
Figures and figure supplements

Dopamine in the dorsal bed nucleus of stria terminalis signals Pavlovian sign-tracking and reward violations

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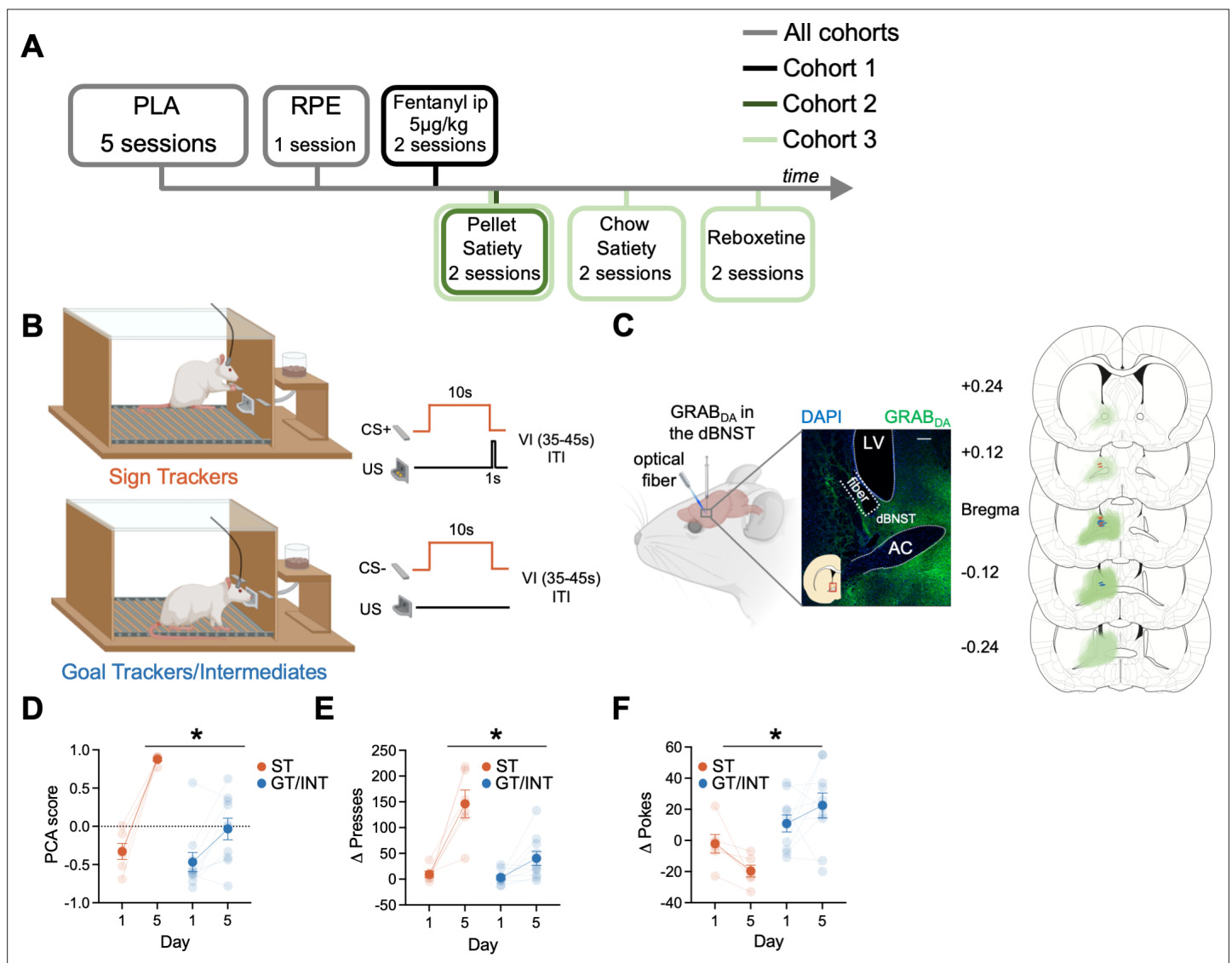


Figure 1. Individual differences emerge during Pavlovian lever autoshaping (PLA). **(A)** Experimental timeline. We trained all rats for five daily reinforced PLA sessions to determine their tracking groups followed by a single reward prediction error (RPE) session. We injected the first cohort of rats with i.p. fentanyl in PLA and tested the second and the third cohort of rats on two counterbalanced PLA pellet satiety sessions. We tested the third cohort of rats on two counterbalanced PLA chow satiety and with reboxetine i.p. injection sessions. **(B)** PLA sessions consisted of the presentation of 10 s of cue (either conditioned stimulus, CS+ or CS– lever, pseudorandom order with an intertrial interval (ITI) varying (variable interval (VI)) between 35 and 45 s) followed by lever retraction and delivery of two food pellets in the food cup. Some rats (Sign Trackers, STs) engage with the cue while others (Goal trackers, GTs) wait in the food cup during the cue period. Others display both lever and food cup behaviors (Intermediates, INTs) **(C)** Left: representative expression of GRAB_{DA} construct and fiber placement in dorsal bed nucleus of stria terminalis (dBNST). White scale bar: 250 μm. Right: The extent of GRAB_{DA} expression and fiber placement across five coronal planes with anterior distance from bregma (millimeters) in the dBNST in STs (orange) and GT/INTs (blue). Drawings were adapted from Figures 31, 32, 33, 34, and 35 from Paxinos and Watson, 2006. **(D)** Average Pavlovian conditioned approach (PCA) scores for STs and GT/INTs on Day 1 and Day 5 of PLA. **(E)** Average Δ Presses (CS+ – (CS–)) on Day 1 and Day 5. **(F)** Average Δ Pokes (CS+ – (CS–)) on Day 1 and Day 5. Data are mean ± SEM. *p<0.05.

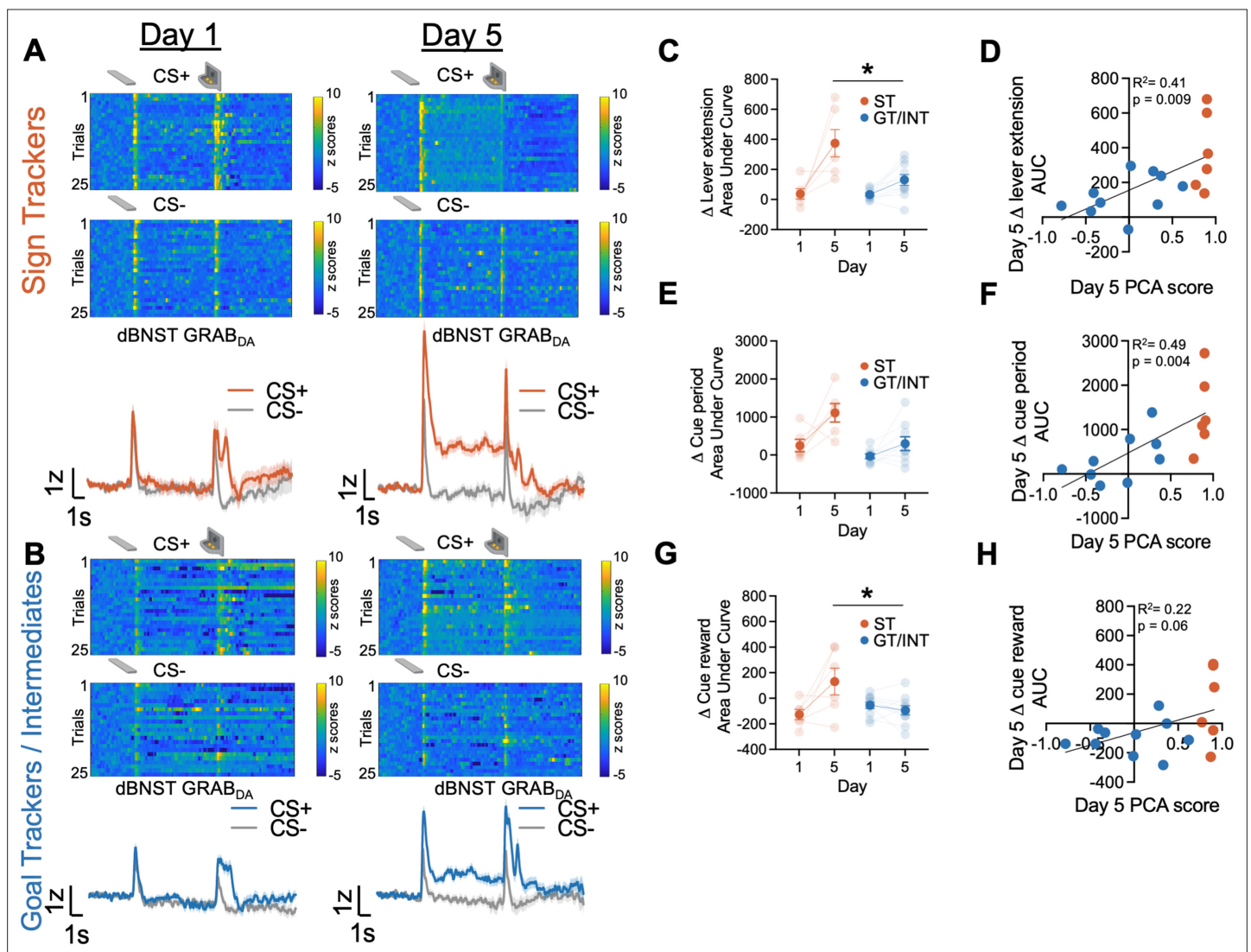


Figure 2. Dorsal bed nucleus of stria terminalis (dBNST) GRAB_{DA} signals during Pavlovian lever autoshaping (PLA) between sign-trackers (STs) and goal-trackers/intermediates (GT/INTs). Representative heat maps illustrating GRAB_{DA} signal changes (z-scores) during CS+ and CS– presentations on Day 1 (top left) and Day 5 (top right) and trial-averaged GRAB_{DA} signal change (z-scored $\Delta F/F$) during CS+ and CS– presentations on Day 1 (bottom left) and Day 5 (bottom right) in (A) STs and (B) GT/INTs. (C) Trial averaged quantification Δ lever extension ((CS+) – (CS–); 2 s) GRAB_{DA} area under curve (AUC) between STs and GT/INTs. (D) Correlation between Day 5 Pavlovian conditioned approach (PCA) scores and Day 5 Δ lever extension AUC. (E) Trial averaged quantification of Δ cue period ((CS+) – (CS–); 10 s) in AUC during cue period between STs and GT/INTs. (F) Correlation between Day 5 PCA scores and Day 5 Δ cue period AUC. (G) Trial averaged quantification of Δ cue-reward ((CS+) – (US), 2 s) in AUC between STs and GT/INTs. (H) Correlation between Day 5 PCA scores and Day 5 change in Δ cue-reward AUC. Data are mean \pm SEM. * $p < 0.05$.

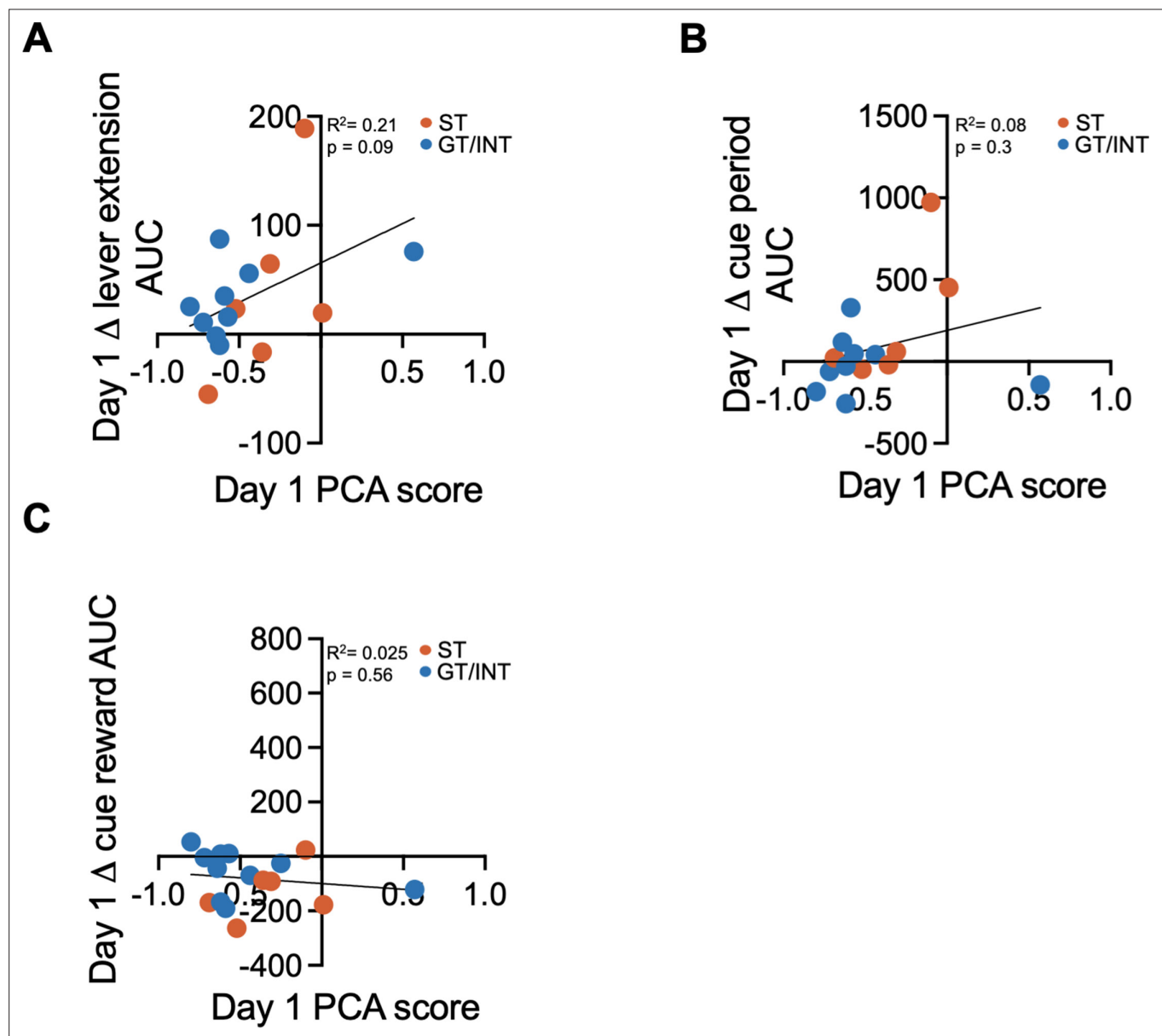


Figure 2—figure supplement 1. No correlation between Day 1 Pavlovian conditioned approach (PCA) scores and Day 1 bed nucleus of the stria terminalis (BNST) GRAB_{DA} signals. Correlation between (A) Day 1 PCA scores and Day 1 Δ lever extension area under curve (AUC). (B) Day 1 PCA scores and Day 1 Δ cue period AUC and (C) Day 1 PCA scores and Day 1 Δ cue-reward AUC.

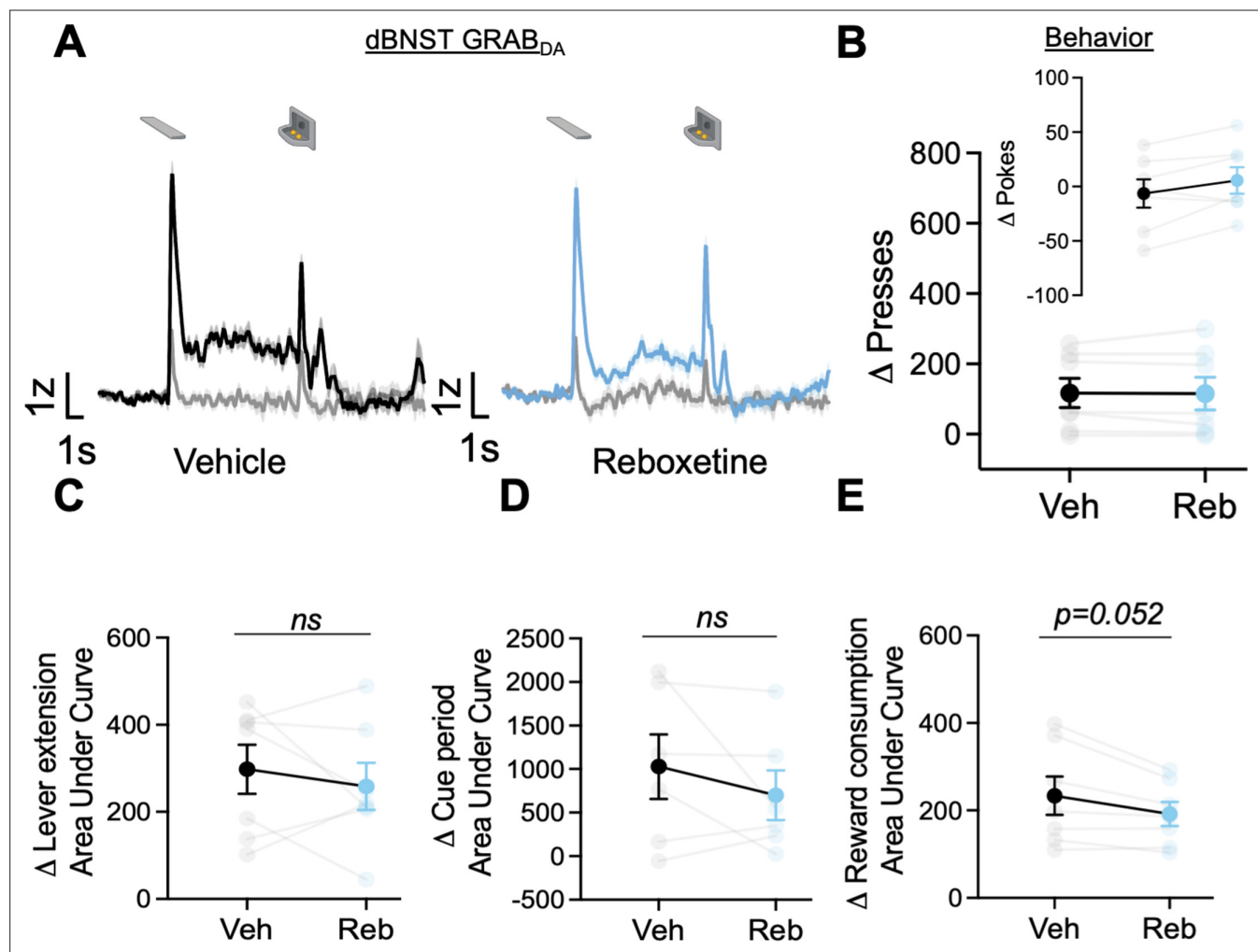


Figure 2—figure supplement 2. Norepinephrine reuptake blocker, Reboxetine doesn't alter Pavlovian lever autoshaping (PLA) behavior or GRAB_{DA} signals. **(A)** Trial-averaged GRAB_{DA} signal change (z-scored $\Delta F/F$) and **(B)** Average Δ Presses (CS+) – (CS–) and average Δ pokes (CS+) – (CS–) (inset) when rats were injected with vehicle or Reboxetine during PLA. Trial average quantification of change (CS+) – (CS–) in area under GRAB_{DA} z-scored curve (AUC) during **(C)** lever extension (2 s), **(D)** cue period (10 s), and **(E)** reward consumption between vehicle and reboxetine conditions. Data are mean \pm SEM. Veh = Vehicle, Reb = Reboxetine.

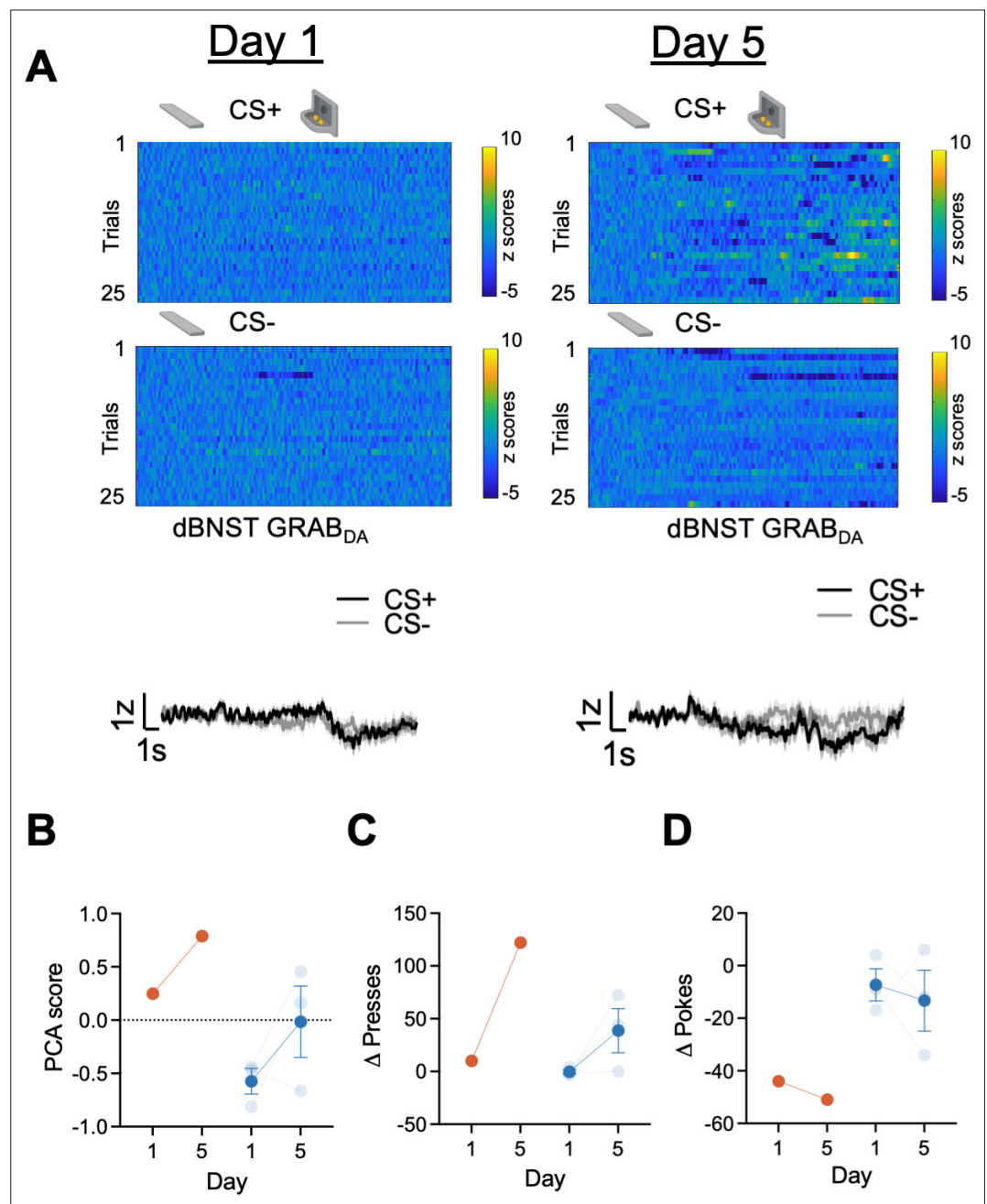


Figure 2—figure supplement 3. Representative and population graph of signals along with behavior from rats that had correct fiber placement and viral expression but under 2z peak. **(A)** Representative heat maps illustrating GRAB_{DA} signal changes (z-scores) during CS+ and CS- presentations on Day 1 (top left) and Day 5 (top right) and trial-averaged GRAB_{DA} signal change (z-scored $\Delta F/F$) for $n=4$ rats during CS+ and CS- presentations on Day 1 (bottom left) and Day 5 (bottom right). **(B)** Average Pavlovian conditioned approach (PCA) scores for sign-trackers (STs) and goal-tracking/intermediates (GT/INTs) on Day 1 and Day 5 of PLA. **(C)** Average Δ Presses (CS+) – (CS-) on Day 1 and Day 5. **(D)** Average Δ Pokes (CS+) – (CS-) on Day 1 and Day 5.

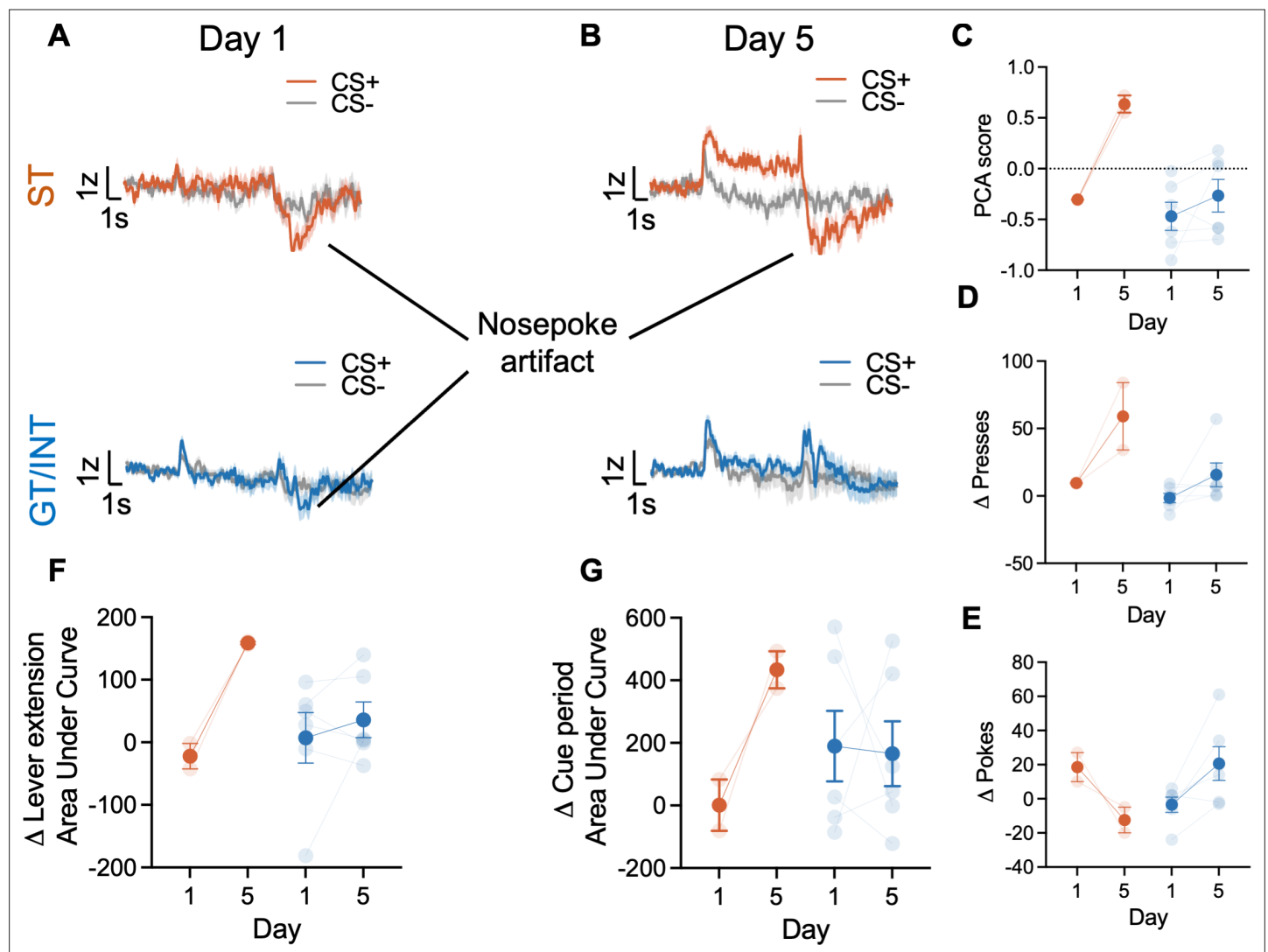
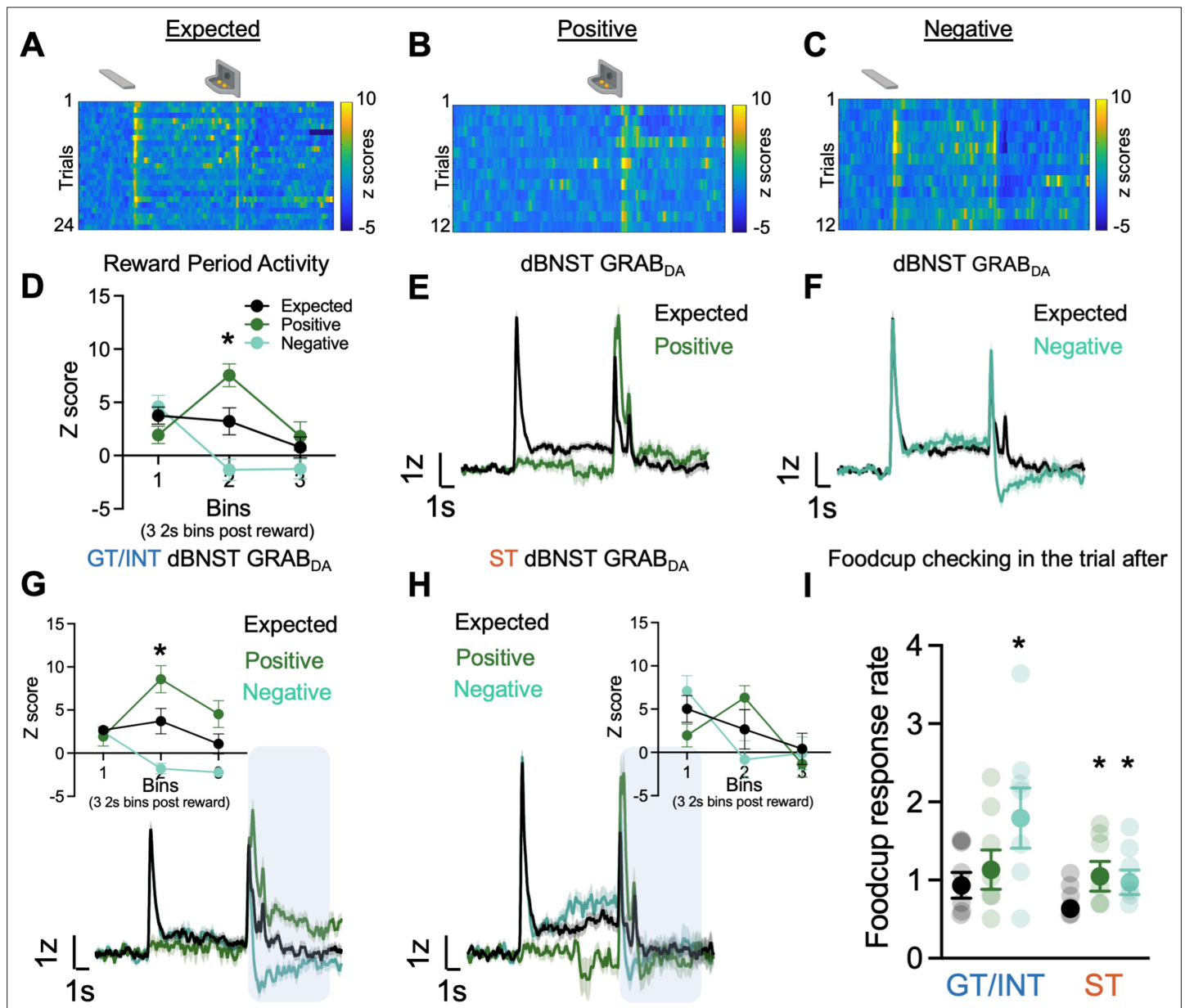


Figure 2—figure supplement 4. Dopamine signals and behavior from rats that were removed from the study due to food cup entry artifact. Trial-averaged GRAB_{DDA} signal change (z-scored $\Delta F/F$) for sign-tracking (ST) (top) and goal-tracking/intermediate (GT/INT) rats (bottom) during CS+ and CS- presentations on (A) Day 1 and (B) Day 5 depicting the food cup entry nose poke artifact during pellet retrieval. (C) Average Pavlovian conditioned approach (PCA) scores for STs and GT/INTs on Day 1 and Day 5 of PLA. (D) Average Δ Presses (CS+) – (CS-) on Day 1 and Day 5. (E) Average Δ Pokes (CS+) – (CS-) on Day 1 and Day 5. (F) Trial averaged quantification Δ lever extension ((CS+) – (CS-); 2 s) GRAB_{DDA} area under curve (AUC) between STs and GT/INTs. (G) Trial averaged quantification of Δ cue period ((CS+) – (CS-); 10 s) in AUC during cue period between STs and GT/INTs.



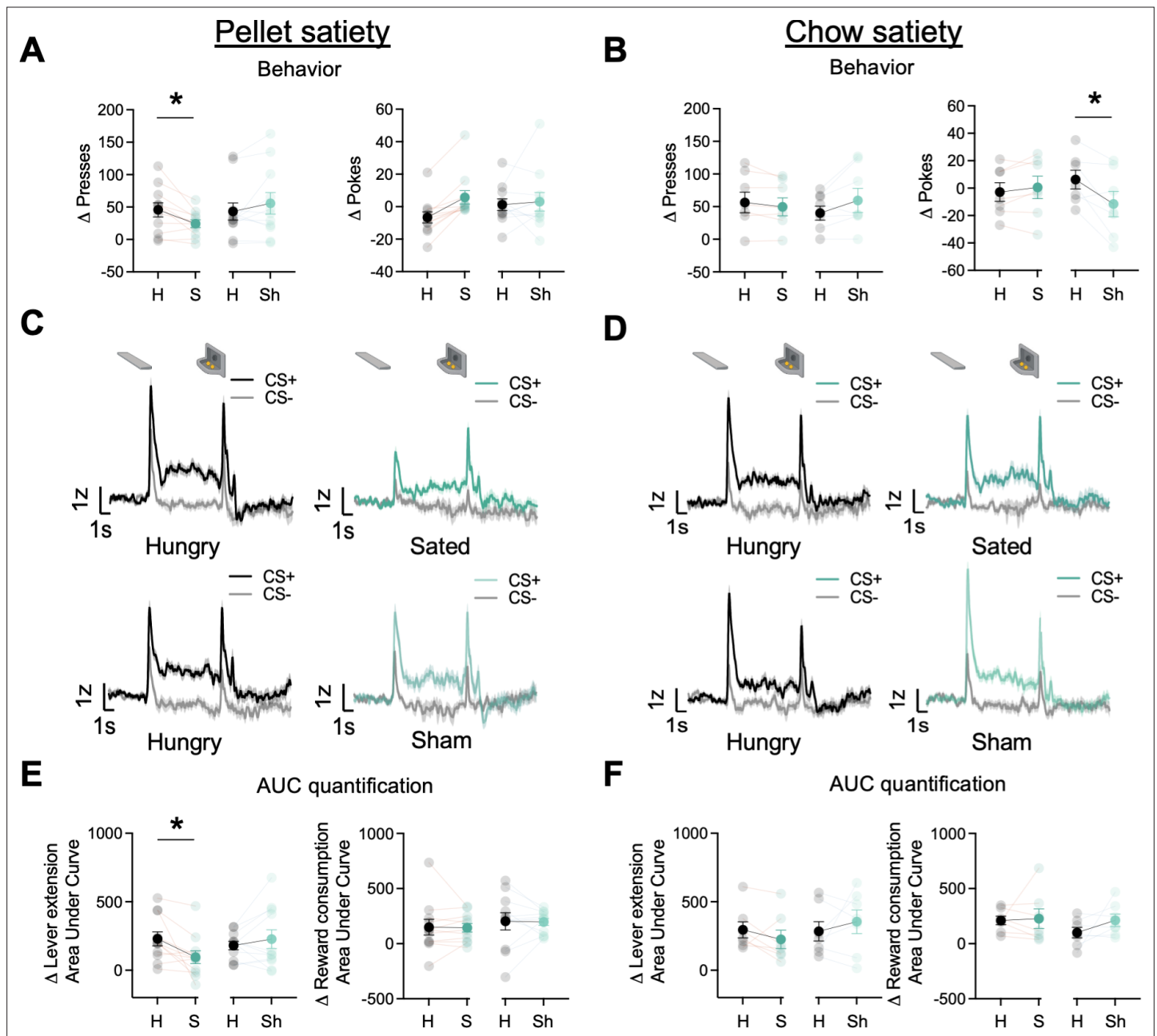


Figure 4. Dorsal bed nucleus of the stria terminalis (dBNST) GRAB_{DA} signals attenuate after reinforcer-specific but not general satiety. **(A)** Average Δ Presses (CS+) – (CS–) (left) and average Δ pokes (CS+) – (CS–) (right) when rats were either sated on training food pellets in the ramekin or sham-sated (ramekin only). **(B)** Average Δ Presses (CS+) – (CS–) (left) and average Δ pokes (CS+) – (CS–) (right) when rats were either sated or sham-sated on homecage chow. **(C)** Trial-averaged GRAB_{DA} signal change (z-scored $\Delta F/F$) during CS+ and CS– presentations when rats were hungry versus sated (top) and when rats were hungry versus sham-sated (bottom) on food pellets and **(D)** on homecage chow. **(E)** Trial average quantification of change (CS+) – (CS–) in an area under GRAB_{DA} z-scored curve (AUC) during lever extension (2 s) (left) and reward consumption (right) between food pellet sated and sham and **(F)** between homecage chow sated and sham conditions. Data are mean \pm SEM, * $p < 0.05$. H=Hungry, S=Sated, Sh = Sham conditions.

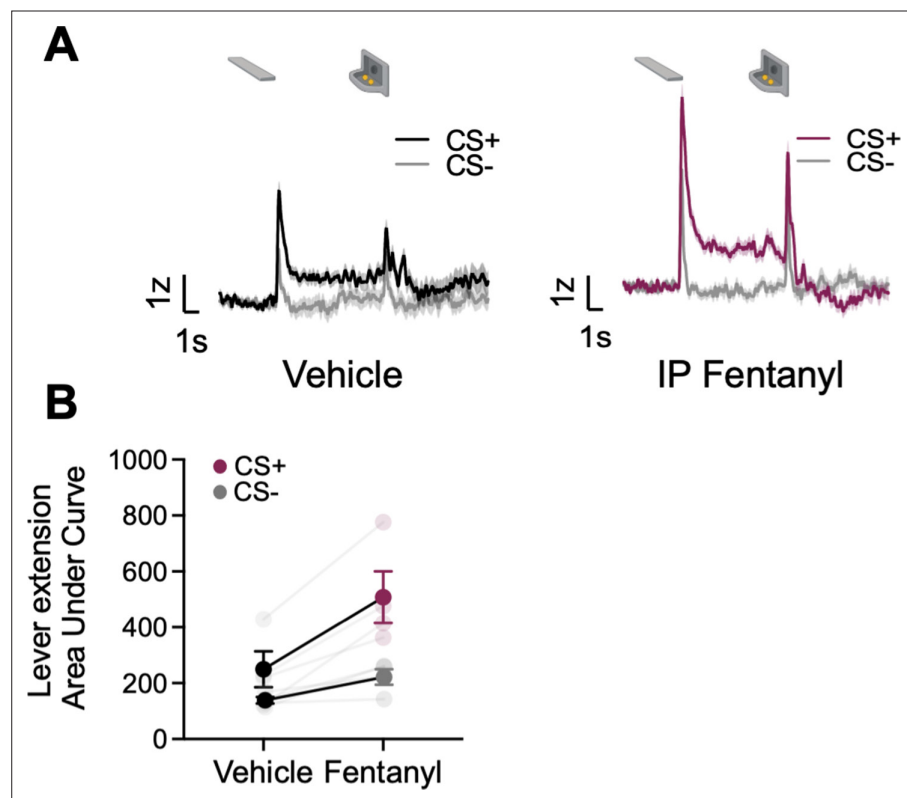


Figure 5. Systemic administration of fentanyl results in the potentiation of dorsal bed nucleus of the stria terminalis (dBNST) dopamine. **(A)** Trial-averaged GRAB_{DA} signal change (z-scored $\Delta F/F$) when rats were injected with vehicle (left) or fentanyl (right) during Pavlovian lever autoshaping (PLA) **(B)** Trial average quantification of the area under GRAB_{DA} z-scored curve (AUC) during CS+ and CS- lever extension (2 s) between vehicle and fentanyl conditions. Data are mean \pm SEM, * $p < 0.05$.