

Characterizing a novel alcohol cue conditioning paradigm

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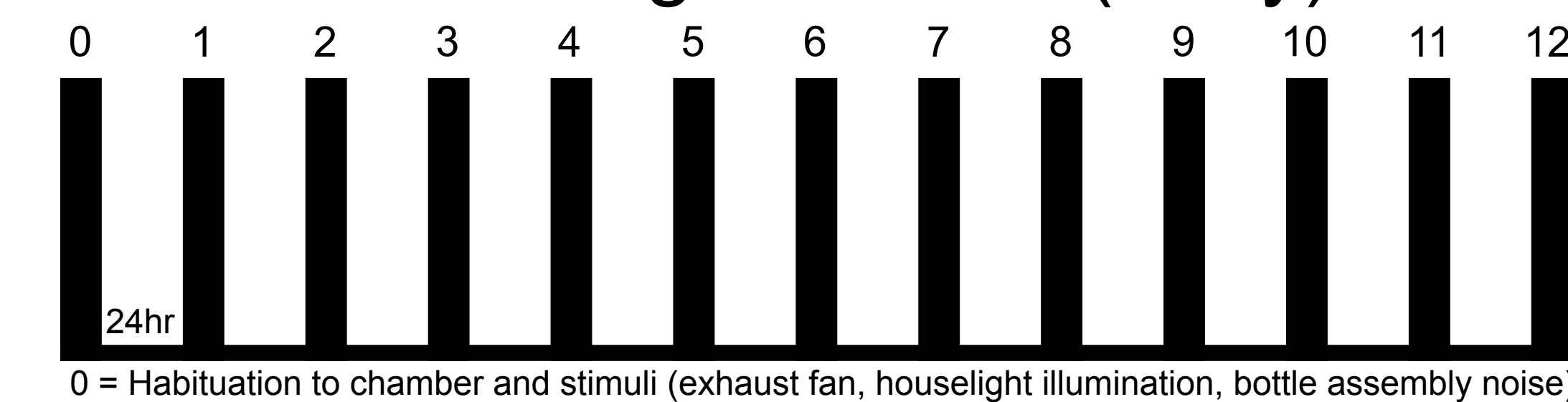
Rationale

Conditioned responses to alcohol-associated cues can promote drinking and hinder recovery. In order to study how cues control alcohol seeking and drinking, we developed a conditioning procedure in which a visual cue predicts access to a sipper from which unsweetened alcohol can be obtained. Appetitive and consummatory response acquisition in this novel paradigm is characterized below.

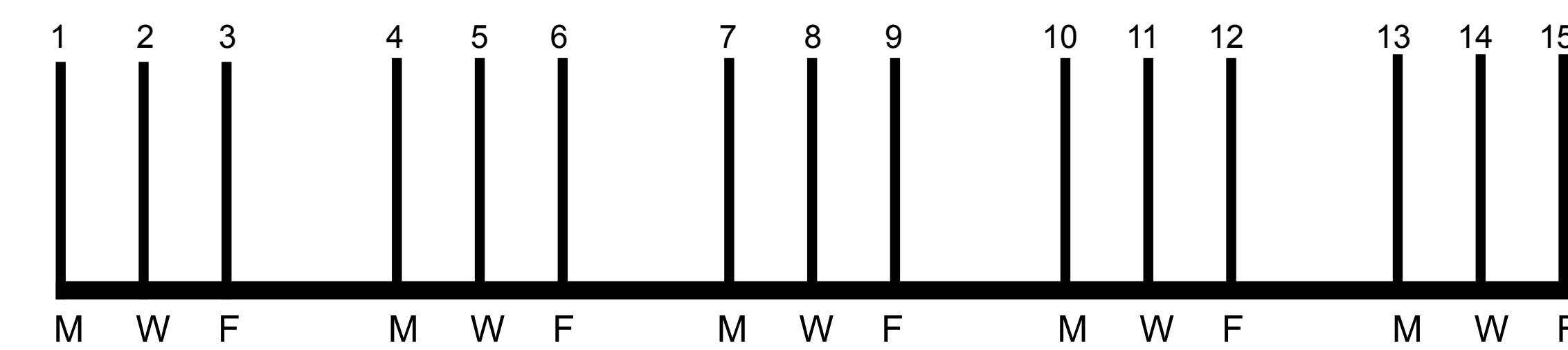
Subjects

Male Long-Evans rats (approx. 300g prior to 1st EtOH exposure) from Envigo (formerly Harlan), singly housed

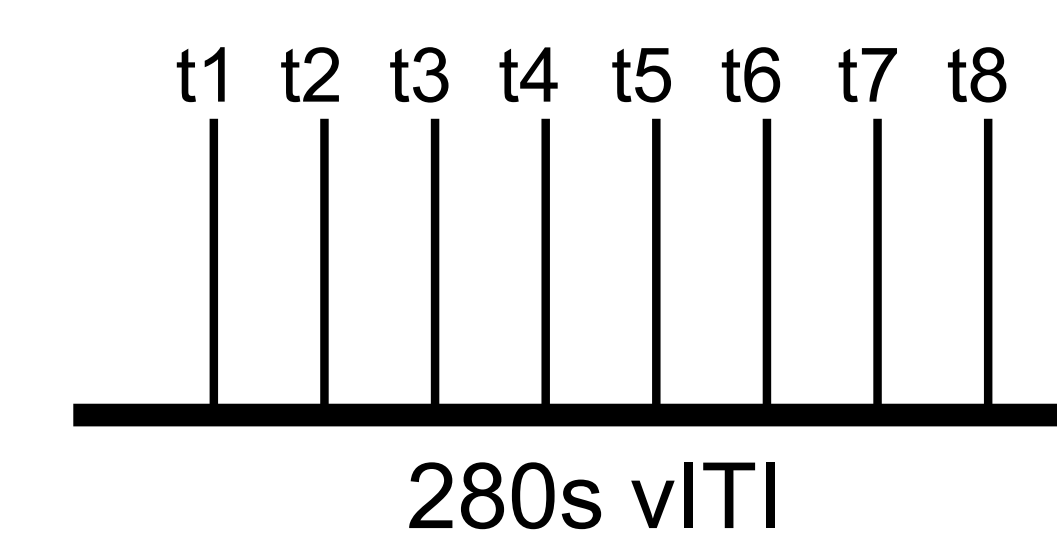
Cue Conditioning Sessions (Daily)



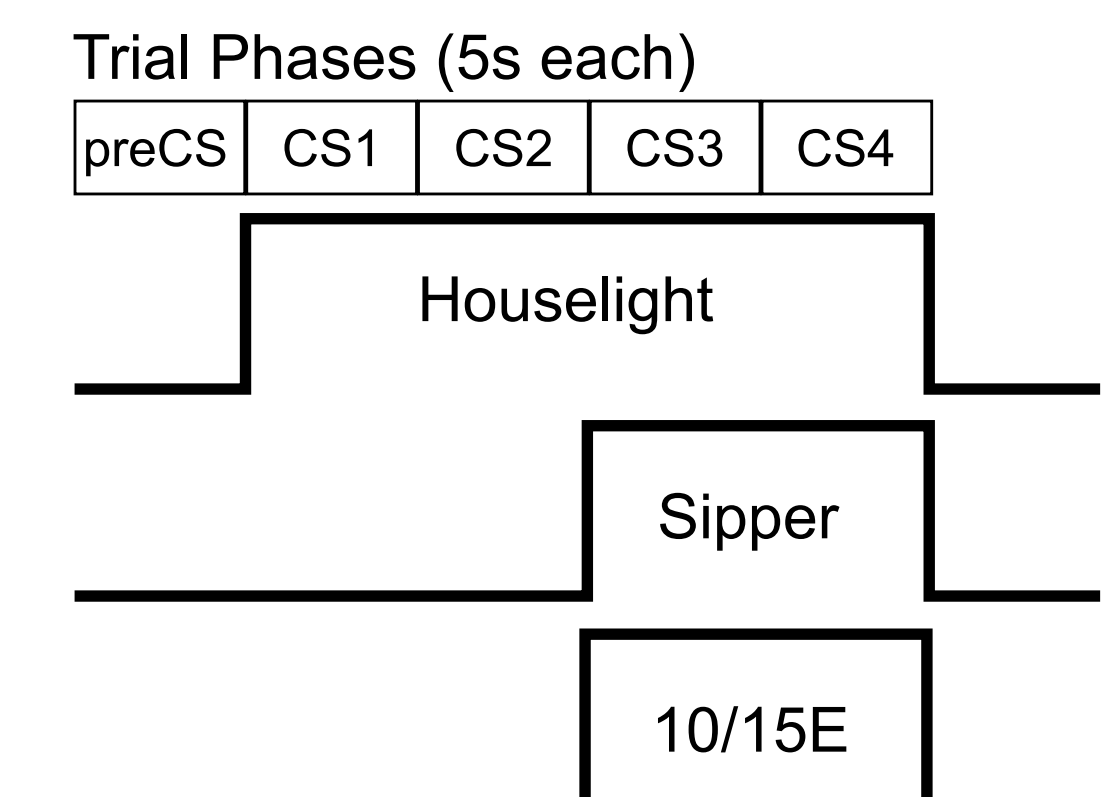
Homeage Drinking Induction (Intermittent Days)



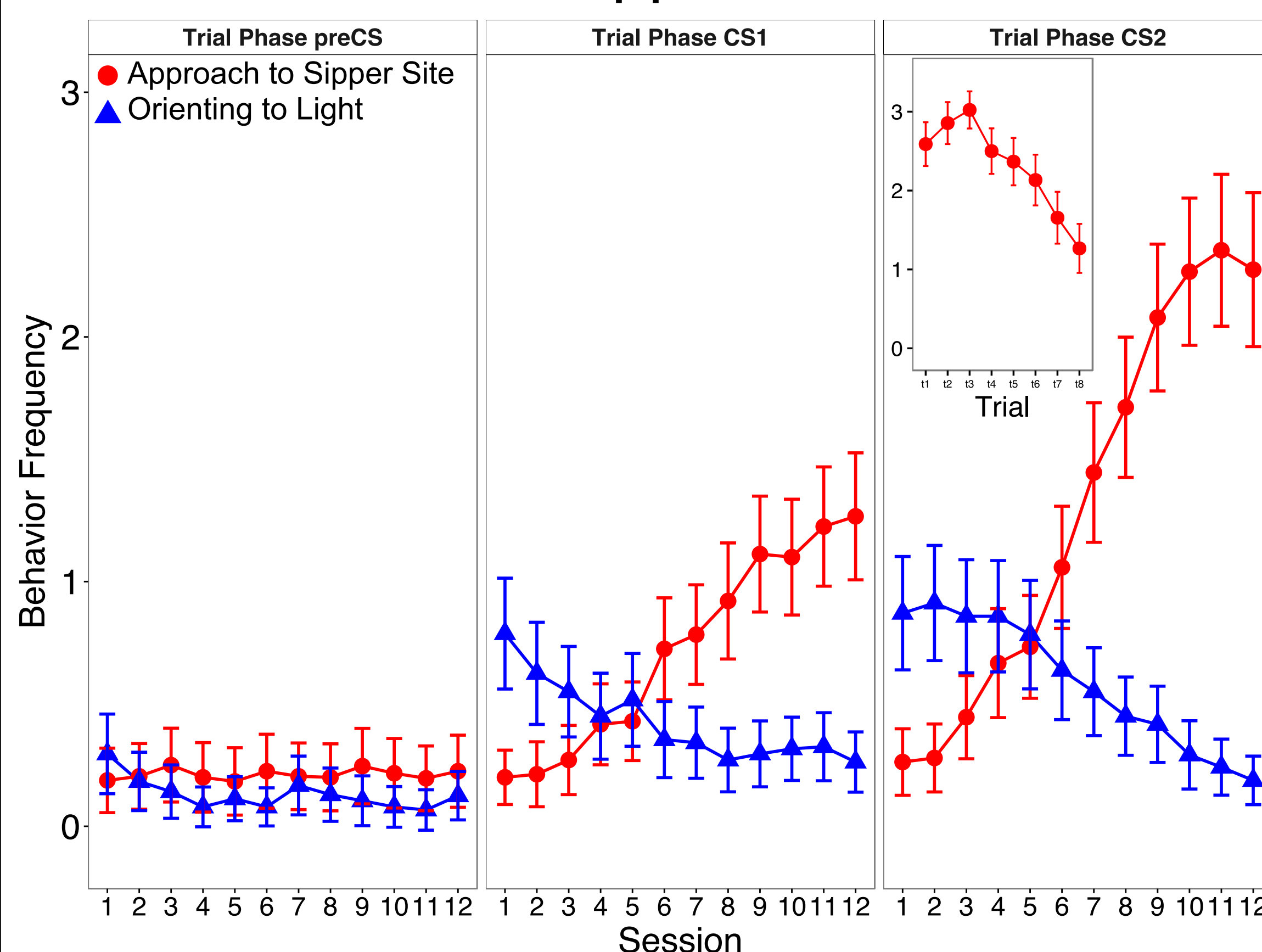
1 Session = 8 Trials



1 Trial = 5 Trial Phases

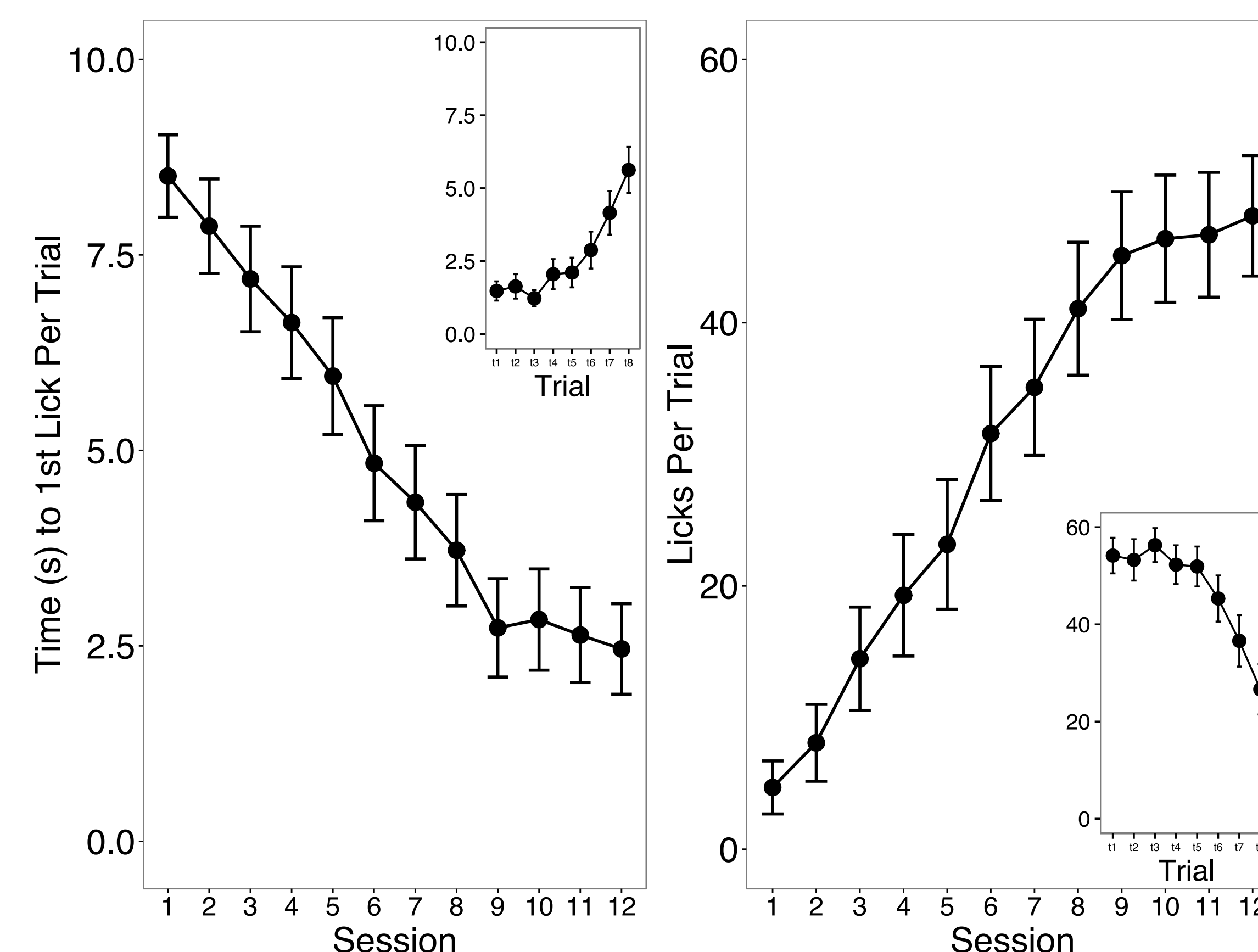


Appetitive Behavior



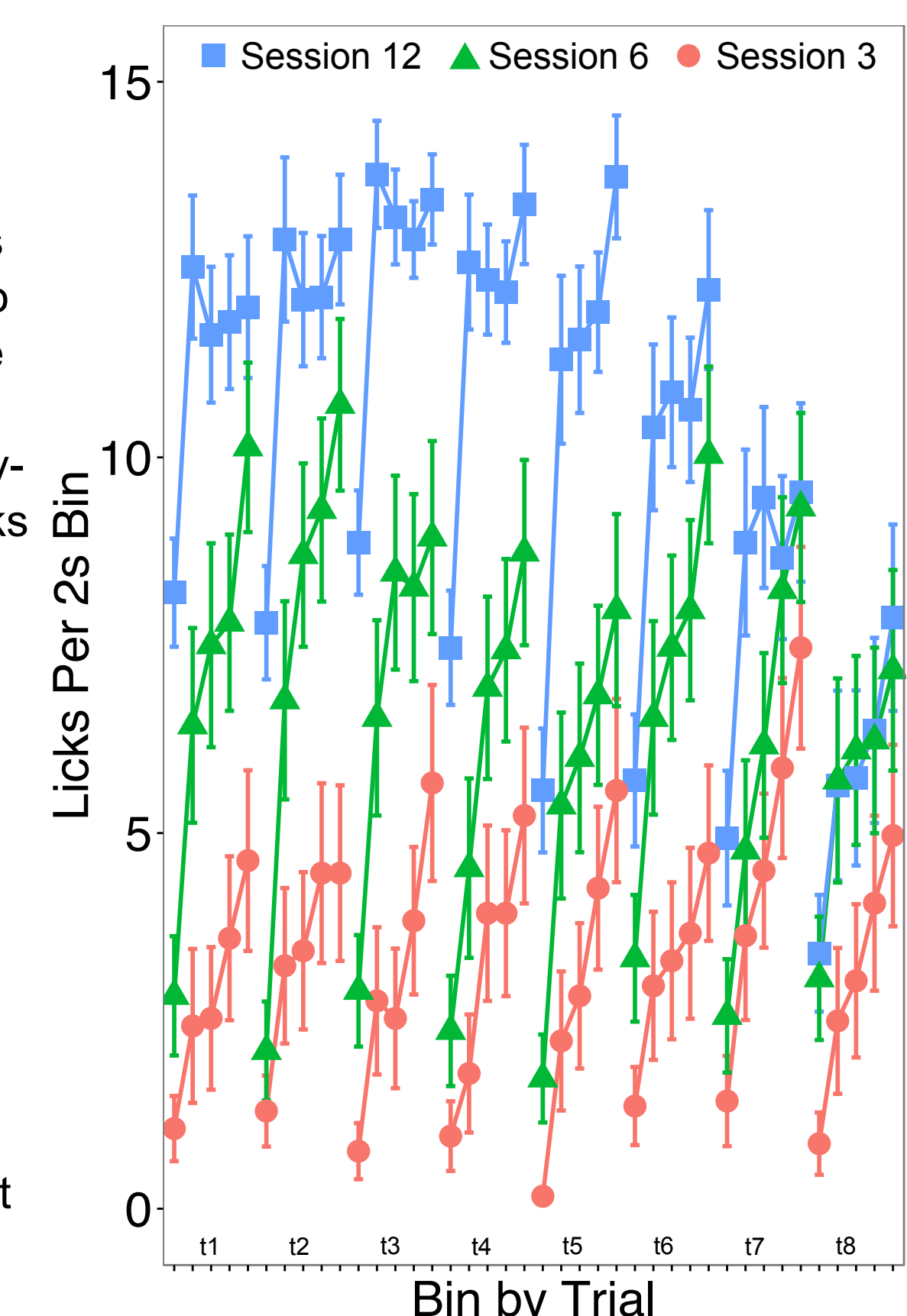
Mean \pm SEM shown across 30 rats for behavior state frequency (count in 4 instantaneous observations per trial phase made from digital video recordings at 1.25s intervals) averaged across trials per session for each rat. Incidence of approach to the site of alcohol access (defined as attending/ exploring sipper hole) during cue presentation (houselight illumination) increased across conditioning sessions, most prominently during trial phase CS2 (2nd 5s of light just prior to sipper insertion). Inset shows by-trial approach during the latter at asymptote (session 10-12). In contrast, incidence of orienting to the light (defined as rearing, but not grooming) decreased across sessions.

Consummatory Behavior

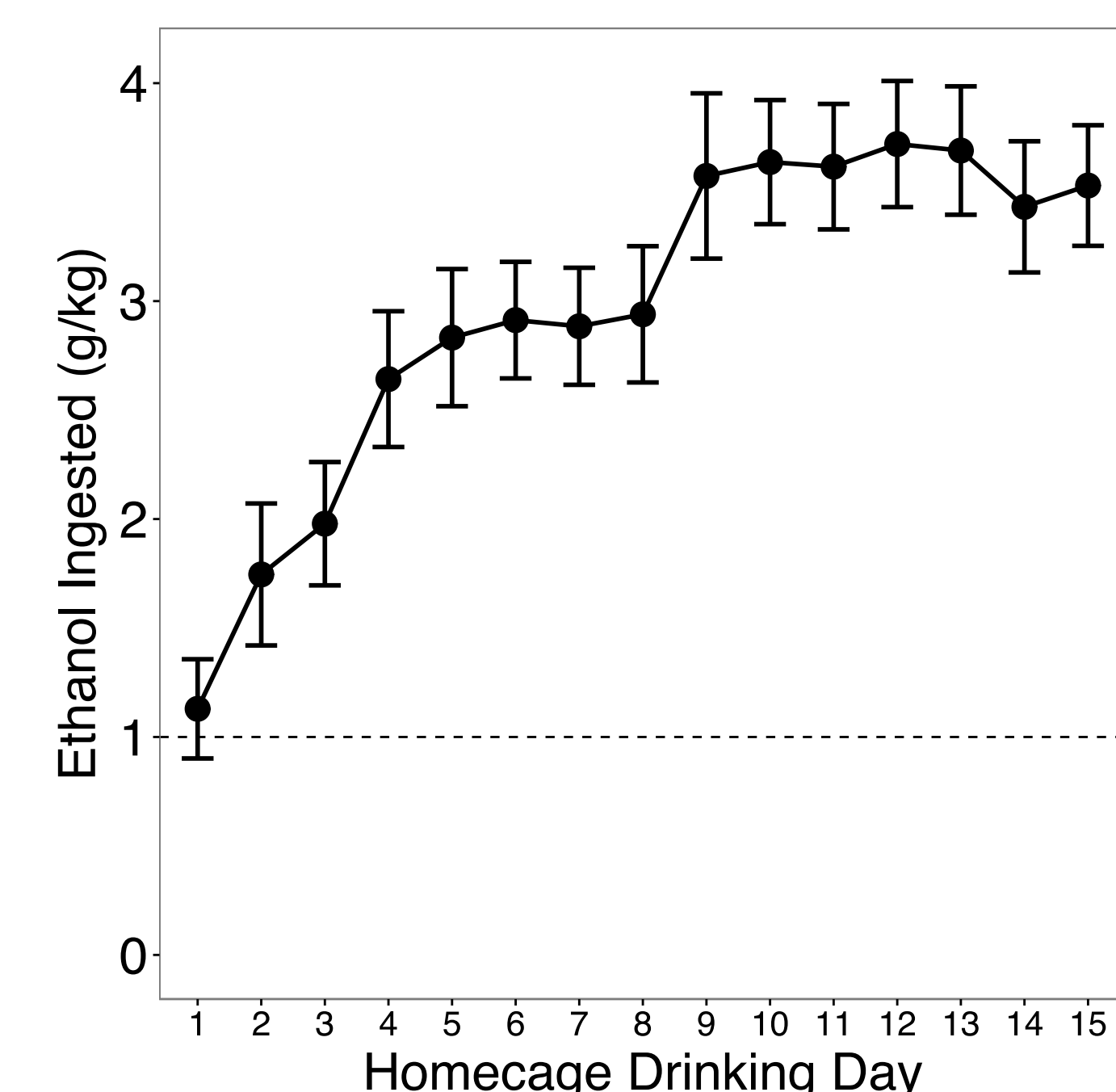


Mean \pm SEM shown across 30 rats for time to 1st lick (far right) and total licks (near right) per trial averaged across the 8 trials per session for each rat. Time to 1st lick per trial decreased while total licks per trial increased across sessions. Insets show by-trial 1st lick latency and total licks per trial at asymptote (session 10-12).

Mean \pm SEM shown across 30 rats for lick rates during sipper presentations (total licks per 2s bin, 5 bins per trial). In session 12, lick rate increased across bins within sipper presentations even as it decreased across trials. In session 3 and 6, lick rate accelerated within trials, but did not change across trials.

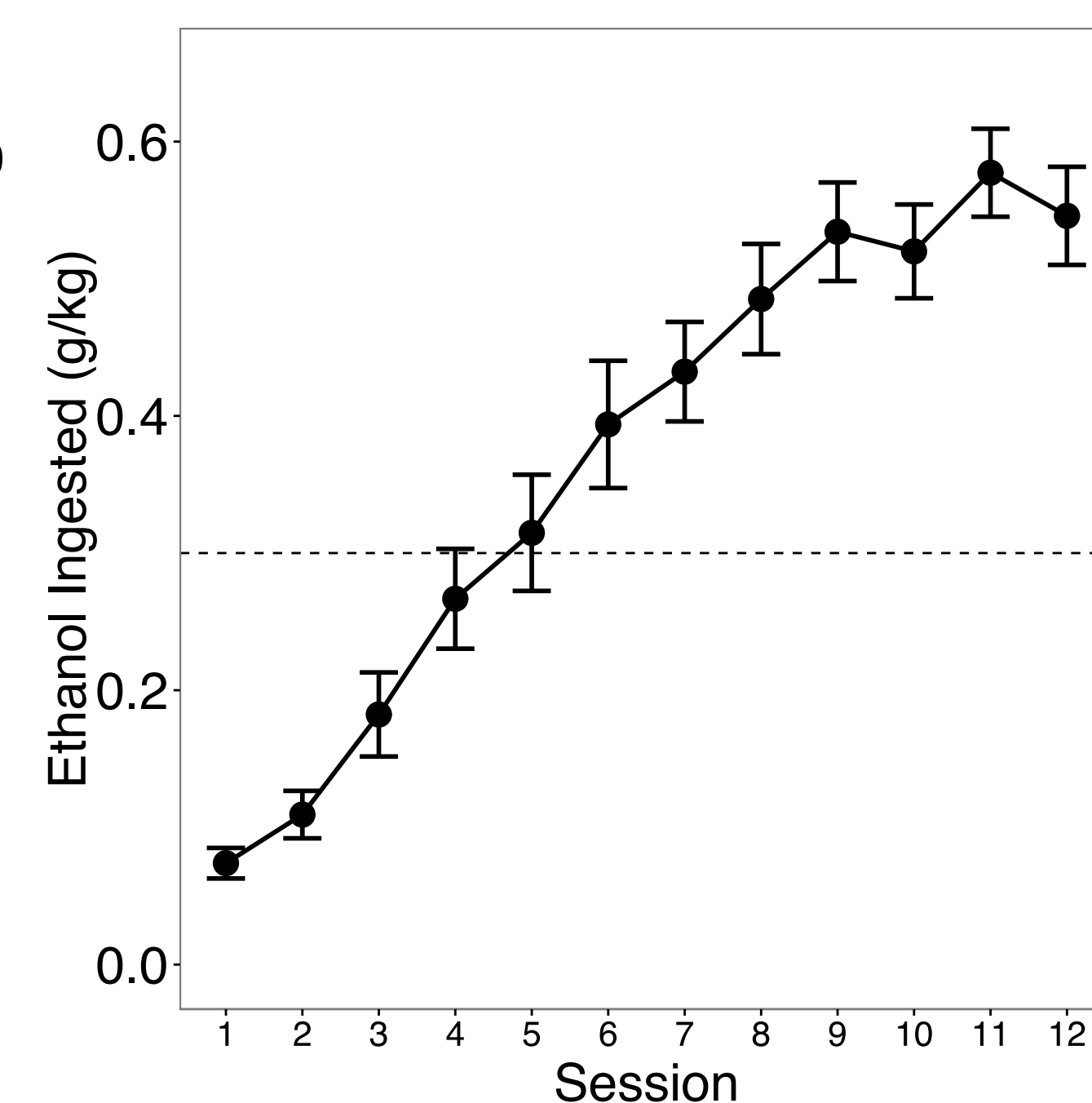


Induction Doses



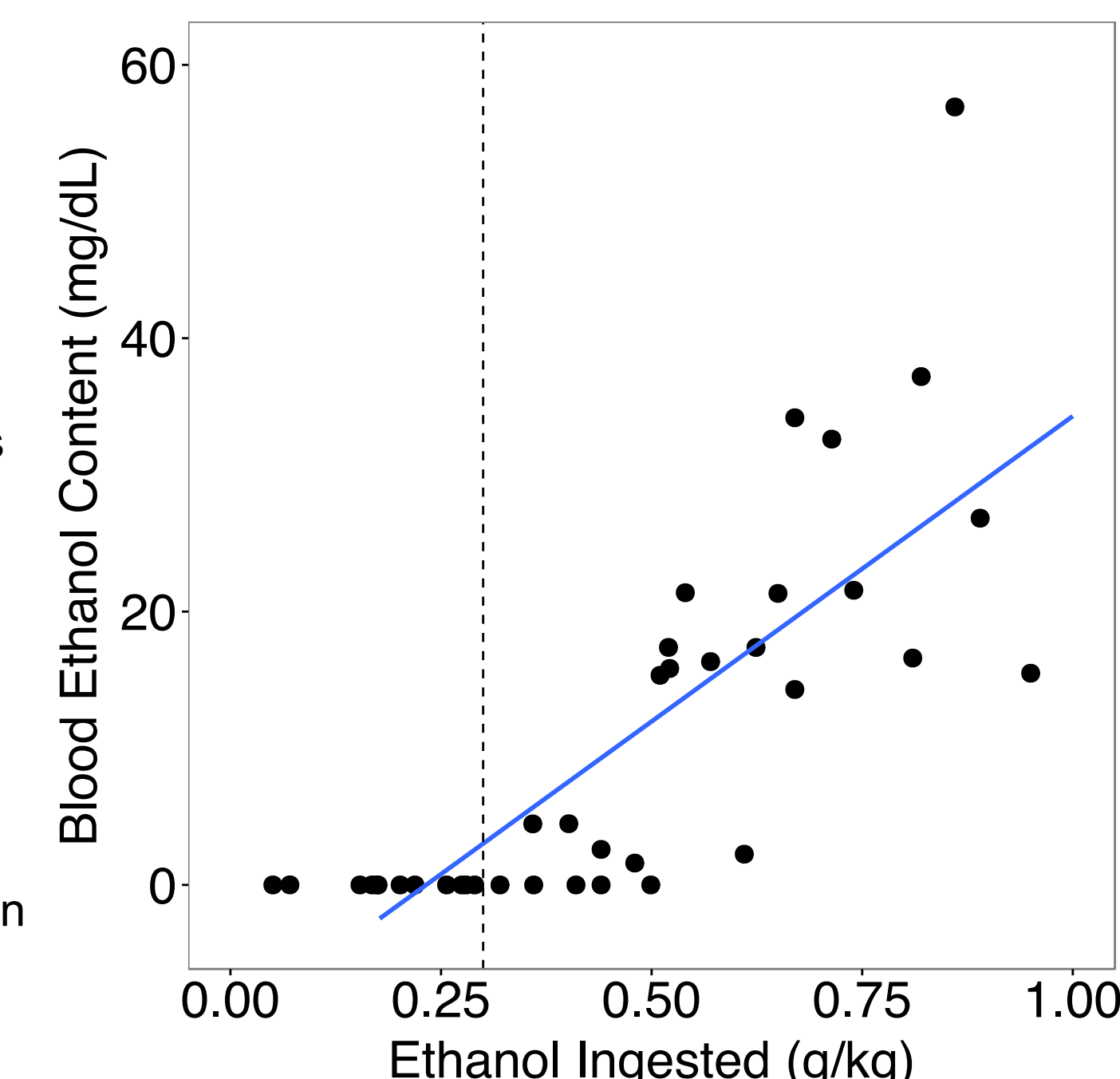
Mean \pm SEM shown across 30 rats for drinking during induction. Access to unsweetened alcohol (15% ethanol v/v) was provided every MWF across 5 weeks. Tap water and standard chow were always available ad libitum. Doses achieved increased across days. Horizontal line represents a priori criterion for inclusion (1.00 g/kg across days 13-15).

Conditioning Doses & Blood Ethanol Concentrations



Mean \pm SEM shown across 30 rats for drinking during conditioning. Doses achieved increased across sessions. Rats had only 8 opportunities to drink per session (each 10s long with approx. 280s between them). Horizontal line represents a priori criterion for inclusion (0.30 g/kg across sessions 10-12) based on expected blood ethanol content (BEC).

Blood samples (n=38) were taken within 12min of the 8th drinking opportunity. Ethanol content was determined via GC-FID. There was a significant positive relationship between BEC and total ethanol ingested during session ($R^2=0.60$, $p=5e-9$).



Conclusions

This paradigm establishes:

- (1) anticipatory approach to the site of alcohol access upon presentation of the visual cue (light)
- (2) vigorous licking upon presentation of the access device (sipper)
- (3) ingestion of ethanol doses resulting in BECs within the 10-60 mg/dL

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