## Disrupting the medial Prefrontal Cortex Alters Hippocampal Sequences during Deliberative Decision-Making

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Supplementary Fig. S1

## DREADDs surgery and Pre-training



Hyperdrive surgery, Recovery Training and CNO/VEH Injection Sequence



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Supplementary Fig. S1 Diagram of the training, surgery, and injection sequence.

Supplementary Fig. S2



Supplementary Fig. S2 a) The difference in the number of place fields (see Methods) between the first ½ and the second ½ of the testing session on VEH and CNO days is shown. We found no difference within CNO and VEH days, nor did we find a difference between VEH and CNO days. b) Place fields were slightly, but significantly, larger for the first ½ of the recording session on VEH days, CNO days failed to reach significance, nor did we find a difference between CNO and VEH days. c) The max in-field firing rate was significantly higher in the first ½ of the session for both VEH and CNO days but we found no difference between CNO and VEH days. d) We measured the mean in-field firing rate and found no within session differences for VEH days, or CNO days or between VEH and CNO days. e) Tuning curve correlations (relationship between spike firing and spatial location) between the first ½ and second ½ of the session were consistent between VEH and CNO days. f) Disrupting the mPFC with CNO had no effect on the max in-field firing rate (for the main place field of the cell) for hippocampal cells on VEH and CNO days g) nor the mean in-field firing rate. h) Similarly, we found no difference in the place field area between CNO and VEH days (Wilcoxon Rank Sum z = 0.39, p > 0.10). mean±std



Supplementary Fig. S3 Flavor preferences were consistent within rat and varied between rats. Each DREADD + CNO rat's thresholds for each of the four flavors (VEH n = 9; CNO n =9). Revealed preferences were consistent within rats but different across rats (session mean  $\pm$  s.e.m.). Circle = VEH, diamond = CNO, white, plain; brown, chocolate; yellow, banana; red, cherry.



Supplementary Fig. S4 mPFC dysfunction had no effect on a non-cognitive foraging task. a) We trained three mPFC-DREADDs transfected rats (DREADDs+) on a similar foraging task as Restaurant Row that did not have the same cognitive demands. Rats were trained to run in a circle for food reward. At the north, south, east, and west coordinates two .45 mg food pellets were dispersed when the rats entered the zone. b) We measured the running speed for the rats on CNO and VEH days, CNO had no effect on running speed. c) mPFC disruption did not improve behavioral performance; the average rate of reinforcement (nPellets per day) did not change under CNO. d) CNO had no effect on consumption time.

## Supplementary Fig. S5 b a 14000 15 Vehicle CNO Vehicle Shuffle CNO Shuffle Sequence Score (median + sem) 12000 \*\*\* 10 10000 Data Shuffle Count 8000 \*\*\* 5 6000 \*\*\* 4000 0 2000 0 -5 Sequence Score -300 -200 200 300 Vehicle CNO d С 200 150 180 \*\*\* Sequence Score (median + sem) 160 Vehicle CNO Vehicle Shuffle 100 140 Count 120 **CNO Shuffle** Data 100 50 - Shuffle \*\* 80 60 0 40 20 0 -50 -1000 -800 -600 -400 -200 0 200 400 600 800 1000 Sequence Score Vehicle CNO



Supplementary Fig. S5 CNO disrupted coherence place cell sequences. a) We measured the sequence score for theta cycles with a minimum of three cells firing three spikes. b) Sequence scores were significantly reduced on CNO days. Sequence scores were significantly different from the shuffled data, however, the shuffled VEH and CNO data were not significantly different from each other. c/d) Same as above with a criteria of a minimum of eight cells firing eight spikes. e) The average theta cycle size was reduced on CNO days. \*\*\* p < 0.001.