Post-retrieval extinction can reduce alcohol cue reactivity

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Introduction

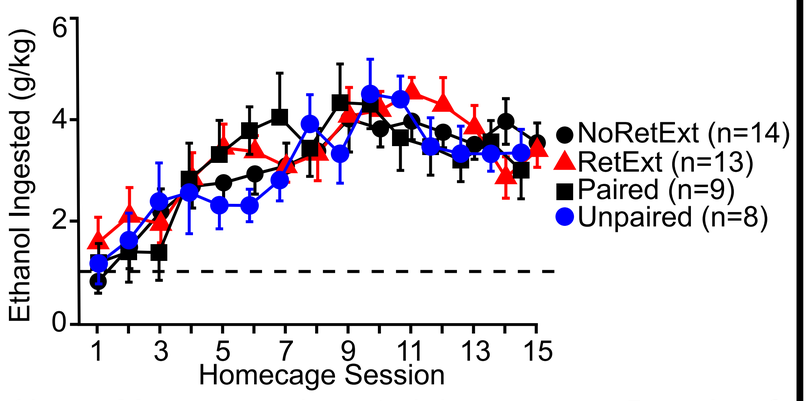
Alcohol-associated cues elicit conditioned reactions that create risk for relapse to drinking. Standard extinction can suppress reactivity to cues, but reactivity can endure and/or return. There is need for behavioral treatment strategies that can persistently attenuate conditioned reactivity to alcohol cues. Here we test whether treatment outcomes can be improved by conducting cue extinction during the post-retrieval memory reconsolidation window.

Methods & Materials

Subjects

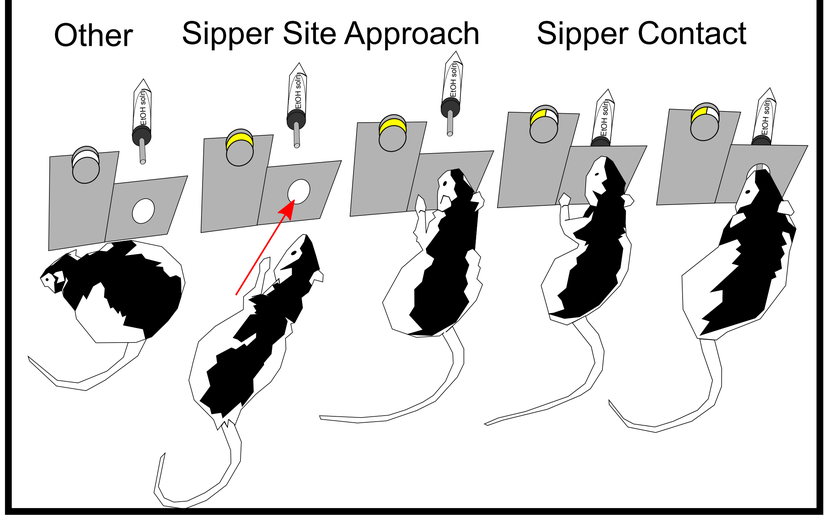
Singly-housed, adult male Long-Evans rats with unlimited food+water; Envigo, Indiana, USA).

Alcohol Acclimation

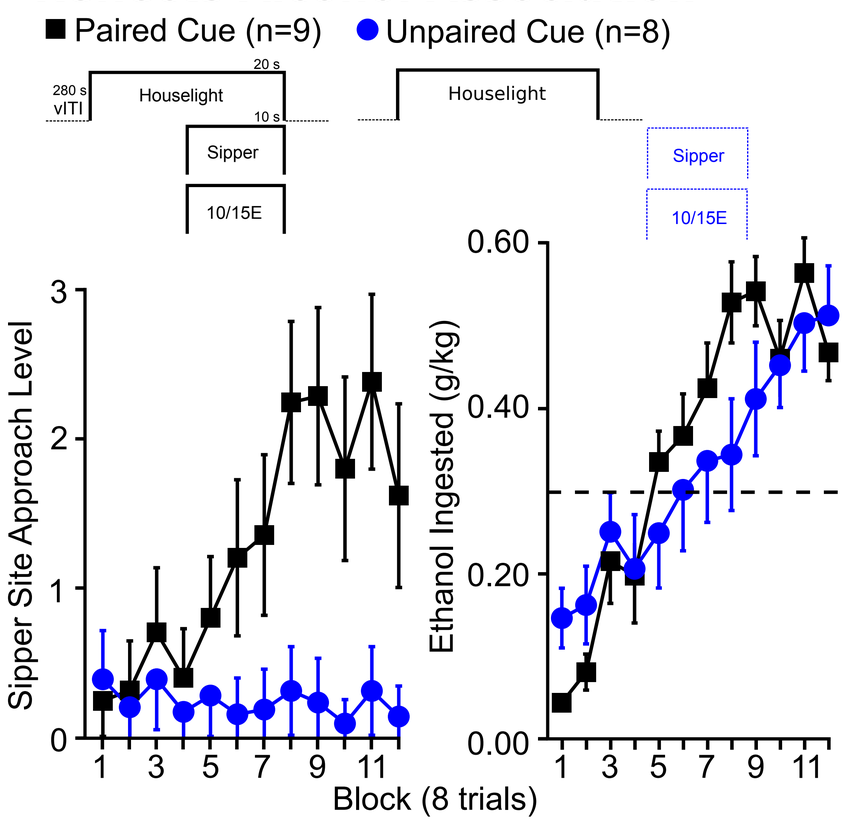


Above: Mean ± sem ingested doses across 5 weeks of 24hr access to unsweetened alcohol (5-15% v/v) every MWF before conditioning experiments. Horizontal line indicates minimum dose required across session 13-15 for subject retention.

Scored Behavior States

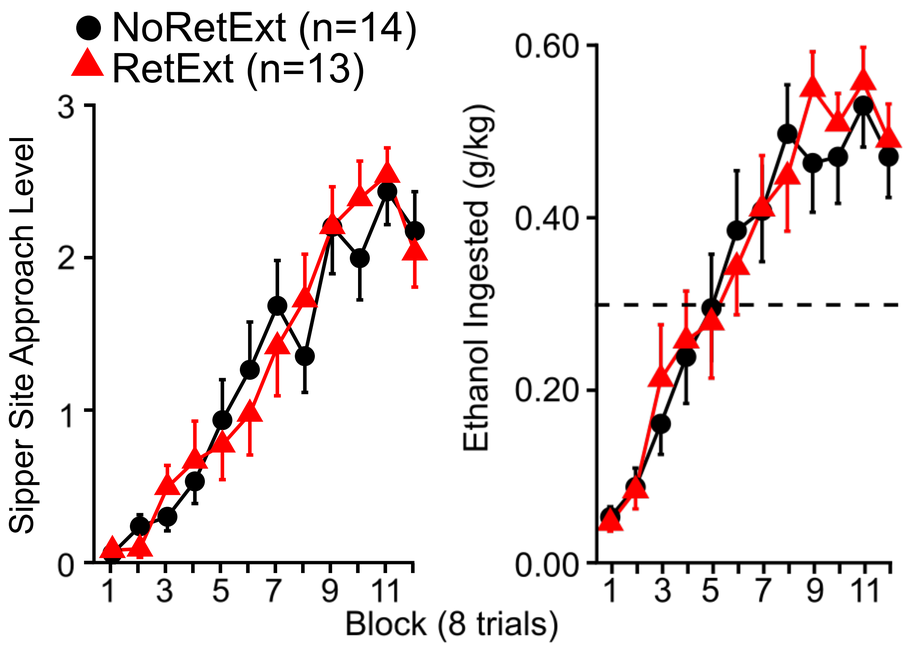


Behavioral Reactivity to Cue Reflects Alcohol Association



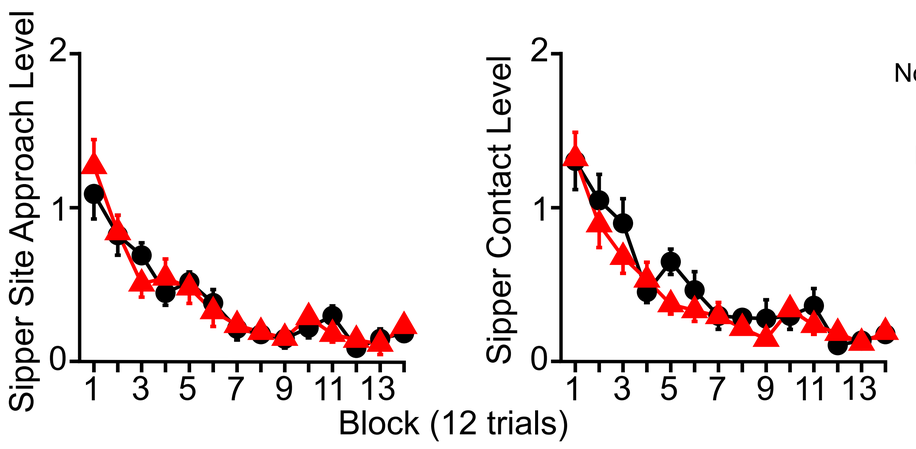
Left: Group mean ± sem for cue-elicited sipper site approach level per trial during first half of cue presentation period across 12 consecutive days. Right: Group mean ± sem for ingested doses across conditioning. Horizontal line indicates minimum dose 0.30 g/kg required across day 10-12 for subject retention.

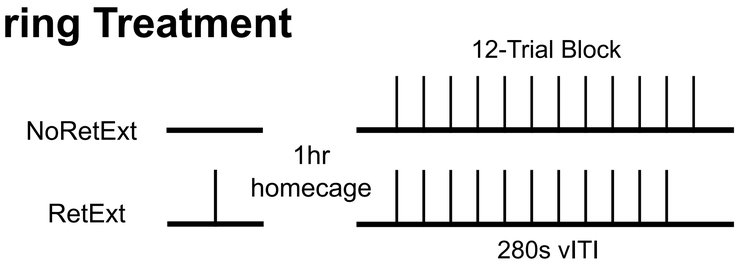
Matched Alcohol Cue Conditioning History



Left: Group mean ± sem for cue-elicited sipper site approach level per trial before sipper insertion across paired cue-alcohol conditioning phase (12 consecutive days). Right: Sipper licking delivered unsweetened alcohol. 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 above 0.30 g/kg ingested in our paradigm can produce blood alcohol content of 10-60 mg/dL.

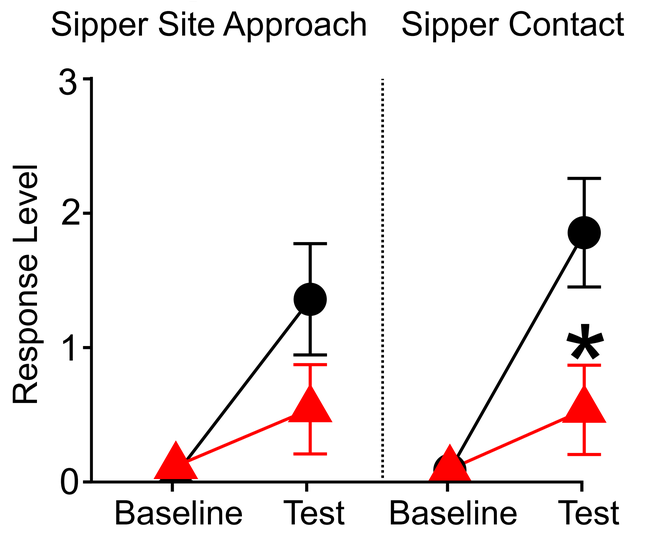
Equivalent Extinction During Treatment





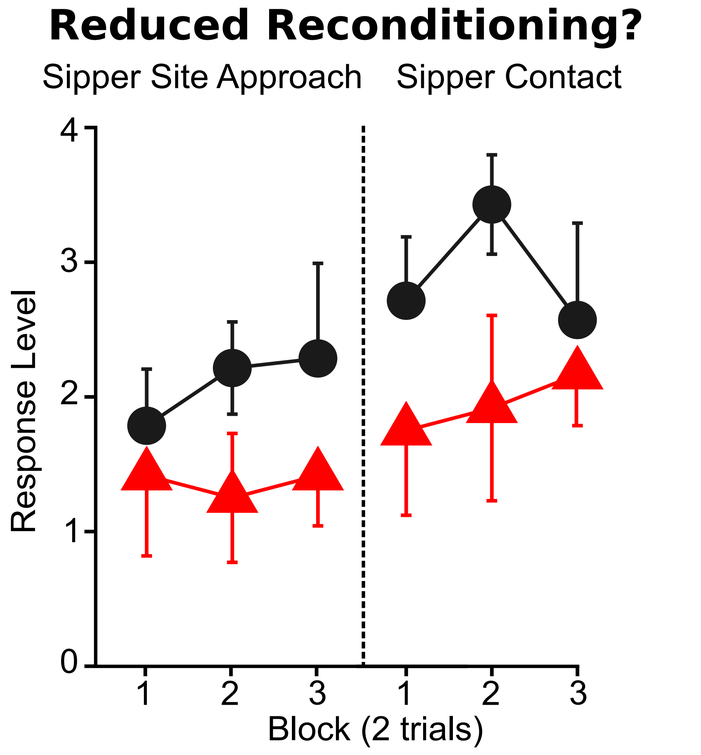
Group mean ± sem for per-trial levels of cue-elicited sipper site approach (left) and sipper-elicited contact (right) across the cue extinction phase (14 consecutive days). Sipper licking did not deliver fluid. No alcohol odor present.

Reduced Spontaneous Recovery



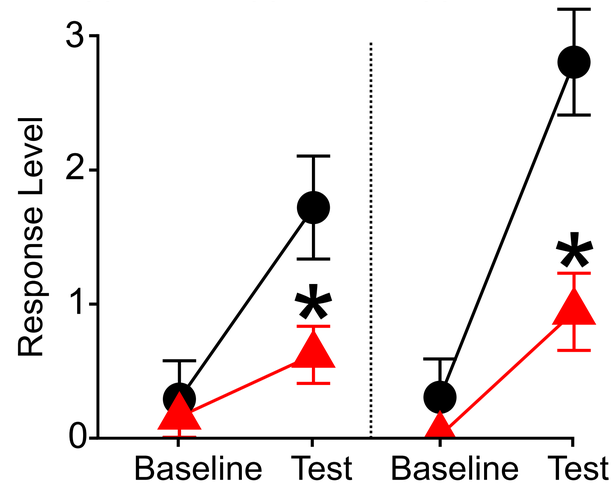
Group mean ± sem for levels of cue-elicited sipper site approach (left) and sipper-elicited contact (right). Baseline refers to end of extinction. Test refers to 48 hr long-term extinction memory probe. Sipper licking did not deliver fluid. No alcohol odor present.

Reduced Reconditioning?



Group mean ± sem for levels of cue-elicited sipper site approach (left) and sipper-elicited contact (right) during reconditioning probe in a subset of subjects (NoRetExt n=7, RetExt n=6). Sipper licking delivered alcohol.

Reduced Reinstatement



Group mean ± sem for levels of cue-elicited sipper site approach (LEFT) and sipper-elicited contact (RIGHT). Baseline refers to end of extinction memory probe. Test referes to alcohol odor-induced reinstatement probe. Sipper licking did not deliver fluid.

Conclusion

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

Clinical Significance

Standard cue exposure conducted after initial retrieval (priming) of alcohol cue memory and brief rest may allow therapeutic learning to better reduce risk for relapse to problem drinking posed by alcohol-associated cues in daily life.

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