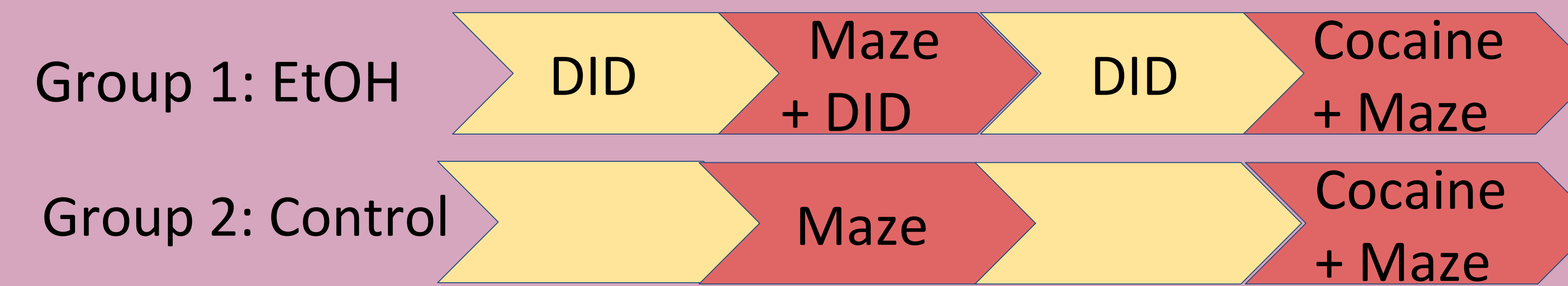




Background

- In the U.S., more than 1 out of 4 adults reported binge drinking in the past 2 months and this prevalence increases to over 50% in college populations
 - Binge drinking is consuming 5 or more drinks in 2 hours
- Binge drinking is a common precursor to alcohol use disorder (AUD) and the risk of polydrug use also increases
- Most preclinical studies model the use of a single substance, thus comorbid models are limited
 - Cocaine is frequently used in combination with alcohol
- Little is known how a history of binge drinking and comorbid cocaine influences memory
- We planned to use a cross-over design to develop a mouse model of alcohol and cocaine co-use to investigate how the comorbidity influences performance of a working memory task. However, due to the Coronavirus pandemic we did not complete part of the design (see Fig. 1).
 - We did test the cognitive abilities of 2 groups of mice that differed in their history of alcohol use (EtOH and Control)
 - To do this, we used the intermittent Drinking in the Dark (DID) paradigm and exposed male mice to 10% EtOH for 2 hours a day for 4 days per week. The mice used for this study were C57BL6/J male mice which are genetically predisposed to drink alcohol.
 - Working memory was assessed using the Barnes Maze (see Fig. 2).

Methods



- Fig. 1. General timeline of methods. Note that the second phase of the cross-over design (Cocaine + Maze) did not occur in the EtOH group due to the Coronavirus pandemic.

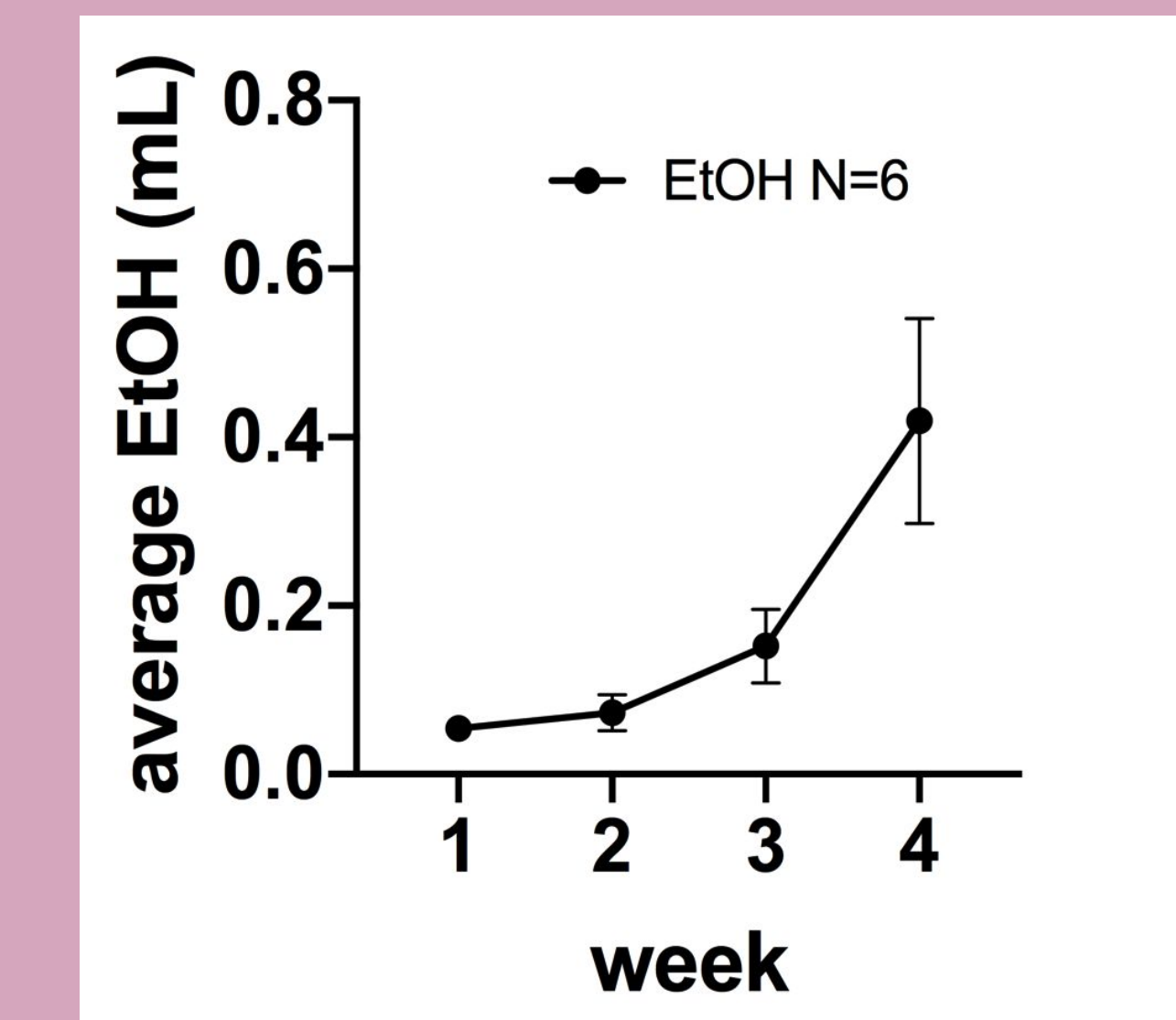


- Fig. 2. The Barnes Maze is a hippocampal-dependent test of learning and memory. The mouse is motivated to find the escape box and must use the spatial cues in the room to find the correct hole.

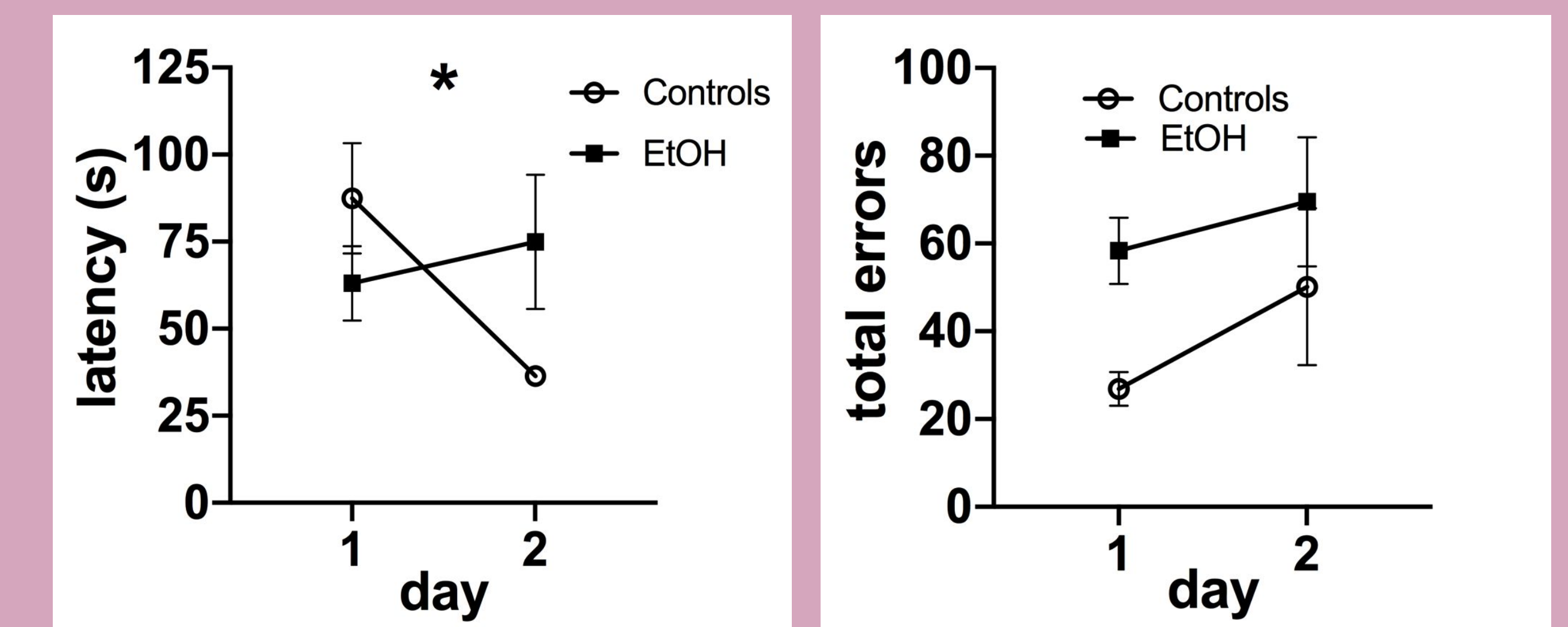
Conclusions

- Here, we found that alcohol use impairs performance in a working memory task.
- We also show a within-subject comparison of mice without a history of alcohol use in the working memory task in two Phases (Baseline and Cocaine-primed).
- This Fall 2020, we will run a third group of mice to compare to the Phase 1 data we have shown here. This group will be exposed to EtOH and also cocaine, and then be tested in the working memory task. This group is very important as it provides the comorbid use of cocaine and alcohol that we sought to model in this study. In this way, we will forgoe the cross-over design.

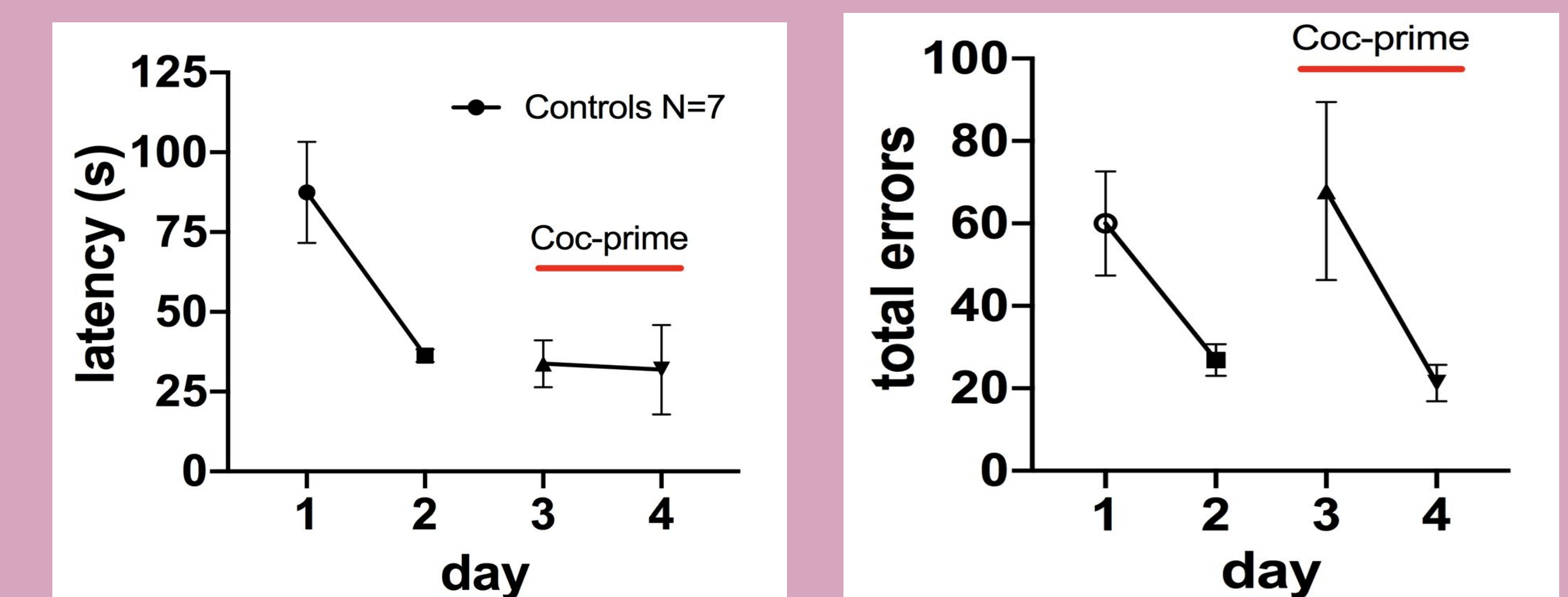
Results



- Fig. 3. Mice drank more across the 4-week period (Repeated Measures ANOVA: $F(1, 6) = 6.5, p = 0.03$).



- Fig. 4. A) An interaction resulted between group and day. Whereas control mice improved on day 2 of the working memory task, alcohol-using mice did not (2-way RM ANOVA: $F(1, 11) = 5.4, p = 0.041$). B) A non-significant trend for EtOH mice to commit more errors was found ($F(1, 11) = 3.8, p = 0.07$).



- Fig. 5. Shows the completed cross-over data for Control mice for A) latency to find the escape box and B) total errors committed. Latency to solve the maze under the influence of cocaine (Days 3 and 4, 20 mg/kg) is comparable to the final day of baseline (Day 2). In spite of this fast latency, the total number of errors on Day 3 is higher and more variable.