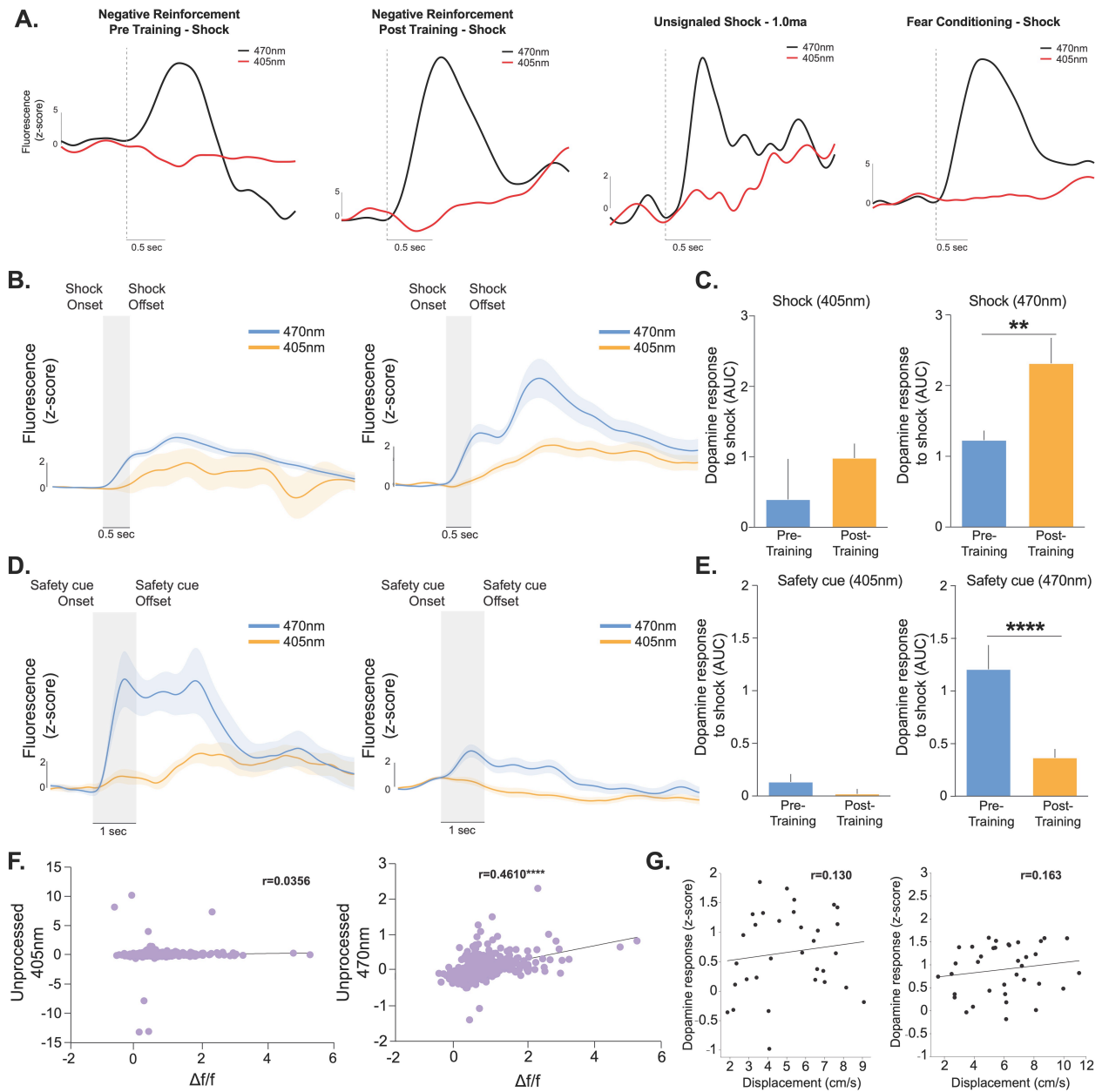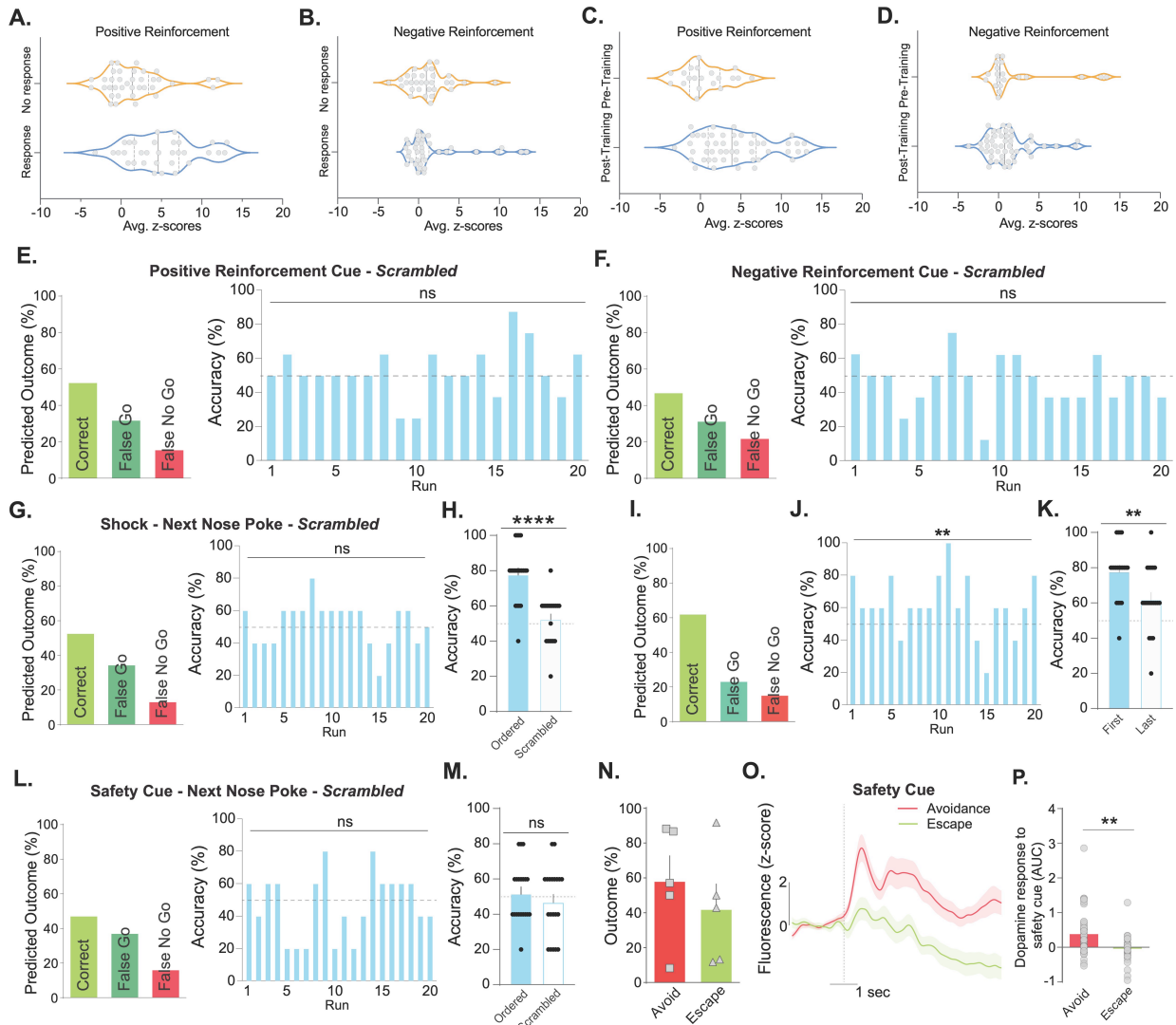**Figure S1. Recording dopamine in the nucleus accumbens (NAc) core during positive and negative reinforcement tasks. Related to Figure1. (A)** dLight1.1 was used to record dopamine transients in the NAc core of awake and behaving animals. Representative image showing the spread of dLight1.1 and placement of the fiber optic implant in an individual animal (Green: dLight; Blue: DAPI). **(B)** Schematic showing fiber optic placements in dLight1.1 (grey) experimental animals. **(C)** Representative traces for 470nm excitation (dLight) and 405nm excitation (isosbestic control) channels in an individual animal at baseline. **(D)** Representative Δf/f trace showing dopamine transients in the nucleus accumbens core. **(E)** Mice nose poked for sucrose delivery and emitted more responses on the active poke (which resulted in sucrose delivery) than the inactive poke (RM ANOVA, Trial x Nose-Poke; $F_{19,114} = 7.81$, $p<0.0001$). **(F)** Performance when the discriminative stimulus ($S^{d, sucrose}$) was presented for 30 or 10 seconds (RM ANOVA, $F_{2.369,10.42}=3.19$, $p=0.07$). **(G)** Simulations of the Rescorla-Wagner (RW) model showing the associative strength of the unconditioned stimulus (V(US)) increases from pre- to post-training and the prediction error between cue and outcome (Δ) simultaneously goes down. **(H)** At the end of the training session associative strength is increased, and prediction error is decreased compared to initial values. **(I)** Mice nose poked during a discriminative cue ($S^{d,shock}$) to avoid or terminate a series of footshocks; mice responded more on the active poke as compared to the inactive (RM ANOVA, Trial x Nose-Poke; $F_{19,114} = 7.81$, $p<0.0001$). **(I)** Task accuracy increased over sessions (RM ANOVA, $F_{1.280,4.054}=8.11$, $p=0.04$). **(K)** Averaged dopamine responses in individual animals (%Baseline AUC) across all positive reinforcement trials to $S^{d,sucrose}$ were increased in post-training sessions as compared to pre-training sessions in the same animals

(independent t-test, t_5=2.31, p=0.03). Dopamine responses following head entries were reduced between pre- and post-training sessions (independent t-test, t_4=2.97, p=0.021). **(L)** Averaged dopamine responses in individual animals (%Baseline AUC) across all negative reinforcement trials. Dopamine responses to $S^{d,shock}$, footshocks, and safety cues during pre- and post-training for negative reinforcement. Dopamine response to shock increased (independent t-test, t_4=2.44, p=0.03) whereas the safety cue dopamine response decreased (independent t-test, t_4=4.18, p=0.007) and dopamine response to the $S^{d,shock}$ did not change (independent t-test, t_4=0.63 p=0.23) during post-training compared to pre-training. Data represented as mean ± S.E.M. * p < 0.05, ** p < 0.01, **** p < 0.0001.
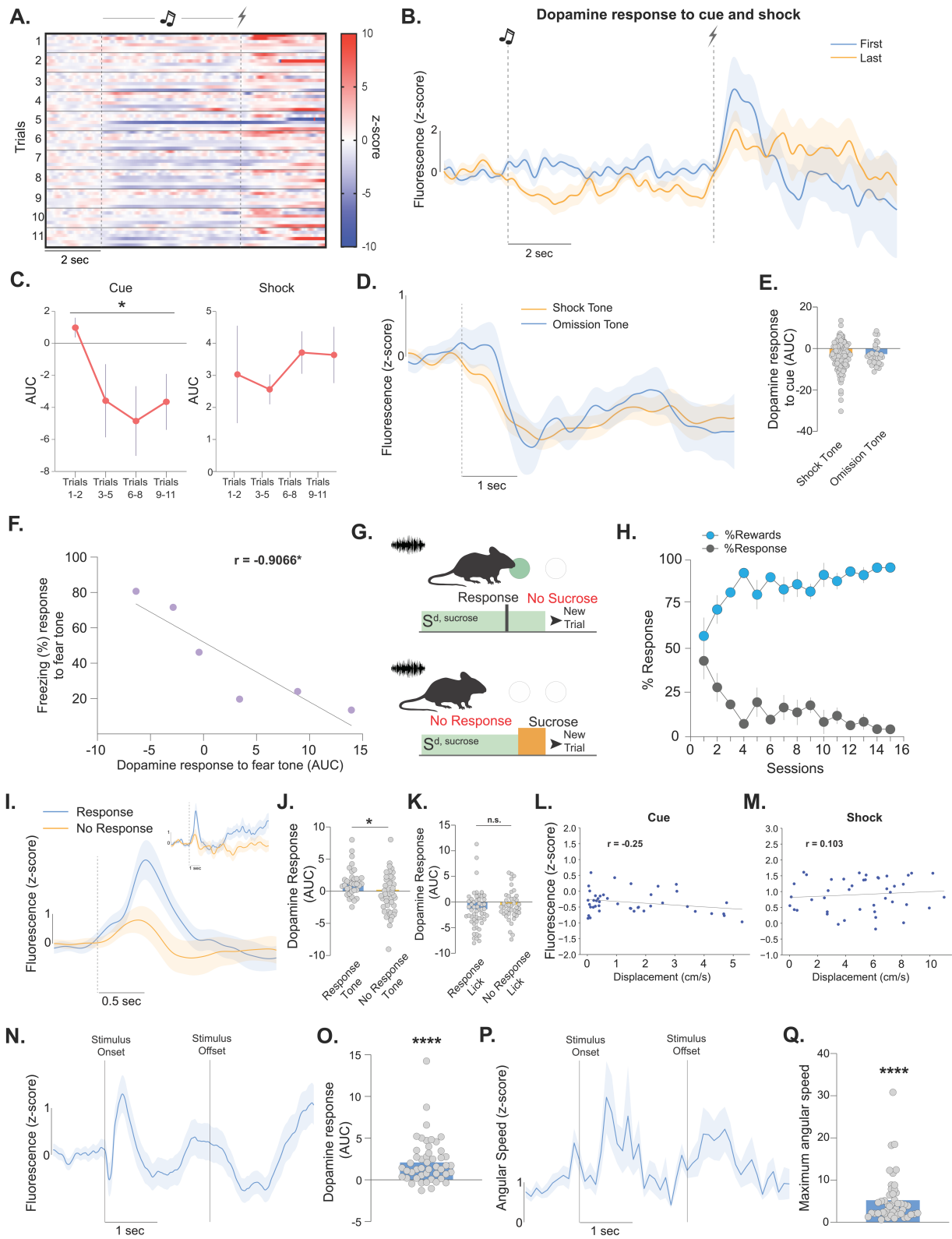
Figure S2. NAc core dopamine responses to footshocks and safety cues are not influenced by movement. Related to Figure1. (A) Representative 470nm (dopamine) and 405nm (control) fluorescent responses to footshocks during negative reinforcement (pre- and post-training), unsignaled shocks, and shocks during fear conditioning. **(B)** Averaged 470nm and 405nm fluorescent responses to footshocks during negative reinforcement (pre- and post-training). **(C)** The 405nm signal did not change (t-test, $t_{531}=0.44$, $p=0.66$); the 470nm signal increased from pre- to post-training during negative reinforcement (t-test, $t_{531}=3.09$, $p=0.002$). **(D)** Averaged 470nm and control 405nm responses to safety cues during negative reinforcement (pre- and post-training). **(E)** The 405nm signal did not change (t-test, $t_{92}=1.16$ $p=0.25$); the 470nm signal to the safety cue decreased (t-test, $t_{94}=4.27$, $p<0.0001$). **(F)** The raw 405nm channel did not correlate with the processed Δf/f responses ($r=0.037$, $p=0.45$). The raw 470nm signal was positively correlated with the processed Δf/f responses ($r=0.46$, $p<0.0001$). **(G)** Pose estimation

analysis was used to assess the amount of displacement following a footshock operationalized as the length of the movement (cm) within the 2 seconds following each footshock. NAc core dopamine responses during negative reinforcement (r=0.13, p=0.48) and fear conditioning (r=0.16, p=0.34) do not correlate with movement following footshock presentations. Data represented as mean ± S.E.M. ** $p < 0.01$, **** $p < 0.0001$.

Figure S3. Dopamine responses to task parameters can predict future behavior, but do not correspond to an error-based updating mechanism. Related to Figure 2. **(A-D)** Histograms showing dopamine response distributions for positive and negative reinforcement for machine learning. **(A)** Dopamine responses (averaged z-scores) during "response" and "no response" positive reinforcement trials, **(B)** "response" and "no response" negative reinforcement trials, **(C)** "pre-training" and "post-training" positive reinforcement trials, and **(D)** during "pre-training" and "post-training" negative reinforcement trials. **(E-J)** Machine learning results were verified by scrambling the behavioral outcome. The SVM algorithm could not predict the behavioral outcome above chance based on dopamine response to the **(E)** $S^{d,\ sucrose}$, **(F)** $S^{d,\ shock}$, or **(G)** the shock itself when the outcome was scrambled. **(H)** The accuracy of the SVM algorithm in predicting behavioral responses based on dopamine responses to the shock was significantly higher when the data were ordered correctly (unpaired t-test, $t_{38}=5.53$, $p<0.0001$). **(I-J)** In negative reinforcement trials where multiple shocks occurred, we determined the ability of dopamine responses to the last footshock in the series to predict future trial behavior. The SVM algorithm was able to predict behavior in the subsequent trial based on the dopamine response to the last footshock (one sample t-test, $t_{19}=2.94$,
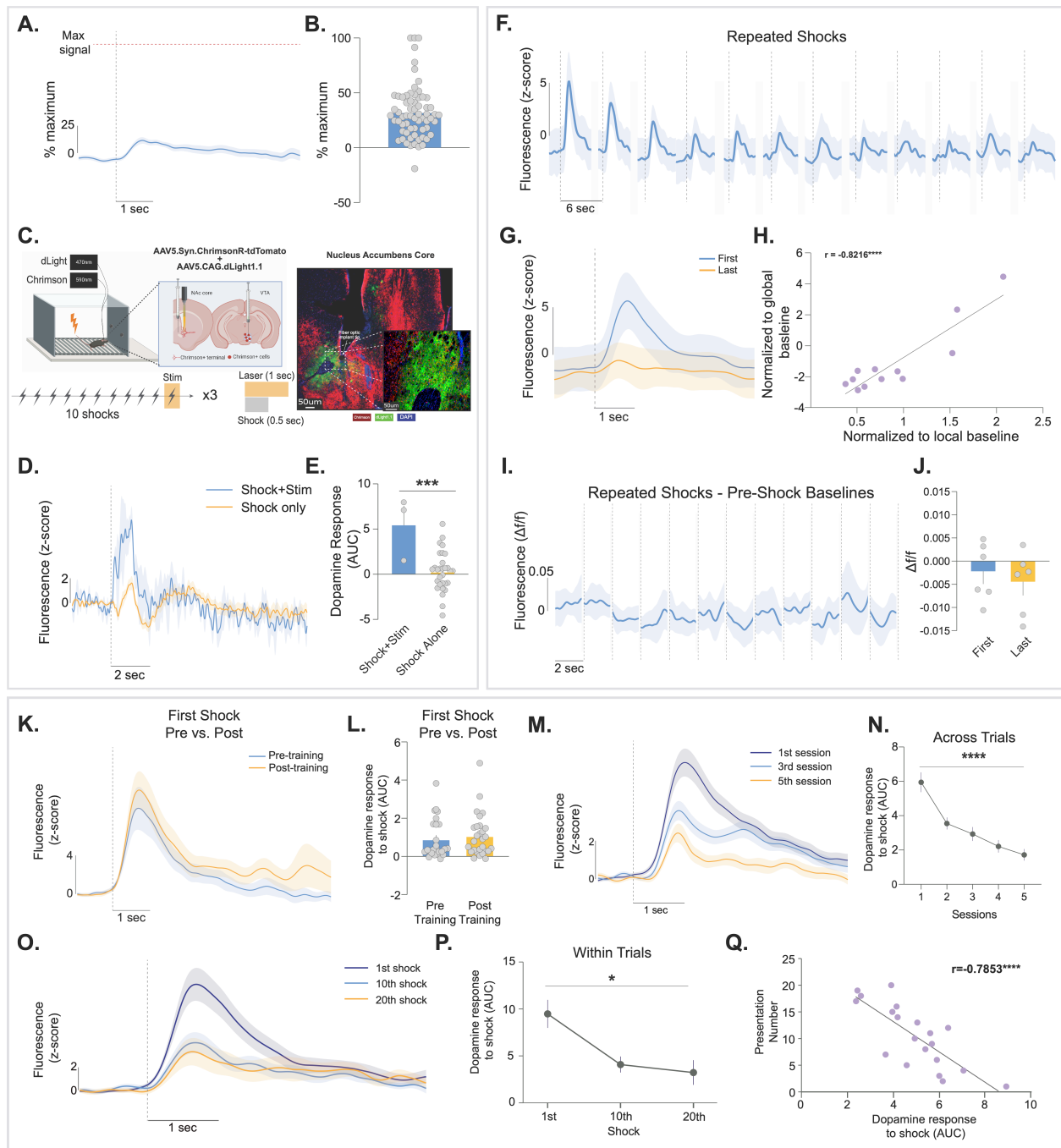
p=0.008). **(K)** The SVM algorithm more accurately predicted next trial behavior using the first footshock (unpaired t-test, t_{38}=2.97, *p*=0.005). **(L-M)** The machine learning algorithm could not predict the behavioral outcome based on dopamine response to the safety cue above chance when behavioral outcomes were scrambled or when they were ordered (unpaired t-test, t_{38}=0.87, *p*=0.39). **(N)** Mice avoided (responded during the discriminative cue to avoid all shocks) about the same percentage of trials as they escaped (responded following the first footshock in the series; unpaired t-test, t_8=0.78, *p*=0.47). **(O-P)** Dopamine response to the safety cue was larger after an avoided trial as compared to an escape trial (unpaired t-test, t_{72}=3.36, *p*=0.0012). Data represented as mean ± S.E.M. ** *p* < 0.01, **** p < 0.0001. ns, not significant.

Figure S4. Dopamine responses to cues are not associated with cue valence. Related to Figure4. (A) Heatmap showing dopamine responses to the cue and
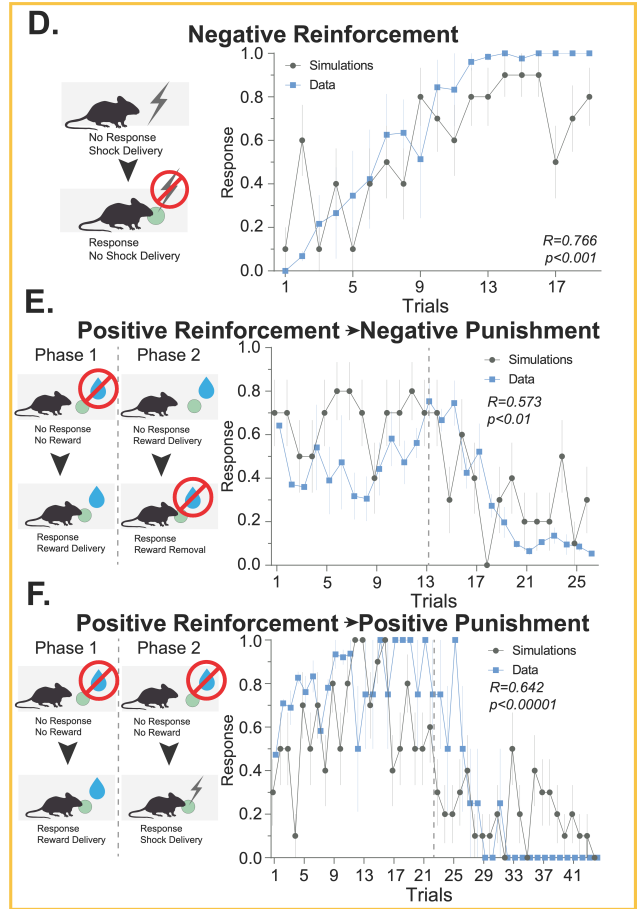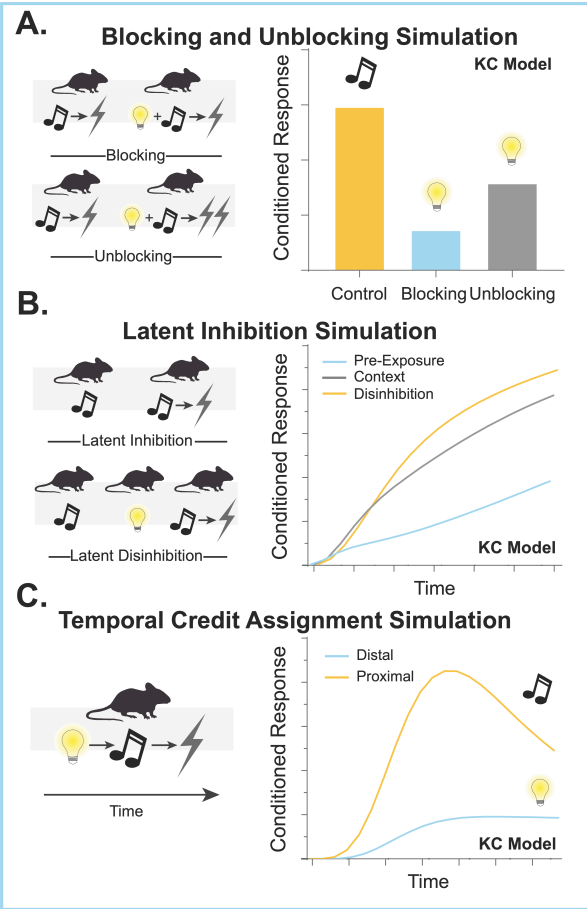
footshock over fear conditioning acquisition. Each trial depicts z-scores from each of the 6 animals. **(B)** Averaged z-scores to the tone and footshocks during the first versus last two trials. **(C)** Cue-evoked dopamine responses progressively decreased over trials (RM ANOVA, $F_{2.052,10.26}=5.56$, $p=0.023$; n=6) whereas dopamine responses to the shock were positive, but unchanged (RM ANOVA, $F_{1.360,6.801}=0.27$, $p=0.69$). **(D)** Average dopamine response to cues predicting shock in fear conditioning experiments when shock is presented or omitted. **(E)** Dopamine response to cues followed by shock or omitted shock did not differ (unpaired t-test, $t_{158}=0.52$, $p=0.60$). **(F)** Freezing responses and dopamine responses to fear conditioning cues are negatively correlated (r=-0.91, $p=0.012$). Each data point represents the averaged dopamine response across the session and freezing response data from an individual animal during the first fear conditioning acquisition session. **(G)** To understand how dopamine changed depending on the task type, we designed a task where mice had to wait following the presentation of a discriminative cue for the delivery of sucrose. First, animals received positive reinforcement training in which a nose poke during an auditory discriminative cue (white noise) resulted in delivery of a sucrose reinforcer. In the second training phase, the animals only received sucrose when they withheld responding during the discriminative cue period. The reward was omitted if they made a response. **(H)** Behavioral performance during the inhibition phase showing that animals quickly learn to inhibit responding to obtain sucrose. **(I-J)** Dopamine response to the discriminative cue decreased below zero during this punishment phase compared to positive reinforcement, even though both trial types resulted in the delivery of sucrose associated with the same white noise cue (unpaired t-test, $t_{78}=2.16$, $p=0.034$; n=3). The inlet in Panel I shows the longer period of the dopamine trace (12 seconds). **(K)** Dopamine response to the sucrose licks between the two trial types did not differ (unpaired t-test, $t_{97}=1.29$, $p=0.197$). **(L)** Pose estimation analysis was used to assess the amount of displacement operationalized as the length of the movement (cm) within 2 seconds following each stimulus presentation (cue or footshock) in fear conditioning. Dopamine response to the fear conditioning cue does not correlate with movement following cue presentations (R=-0.25, $p=0.092$; n=4). **(M)** Dopamine response to footshocks does not correlate with movement in response to shock presentations (R=-0.10, $p=0.51$; n=4). **(N-O)** Presentation of an unexpected neutral cue (house light) results in a positive dopamine response (one sample t-test, $t_{47}=5.66$, $p<0.0001$). **(P-Q)** At the time of the neutral cue presentation animals show an orienting response computed as the speed of the angular change of the head in response to each cue presentation (one sample t-test, $t_{46}=6.69$, $p<0.0001$; n=4). Data represented as mean ± S.E.M. *$p < 0.05$, ****$p < 0.0001$.

Figure S5. Dopamine responses to shocks are not dictated by dopamine detection limits and change similarly across all task types. Related to Figure5. (A) Dopamine response to footshocks scaled based on the maximum recorded dopamine response in each animal (n=3). Footshock responses were below the maximum dopamine peak in each animal. **(B)** Distribution of dopamine responses to footshocks. Only 4.5% of footshocks (3 footshocks) evoked the maximum observed dopamine response in an animal. **(C)** The red-shifted opsin, Chrimson, was expressed in the VTA, while dLight1.1 was expressed and a fiberoptic was implanted in the NAc core. This approach allowed for simultaneous dopamine terminal excitation and dopamine recordings in the same animal. Mice received 10 repeated footshocks and received an optogenetic stimulation of

dopamine terminals on the 11th footshock. This was repeated 3 times. **(D-E)** Optogenetic dopamine terminal stimulation during footshocks elicited more dopamine than the footshock alone condition (unpaired t-test, t_{31}=3.76, p=0.0007). **(F)** Dopamine response to repeated footshocks when normalized to the first 20 seconds of individual recordings (global baseline). **(G)** Dopamine response to first and last footshocks. **(H)** Dopamine response to footshocks normalized to global baseline and local baseline show a strong positive correlation (r=0.91, p<0.0001). **(I)** Baseline dopamine levels before each footshock over the entire session showing that the baseline does not change. **(J)** Local baseline for the first and last footshock did not differ (paired t-test, t_5=0.70, p=0.51). **(K-L)** Averaged dopamine response to the first shock of each pre- vs. post-training session during negative reinforcement. The dopamine response to the first shock did not differ (unpaired t-test, t_{51}=0.59, p=0.56). **(M-N)** Dopamine responses to footshocks decreased across negative reinforcement pre-training trials (RM ANOVA, main effect of trial; $F_{3.295,285.9}$=9.60, p<0.0001) showing similar shock responses across tasks. **(O)** Dopamine responses to footshocks in the first negative reinforcement training session. **(P)** Dopamine responses to footshocks decrease within a single trial (RM ANOVA, Trial x Nose-Poke; $F_{1.533,32.96}$=4.96, p=0.020). **(Q)** Negative reinforcement trial number and dopamine response to footshocks are negatively correlated (r=-0.79, p<0.0001). Data represented as mean ± S.E.M. *p < 0.05, ***p < 0.001, **** p < 0.0001.

A. Blocking and Unblocking Simulation
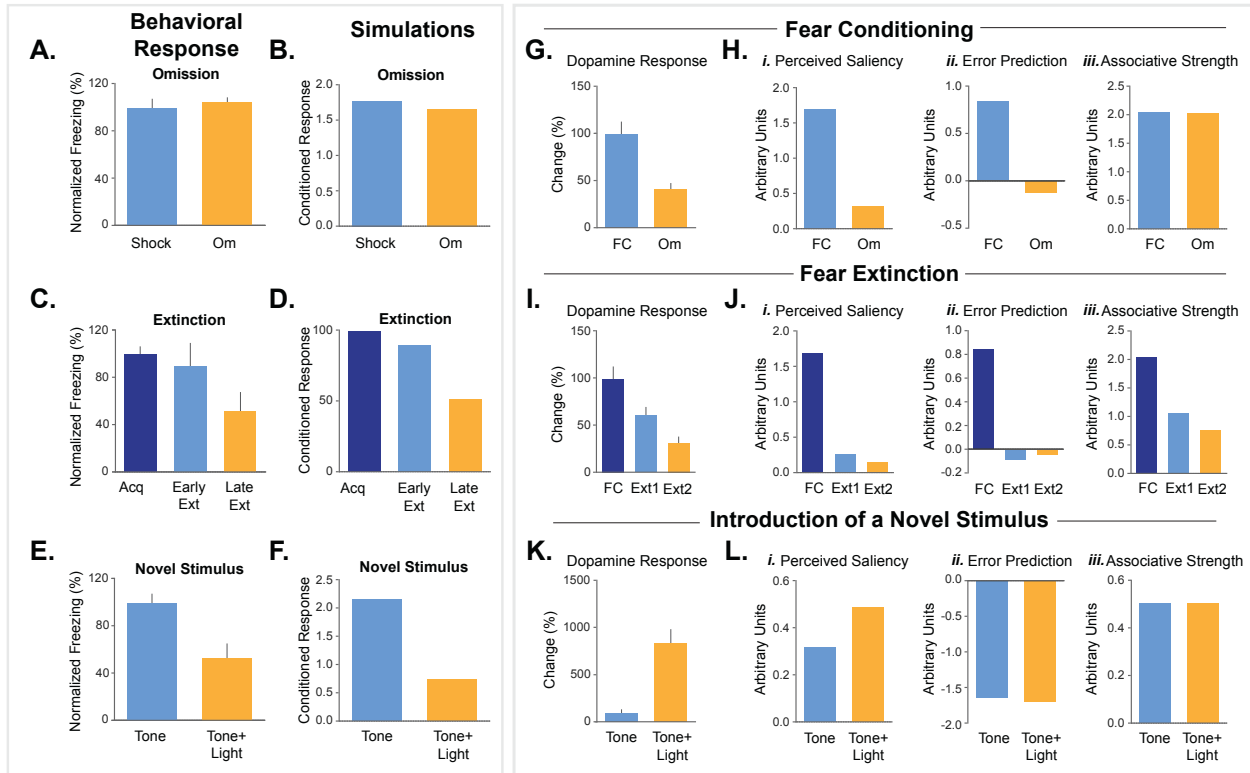
KC Model

Conditioned Response

Control | Blocking | Unblocking

B. Latent Inhibition Simulation

Latent Inhibition

Latent Disinhibition

Pre-Exposure
Context
Disinhibition

Conditioned Response

Time

KC Model

C. Temporal Credit Assignment Simulation

Time

Distal
Proximal

Conditioned Response

Time

KC Model

D. Negative Reinforcement

No Response
Shock Delivery

Response
No Shock Delivery

Simulations
Data

Response

Trials

R=0.766
p<0.001

E. Positive Reinforcement → Negative Punishment

Phase 1 | Phase 2

No Response
No Reward

No Response
Reward Delivery

Response
Reward Delivery

Response
Reward Removal

Simulations
Data

R=0.573
p<0.01

Response

Trials

F. Positive Reinforcement → Positive Punishment

Phase 1 | Phase 2

No Response
No Reward

No Response
No Reward

Response
Reward Delivery

Response
Shock Delivery

Simulations
Data

R=0.642
p<0.00001

Response

Trials

Accumbal dopamine signals stimulus saliency but not stimulus value

G. Dopamine response to repeated shocks

Perceived
Saliency

Fluorescence (z-score)

6 sec

H. Shock response

%Change

First | Last

*

I. Perceived saliency

Arbitrary Units

r= 0.8838***

First | Last

J. Prediction error

Arbitrary Units

r= 0.2451

First | Last

K. Dopamine response to shock

% Change

0.3mA | 1.0mA | 1.7mA

*

L. Perceived saliency

Arbitrary Units

r= 0.7616**

0.3mA | 1.0mA | 1.7mA

M. Prediction error

Arbitrary Units

r= 0.7490**

0.3mA | 1.0mA | 1.7mA

N.

Fiber optic implant tip
for ChR2

Figure S6. KCS Model behavioral simulations. Related to Figure7. *Simulations of basic properties of Pavlovian conditioning:* **(A)** Blocking and unblocking of a second stimulus. **(B)** Latent inhibition and disinhibition of a pre-exposed conditioned stimulus. **(C)** Temporal credit assignment of a proximal vs. a distal conditioned stimulus. *Simulations of basic properties of operant conditioning:* The KCS model simulations following 10 runs (grey) vs. data from mouse reinforcement learning for each condition (blue). **(D)** Negative reinforcement (R=0.64; *p*<0.0001). **(E)** Positive reinforcement and a contingency switch (which occurs at the dotted line) to negative punishment (i.e. removal of sucrose following nose-poke) (R=0.57; *p*<0.01). **(F)** Positive reinforcement followed by a contingency switch to positive punishment (shock presentation following response; R=0.77; *p*<0.001). Model simulations are presented as arbitrary units of conditioned response for Pavlovian conditioning simulations and percentage of response trials. Animal behavior data presented as the mean percentage correct trials. Next, experiments from figures 3 and 4 were reanalyzed and mapped onto KCS model simulations to show best fit. **(G)** Dopamine responses to repeated footshocks (with constant intensity) decreased, even though the physical intensity of the stimulus did not change (blue). KCS model simulations show perceived saliency decreases with repeated stimulus presentations (grey). **(H)** Dopamine responses to the shock decreased over presentations (paired t-test, t_5=2.60, *p*=0.047). Dopamine response patterns aligned with perceived saliency (**I,** r=0.88, *p*=0.0001)) but not prediction error (**J,** r=0.25, *p*=0.44). **(K)** Dopamine increased with increasing shock intensities (ANOVA, $F_{2,81}$=3.18, *p*=0.047). Simulations show that both perceived saliency (**L,** r=0.76, *p*=0.0039) and prediction error (**M,** r=0.75, *p*=0.005) increased with increasing stimulus intensity. **(N)** Schematic showing NAc core fiber optic placements in ChR2 (red) for experimental animals from **Figure 7**. Data represented as mean ± S.E.M. *p* < 0.05.

Figure S7. Dopamine responses map onto perceived saliency across conditions. Related to Figure7. (A-F) KCS model simulations of behavioral responses presented next to behavioral data from fear conditioning, omission, extinction, and novel stimulus experiments. **(A)** Normalized freezing (%) during shock and omission trials. **(B)** Simulated conditioned responses during the unconditioned stimulus when present and omitted unconditioned stimulus. **(C)** Normalized freezing (%) from fear acquisition and early and late fear extinction. **(D)** Simulated conditioned response during fear conditioning, early, and late extinction. **(E)** Normalized freezing (%) response during tone only and tone+light trials from the novel stimulus session. **(F)** Simulated conditioned response from conditioned stimulus only, as well as conditioned stimulus + novel stimulus trials. **(G-L)** The KCS model simulations of the model component computations showing that accumbal dopamine signals perceived saliency of predicted stimuli. **(G)** Dopamine response to footshocks and expected but omitted shocks [Change(%)]. **(H)** Simulations from the KCS model for (i) Perceived saliency (ii) Prediction Error and (iii) Associative strength at the time of the footshock and predicted but absent footshock. Only Perceived saliency simulations align with the dopamine response. **(I)** Dopamine response to footshocks during fear conditioning and omitted footshocks during Extinction1 and Extinction2 sessions. **(J)** Simulations from the KCS model at the time of the footshock during fear conditioning and omitted footshocks during early and late extinction. Perceived saliency (i) and Associative Strength (iii), but not Prediction error (iii), show a progressively decreasing signal. **(K)** Dopamine response to a fear conditioning cue (Tone) during Tone only and Tone+Unexpected stimulus (Tone+Light) trials. **(L)** Simulations from the KCS model (i) Perceived saliency (ii) Prediction Error and (iii)

Associative strength at the time of the Tone and Tone+Light (novel stimulus) trials. Only the Perceived saliency simulations show an increasing signal during Tone+light trials and track the recorded dopamine signatures. FC, fear conditioning; Om, omission trial; Ext1, first extinction session; Ext2, second extinction session.