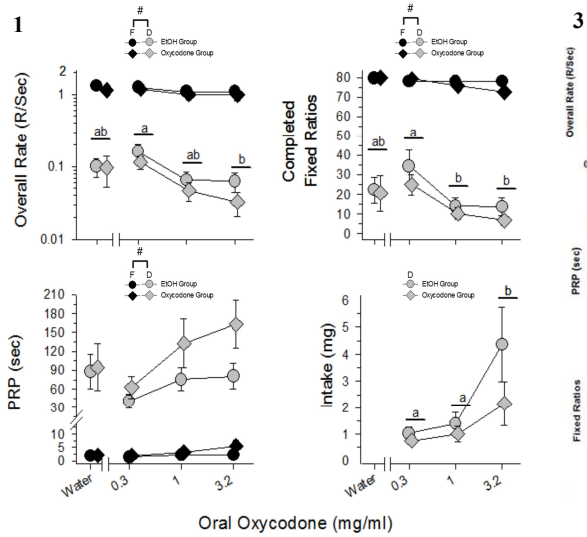

Figure 1: Effects oxycodone intake on overall rate, PRP, and total reinforcers in both ethanol- and oxycodone-trained rats responding under a multiple schedule. Responding for food or oxycodone concentrations did not significantly differ for ethanol- or oxycodone-trained rats on any of the dependent measures examined.

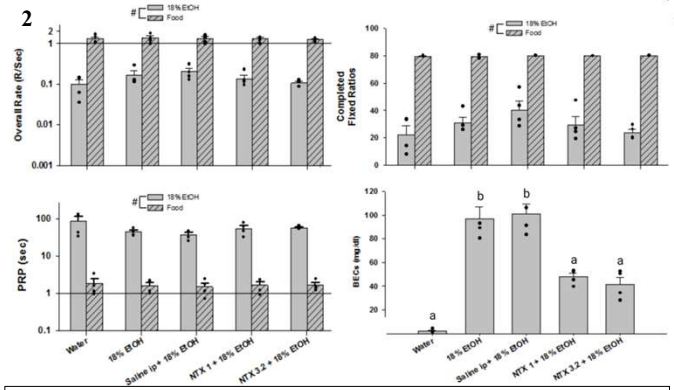

Figure 2: Effects of naltrexone administration (1 and 3.2 mg/kg, 15 minutes prior to the session) on four rats responding under a multiple schedule for food (FR10) and 18% ethanol (FR10). There were significant main effects of reinforcer on overall rate, PRP, and completed fixed ratios; however, there was no significant effects of pretreatment nor any significant interactions for these three dependent measures. Interestingly, naltrexone significantly decreased blood alcohol levels (BALs) compared to baseline levels of alcohol intake or intake after saline administration.

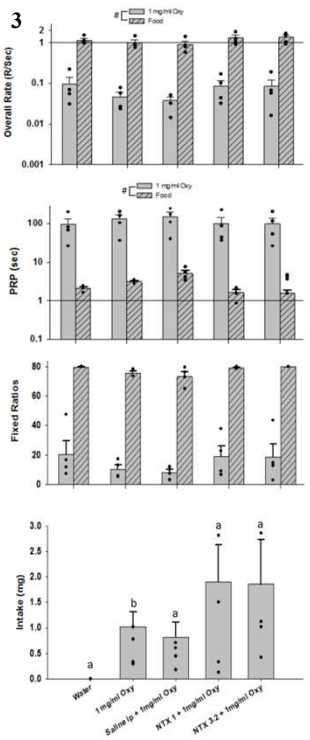

Figure 3: Effects of naltrexone administration (1 and 3.2 mg/kg, 15 minutes prior to the session) on four rats responding under a multiple schedule for food (FR10) and 1 mg/ml oxycodone (FR10). Statistical analyses of these data again indicated that there were significant main effects of reinforcer on overall rate, PRP, and completed fixed ratios, but no significant effects of pretreatment nor significant pretreatment x reinforcer interactions. Surprisingly, naltrexone did not significantly decrease oxycodone intake compared to baseline levels or intake after saline administration.

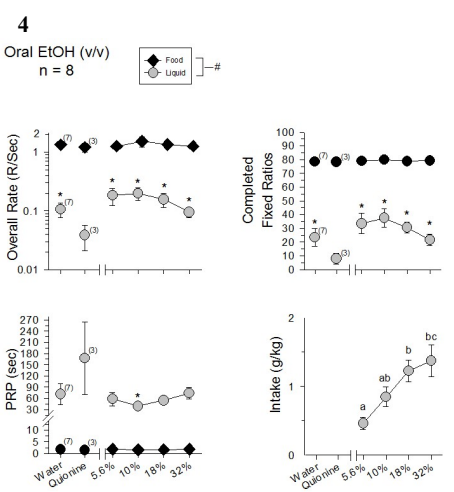

Figure 4: Effects of ethanol intake on overall rate, PRP, and completed fixed ratios (CFRs) in rats responding under a multiple schedule of food and ethanol presentation. Responding for food was significantly higher than ethanol in all the dependent measures (as shown by #). Quinine presentation significantly decreased responding in overall rate and CFRs. A (*) represents a significant difference from quinine responding. There is also a significant difference between PRP for 10% ethanol presentation and quinine presentation. Ethanol intake dose-dependently increased with ethanol concentrations.

Conclusion

Our initial findings indicated that in both subjects with a history of consuming either ethanol and oxycodone, increasing the oral oxycodone dose available had similar effects on overall response rate, PRP, completed fixed ratios, and intake. Prior results also indicated that naltrexone differentially affected responding for ethanol or oxycodone; that is, it decreased responding for ethanol presentation and increased responding for oxycodone presentation. In the present experiment, quinine presentations were reduced to a greater extent than either presentations for ethanol or dH2O, indicating that quinine was significantly less reinforcing than both ethanol and dH2O.

References

McCane, A. M., Auterson, C. D., DeLory, M. J., Lapish, C. C., & Czachowski, C. L. (2021). Differential effects of quinine adulteration of alcohol on seeking and drinking. Alcohol, 92, 73–80. https://doi.org/10.1016/j.alcohol.2021.01.003

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