Reducing alcohol cue reactivity in rats using retrieval+extinction

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Rationale

Alcohol-associated cues elicit conditioned reactions that create risk for relapse to drinking. Standard extinction can suppress reactivity to cues, but reactivity can endure and/or return. There is need for behavioral treatment strategies that can persistently attenuate conditioned reactivity to alcohol cues. Here we test a strategy that has shown promise in both appetitive and aversive conditioning domains: retrieval+extinction.

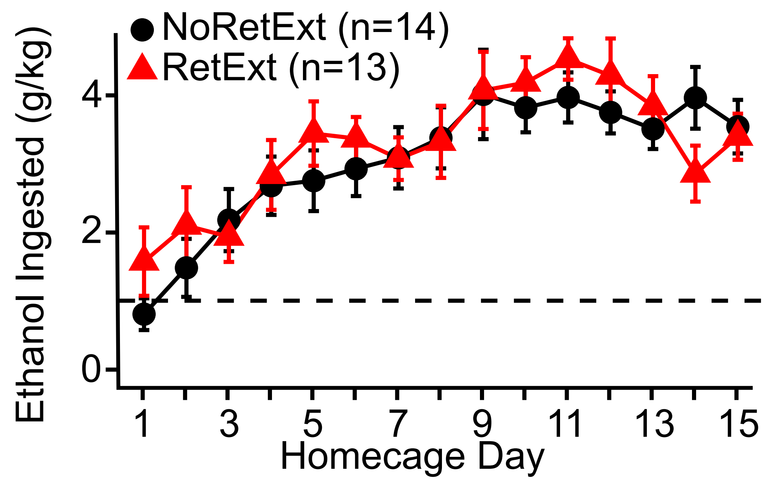
Subjects

Species: Rat
Strain: Long-Evans
Sex: Male
Age: Adult (~300g prior to alcohol drinking)
Source: Envigo (formerly Harlan; Indiana)
Housing: 1 rat per cage
Feeding: Ad libitum standard chow and water

Behavior Measurement

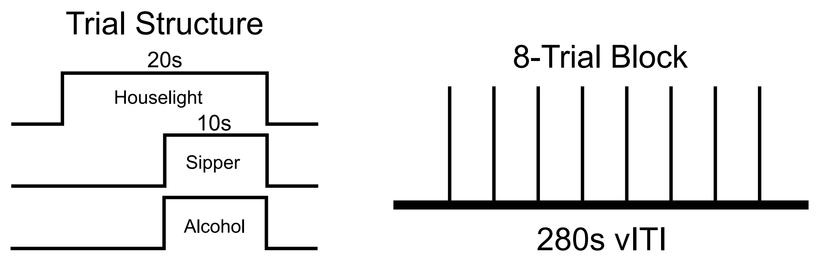
Trials were scored from videotape for sipper site approach state (moving toward sipper insertion hole or clawing, gnawing, sniffing it) during the 5s of houselight illumination prior to sipper presentation. During the first 5s of sipper presentation, sipper contact was scored (pressumed licking: sipper occlusion or proximity plus rapid whisker motion).

Matched Drinking History

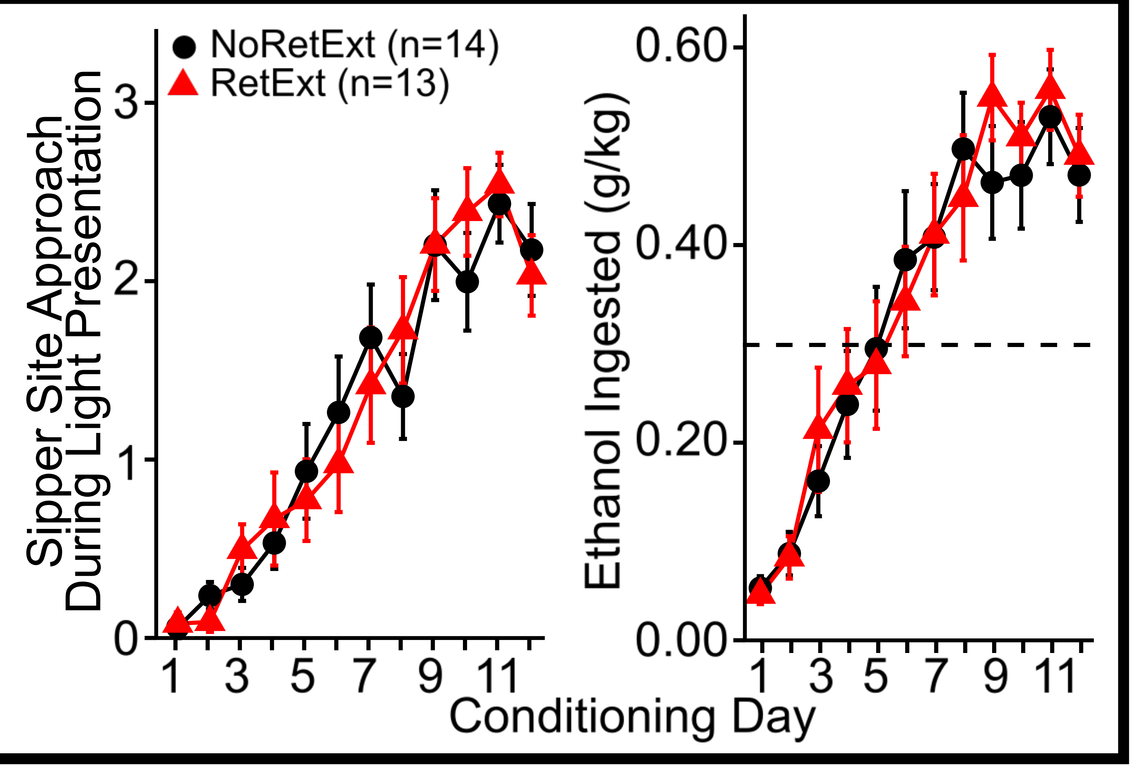


Group mean ± sem for ingested doses across homecage alcohol pre-exposure phase (24hr access MWF across 5 weeks). Horizontal line indicates minimum dose 1 g/kg required across day 13-15 for subject retention.

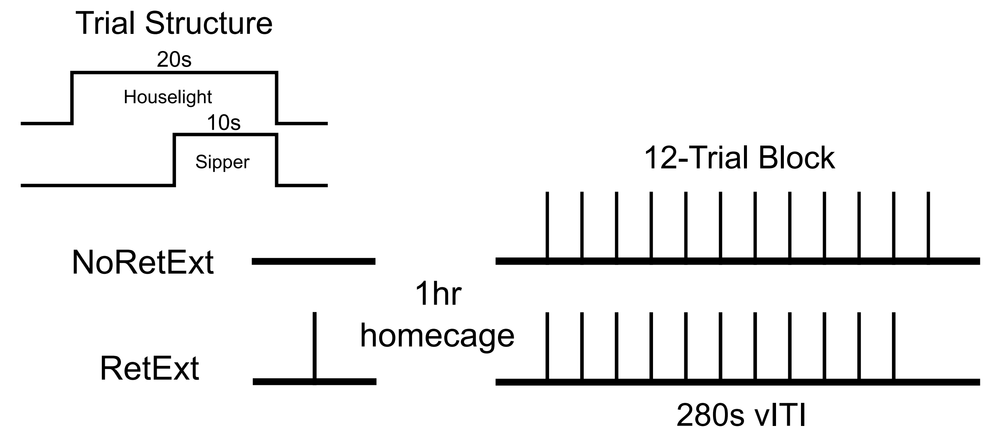
Matched Cue Conditioning History



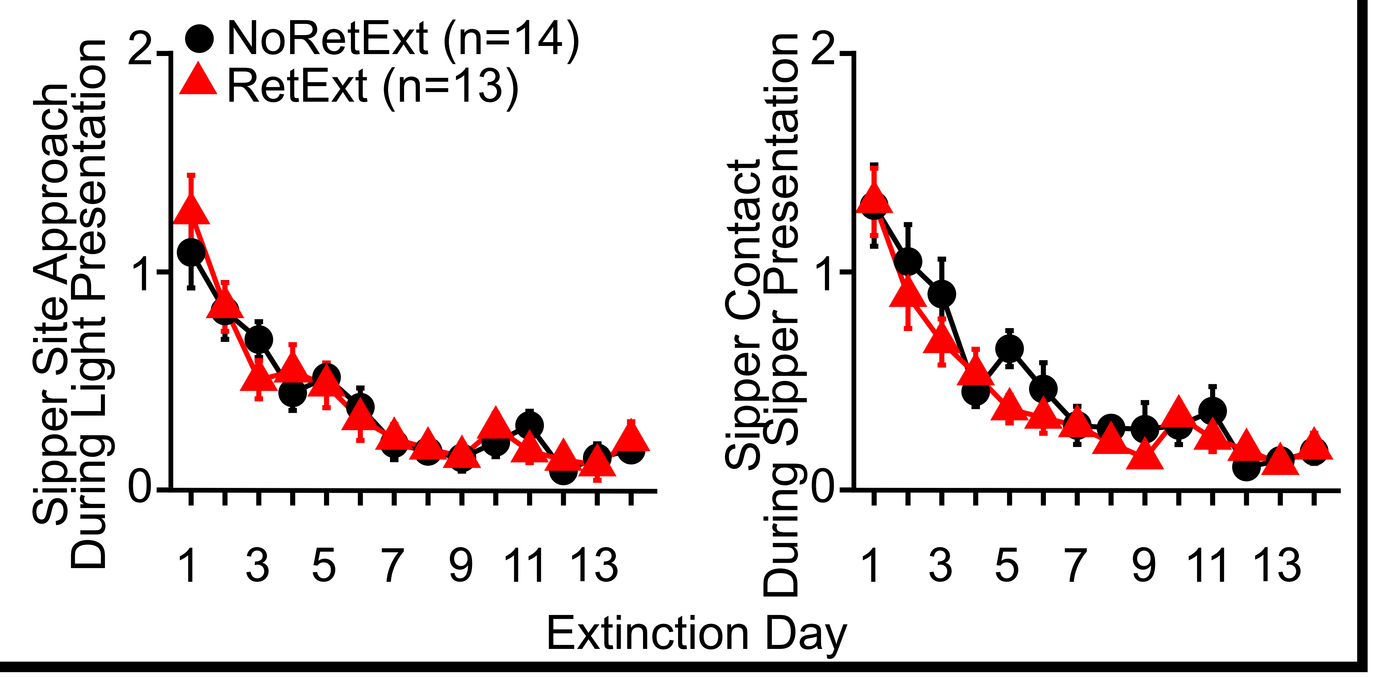
LEFT: Group mean ± sem for sipper site approach level during 5s prior to sipper insertion across the cue conditioning phase (12 consecutive days). RIGHT: Group mean ± sem for ingested doses across conditioning. Horizontal line indicates minimum dose 0.30 g/kg required across day 10-12 for subject retention. We previously demonstrated that doses > 0.30 g/kg ingested in this paradigm can produce blood alcohol content of 10-60 mg/dL.



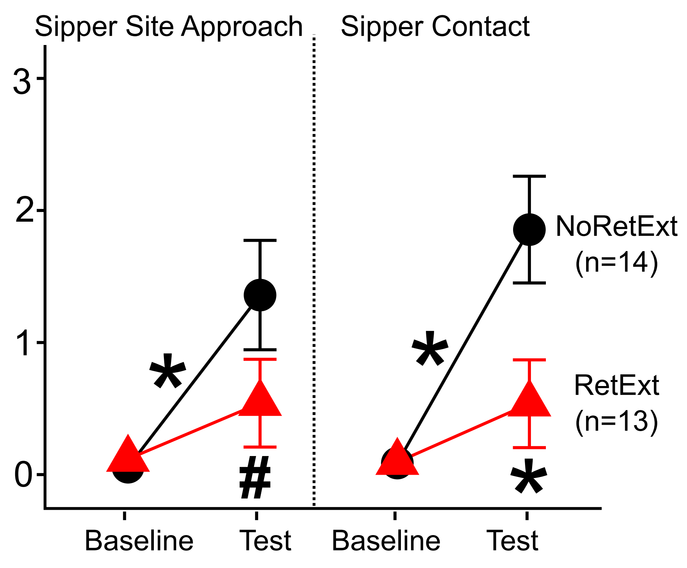
Equivalent Extinction During Treatment



Group mean ± sem for levels of sipper site approach (LEFT) and sipper contact (RIGHT) across the cue extinction phase (14 consecutive days).

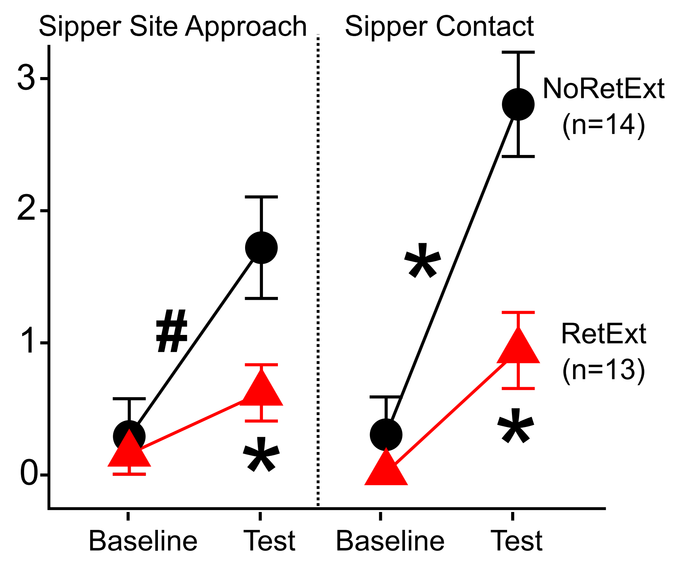


RetExt Reduced Short-Term Spontaneous Recovery



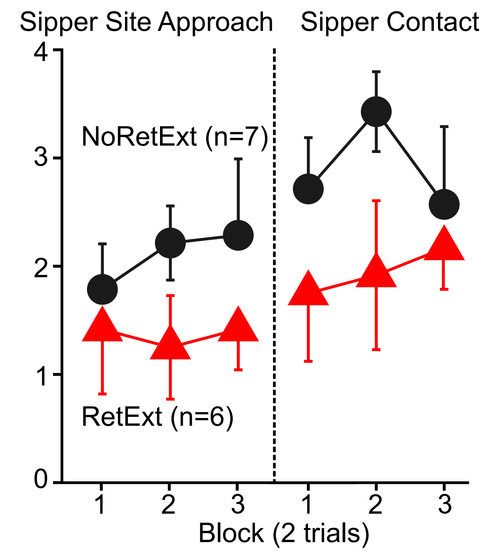
Group mean ± sem for levels of sipper site approach (LEFT) and sipper contact (RIGHT). Baseline refers to the average across the last 4 trials of extinction day 14. Test refers to the first trial of a 4-trial long-term extinction memory probe. Asterisk and pound symbol signify p<0.05 and p<0.07, respectively, for hypothesis tests (NoRetExt > RetExt) on response level at test and increase relative to baseline (slopes).

RetExt Reduced Alcohol Odor-Induced Reinstatement



Group mean ± sem for levels of sipper site approach (LEFT) and sipper contact (RIGHT). Baseline refers to the last trial of a 4-trial long-term extinction memory probe. Test refers to the first trial of a 4-trial alcohol odor-induced reinstatement test. Asterisk and pound symbol signify p<0.05 and p<0.07, respectively, for hypothesis tests (NoRetExt > RetExt) on response level at test and increase relative to baseline (slopes).

RetExt Reduced Reconditioning?



Group mean ± sem for levels of sipper site approach (LEFT) and sipper contact (RIGHT) across 2-trial blocks in a re-conditioning session given 24hr after 4-trial reinstatement test. Groups ingested similar doses during this session (NoRetExt: 0.47±0.08 g/kg; RetExt: 0.38±0.07 g/kg).

Findings

Retrieval+extinction protected against short-term spontaneous recovery and alcohol odor-induced reinstatement relative to standard extinction.

Retrieval+extinction may also slow down initial reconditioning rate.

Conclusion

Given similar prior conditioning + drinking history, retrieval+extinction more persistently attenuates alcohol cue reactivity than standard extinction for the same amount of treatment.

Future Directions

Does RetExt work on the original memory?
Will RetExt work on stronger cue memory?

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