

Figure S1. Experimental preparations and histology. Related to Figures 1-6. (A) Image of bilateral voltammetry electrodes implanted in dorsal striatum. Voltammetric headstage is connected to one electrode and reference (beneath cement) on the left. (B) Detailed wiring diagram for bilateral FSCV implants. (C) Histological location of recording electrode in dorsal striatum. INSET shows closeup of electrode location. (D) Bilateral implants for optogenetic stimulation of dopamine terminals in dorsal striatum. (E) Preparation for simultaneous voltammetry and optogenetic experiments. Chronically implanted voltammetric and reference electrodes (red arrow) are located in striatum and ipsilateral cortex, respectively, and are covered by cement. Posterior to this electrode, bilateral fiber optics targeting substantia nigra pars compacta (SNc) are connected to leads. Further posterior, an adapter connected to the recording and reference electrodes is attached to headstage for voltammetric recording. (F) Fiber optic placement above SNc is shown in a DAT Ai35 mouse. (G) Representative eYFP expression and tyrosine hydroxylase (TH) in a DAT-Cre mouse injected with AAV-FLEX-ChR2-eYFP. (H) A DAT-Ai32 mouse which genetically expresses ChR2 in a Cre dependent manner. INSET shows closeup of TH+ neurons in red and eYFP in green. (I) An electrode array implanted in SNc with cannula attached allows insertion of fiber optic for simultaneous optogenetic stimulation and neuronal recording. (J) Similar to (I) but an optic fiber is directly affixed to the electrode array for simultaneous optogenetic stimulation and neuronal recording.

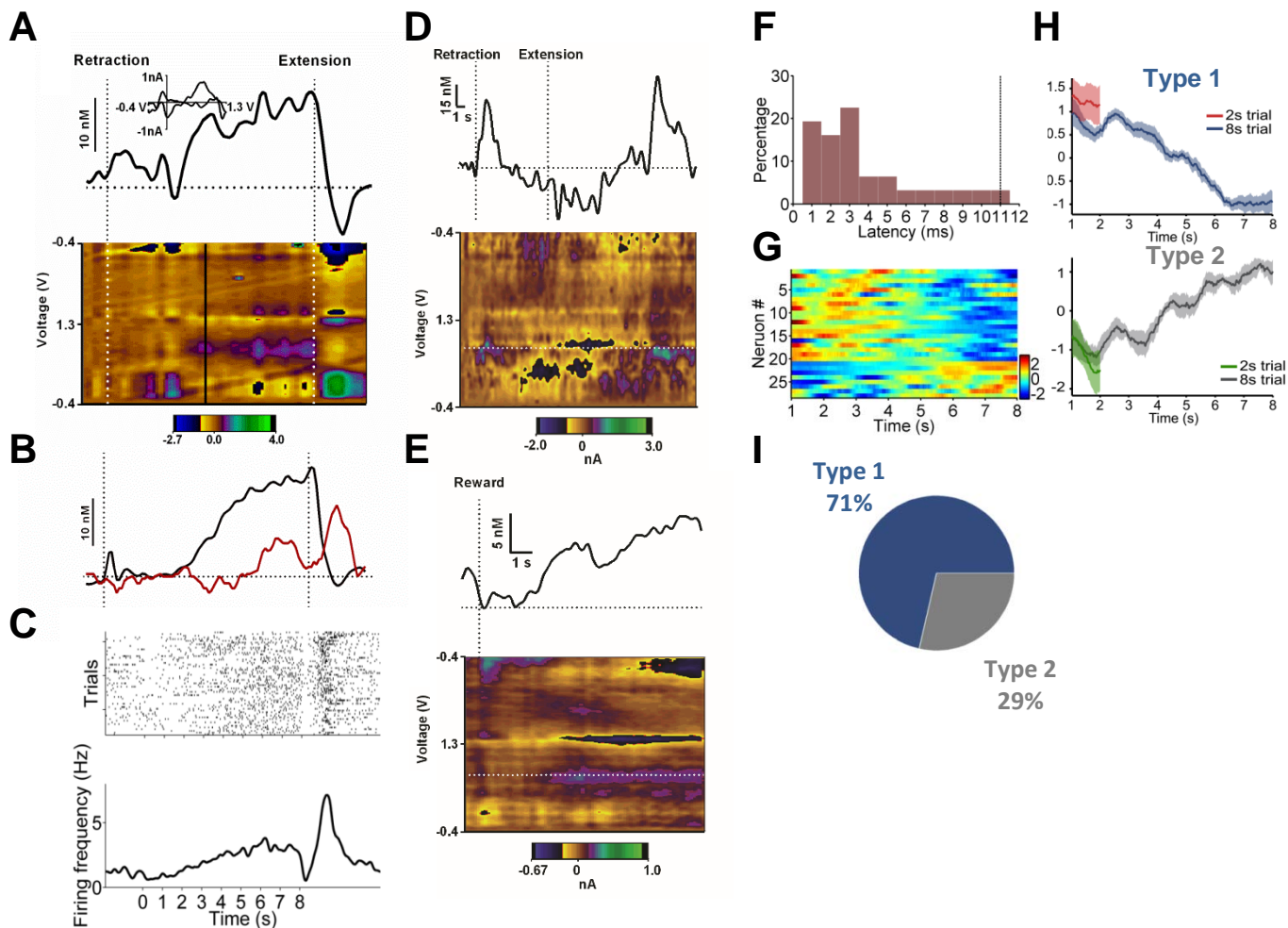


Figure S2. Dopamine profiles and neuron identification with 11 ms criteria. Related to Figures 1, 2, and 4. (A) Representative recording demonstrating ramping of dorsal striatum dopamine levels toward lever extension in a successful 8 s trial in the 2-8s task. Top panel: Thick black line shows change in dopamine concentration over time aligned to lever retraction/extension (vertical dotted lines). Bottom panel: A pseudocolor plot showing change in current recorded at each point in the voltage sweep across time. Baseline is denoted by horizontal dotted line. INSET shows a cyclic voltammogram collected at the vertical line on the pseudocolor plot identifying the current recorded as dopamine. (B) Within the 13 mice recorded, two showed an average dopamine response of ramping toward lever extension (black and red lines). (C) Raster plot (top) and averaged firing rate (bottom) of an optogenetically-identified dopamine neuron demonstrating ramping activity across the 8 s trials. Within the total 23 identified dopamine neurons, five exhibited ramping-like activity. (D) An example trial recorded in a DAT-NR1 KO mouse, showing that this line is capable of reducing dopamine levels below baseline. (E) Example trials recorded in a RGS-NR1 KO mouse, demonstrating that this line is able to elevate dopamine level following rewarded presses. (F) Histogram showing latency of optogenetically-evoked neuronal response. The vertical dash line (11 ms) shows a less stringent criterion considered for data analysis in the following panels. (G) Normalized responses (Z-scores) of 28 putative dopamine neurons. The relative high and low firing rate is coded by red and blue. Decreasing and increasing dynamics are sorted from top to bottom and defined as Type 1 and Type 2, respectively. (H) Averaged Z-score of firing activity in Type 1 (top) and Type 2 (bottom) neurons. (I) Proportion of Type 1 (20/28, 71%) and Type 2 (8/28, 29%) response in putative dopamine neurons.

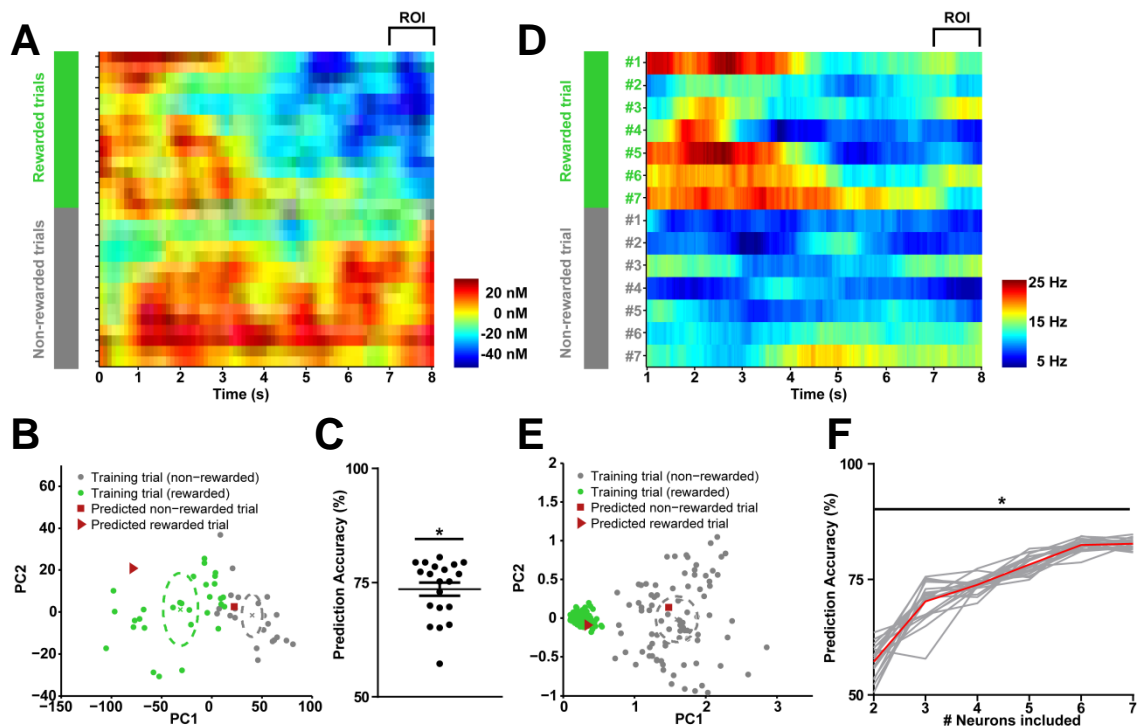


Figure S3. Trial-by-trial analysis of voltammetric and electrophysiological data. Related to Figures 1 and 2. (A) Representative raw fast scan-cyclic voltammetry (FSCV) data included in principal component analysis. 15 rewarded trials (indicated by green bar on left) and unrewarded trials (indicated by gray bar on left) are shown for FSCV data. Principal component analysis focused on the recordings from the final second (7s – 8s) in the lever retraction period, indicated by ROI (region of interest). (B) Principal component analysis of voltammetry data with training set constructed using half of the successful and unsuccessful trials from one experiment selected randomly. Successful and unsuccessful trials are shown in green and grey respectively. x represents midpoint of data sets and dotted line is one standard deviation from midpoint. One trial predicted as either successful or unsuccessful is shown as a red triangle or red square, respectively. (C) Prediction accuracy of 20 iterations of FSCV trial by trial analysis (one-sample t -test of difference from 50%, $t_{19} = 51.49$, $P < 0.0001$, $n = 20$). Each iteration is shown as a dot and lines represent mean \pm SEM. (D) Representative rewarded and unrewarded trials of 7 optogenetically identified dopamine neurons from a single recording session. These neurons are labeled as #1 ~ #7. Raw firing rates in a single rewarded trial and unrewarded trial from neuron #1 ~ #7 are indicated by green and gray bars on the left respectively. Principle component analysis focused on the final second (7s – 8s) in the lever retraction period, indicated by ROI (region of interest). (E) Principal component analysis of optogenetically identified electrophysiology recordings with training set constructed using half of the successful and unsuccessful trials from one experiment selected randomly. Data is shown in the same manner as (B). (F) Prediction accuracy of electrophysiology trial by trial analysis improves as more neurons are added to the analysis (see methods, one-sample t -test of difference from 50%, $P < 0.0001$ for all points, $n = 21$). Mean is shown in red and individual iterations are shown in grey.

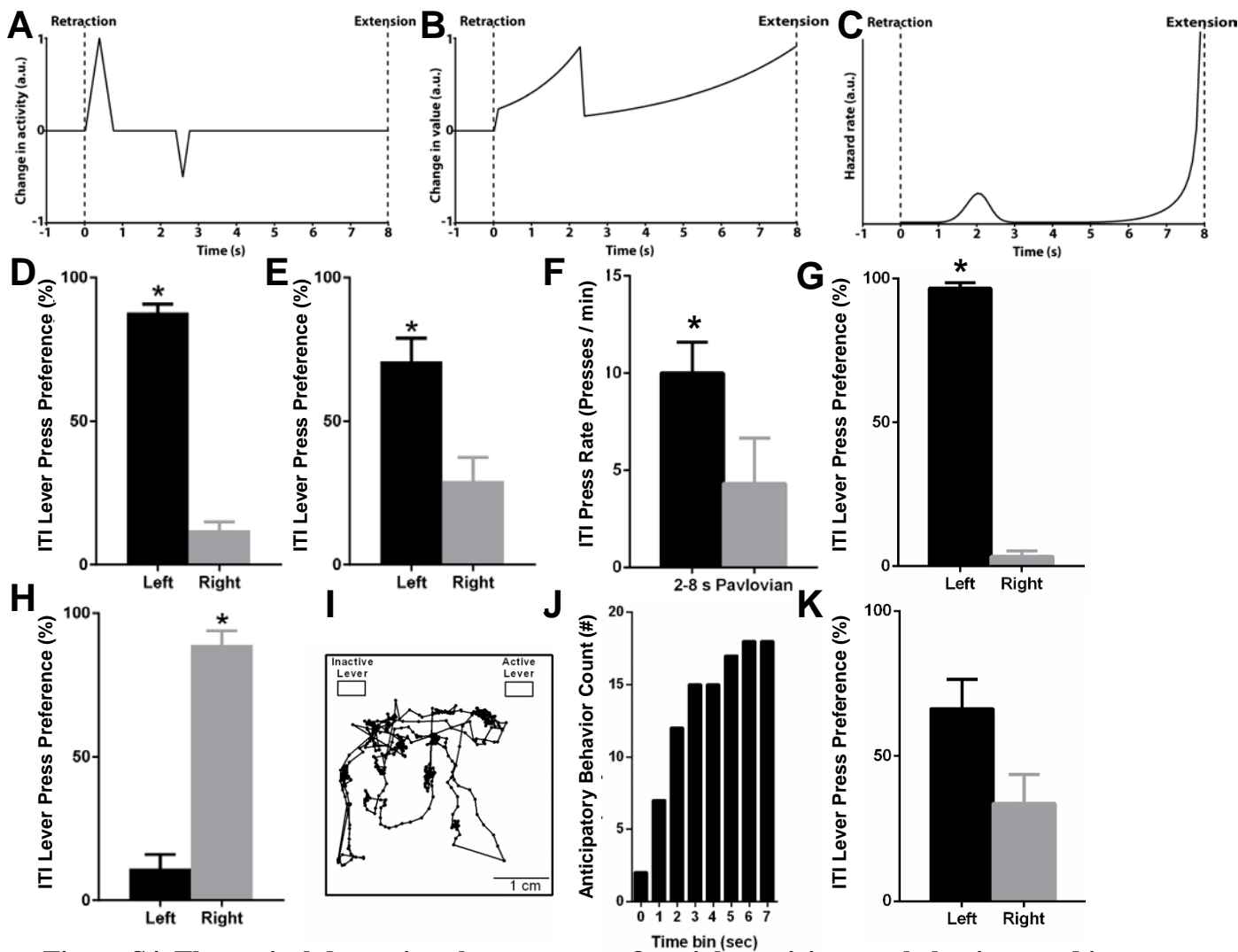


Figure S4. Theoretical dopamine changes across 8 s trials, anticipatory behaviors, and inter-trial interval lever presses during behavioral tasks. Related to Figures 1, 3, and 4. (A) Predicted changes in dopamine activity based on reward prediction error theory (Schultz et al., 1997) across 8 s trials. Dopamine initially increases at lever retraction, then when levers do not extend at 2 s, a phasic decrease occurs. The remainder of the trial is predicted, and no further change in dopamine occurs. (B) Changes in value state (Hamid et al., 2016) across 8 s trials. Lever retraction is associated with a step increase in value, which exponentially continues until 2 s. When levers do not extend, a step decrease occurs followed by exponential increase toward 8 s. (C) Predicted hazard rate (Janssen and Shadlen, 2005) across 8 s trials. (D) Mice trained in the 2-8 s action selection task prefer the lever associated with short trials during the inter-trial interval (ITI, paired t -test, $t_6 = 13.35$, $P < 0.0001$, $n = 7$). (E) Mice trained on the 4-16 s action selection task show a similar preference to mice trained on the 2-8 s task (paired t -test, $t_5 = 2.532$, $P < 0.05$, $n = 6$). (F) Mice engaged in the 2-8 s Pavlovian task make significantly fewer lever presses relative to mice engaged in the 2-8 s task (unpaired t -test, $t_9 = 2.077$, $P < 0.01$, $n = 7$ for 2-8 s task, $n = 4$ for 2-8 s Pavlovian task). (G) Mice engaged in the 2-8 s forced choice task dedicate the majority of responses to the left (rewarded) lever (paired t -test, $t_4 = 24.32$, $P < 0.0001$, $n = 5$). (H) Mice trained in the 8 s only task greatly prefer the rewarded lever (paired t -test, $t_6 = 7.833$, $P < 0.0001$, $n = 7$). (I) During inter-trial intervals in the 8 s only task, mice move throughout the operant chamber. (J) Mice display anticipatory behaviors across the lever retraction period. Approaching and biting or digging at the retracted lever increases across the 8 s retraction period. (K) Mice display no significant preference to either lever during the 2-8 s tone task (paired t -test, $t_3 = 1.630$, $P > 0.05$, $n = 4$). Bar graphs show mean and SEM. * $P < 0.05$.

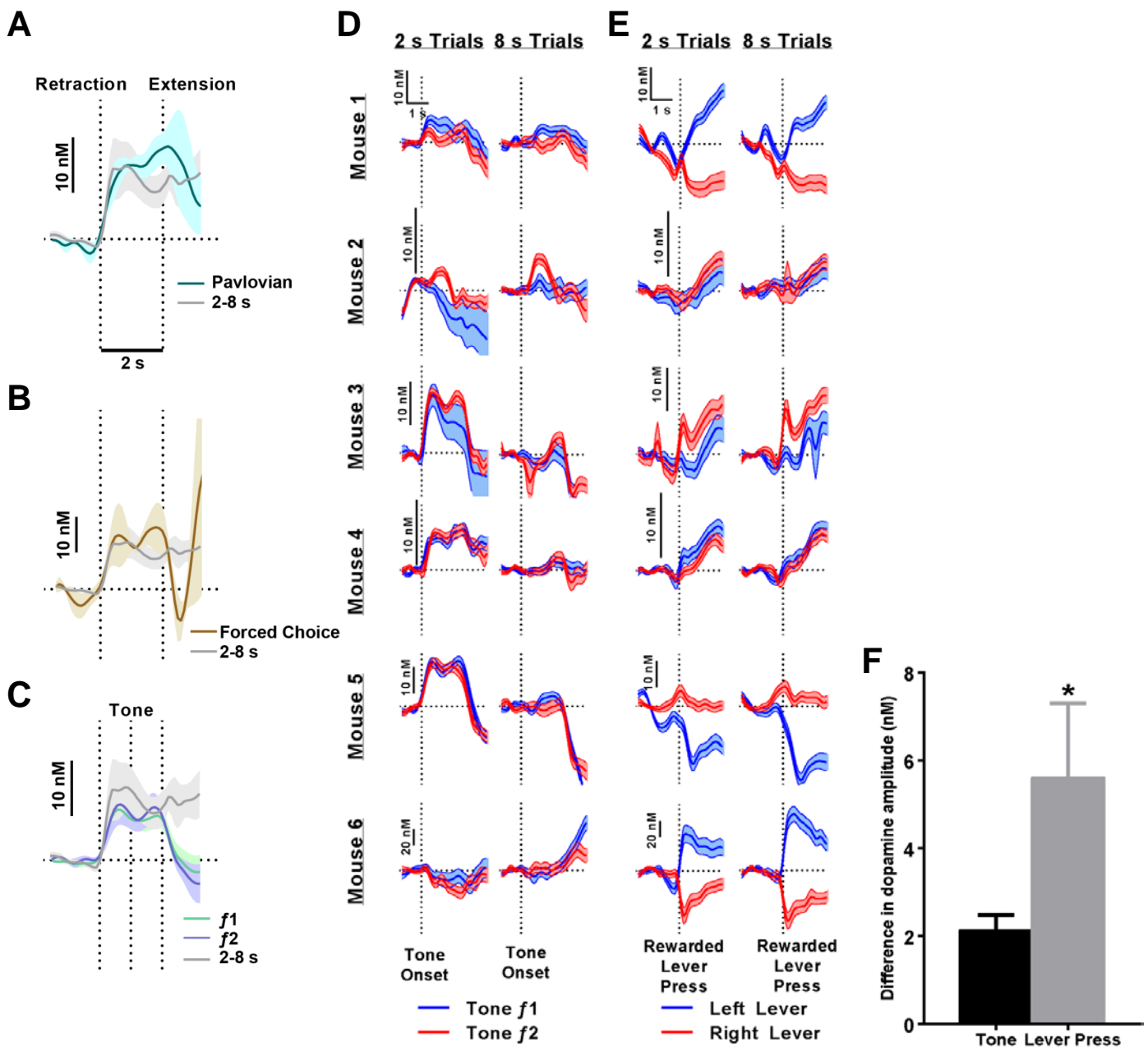


Figure S5. 2 s data for control experiments and dopamine release in relation to tone onset and rewarded lever presses during the 2-8 s tone task. Related to Figure 4. (A-C) Dopamine recorded during 2 s trials of the (A) Pavlovian control task, (B) forced choice task, and (C) the tone control task (see Methods). (D) For each individual mouse, voltammetric data is divided into 2 and 8 s trials and is split for tone f_1 (3 KHz) and tone f_2 (10 KHz). (E) Voltammetric data for each mouse is aligned to rewarded lever press and is divided by left or right lever presses. Tone f_1 and f_2 indicated reward at the left and right lever, respectively. (F) On average across mice, a significantly larger difference in dopamine signaling is noted while mice perform left vs. right action relative to different tone presentation (paired t -test, $t_{11} = 2.366$, $P < 0.05$). All recordings are from rewarded trials only.

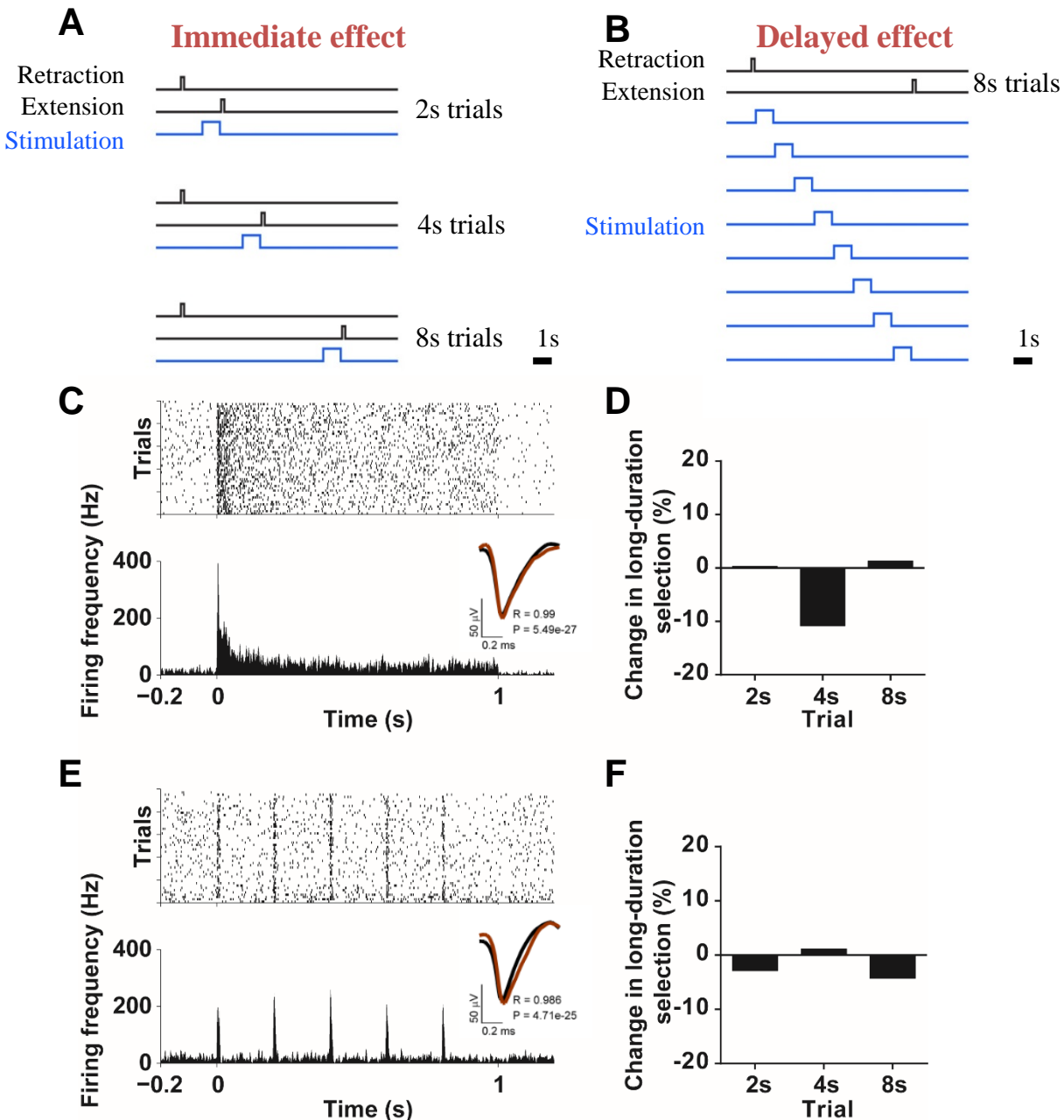


Figure S6. Experimental design for optogenetic experiments and optogenetic stimulation at 5Hz has no effect on behavioral choice. Related to Figure 6.(A) For studying the immediate effect of stimulating dopamine on choice behavior, mice were presented with three types of trials after being trained in the 2-8 s task: 2 s (40%, top panel), 4 s (20%, middle panel), or 8 s (40%, bottom panel) in random order (lever retraction and extension shown in black line). Within 50% of trials, 1 s constant laser stimulation was delivered 1 s before lever extension (shown in blue line). (B) For investigating the delayed effects of dopamine stimulation, mice were presented with 8 s trials. 50% of these trials, mice were optogenetically stimulated for 1 s occurring randomly at 0-7 s, and the remaining 50% of trials served as within-subject control. Mice were only stimulated once per trial. (C) Optogenetic stimulation of dopamine neurons with 1 s constant light drives high frequency firing in nigral dopamine neurons. INSET: Averaged waveform of spontaneous firing (black) and light-evoked firing (red). (D) In a representative animal, this stimulation biases behavioral choice at 4 s probe trials. (E) Optogenetic stimulation with 1 s low-frequency (5 Hz, five 10-ms pulses) light entrains dopamine neuron firing activity faithfully. INSET: Averaged waveform of spontaneous firing (black) and light-evoked firing (red). (F) Behavioral effect of 5 Hz optogenetic stimulation is greatly diminished.

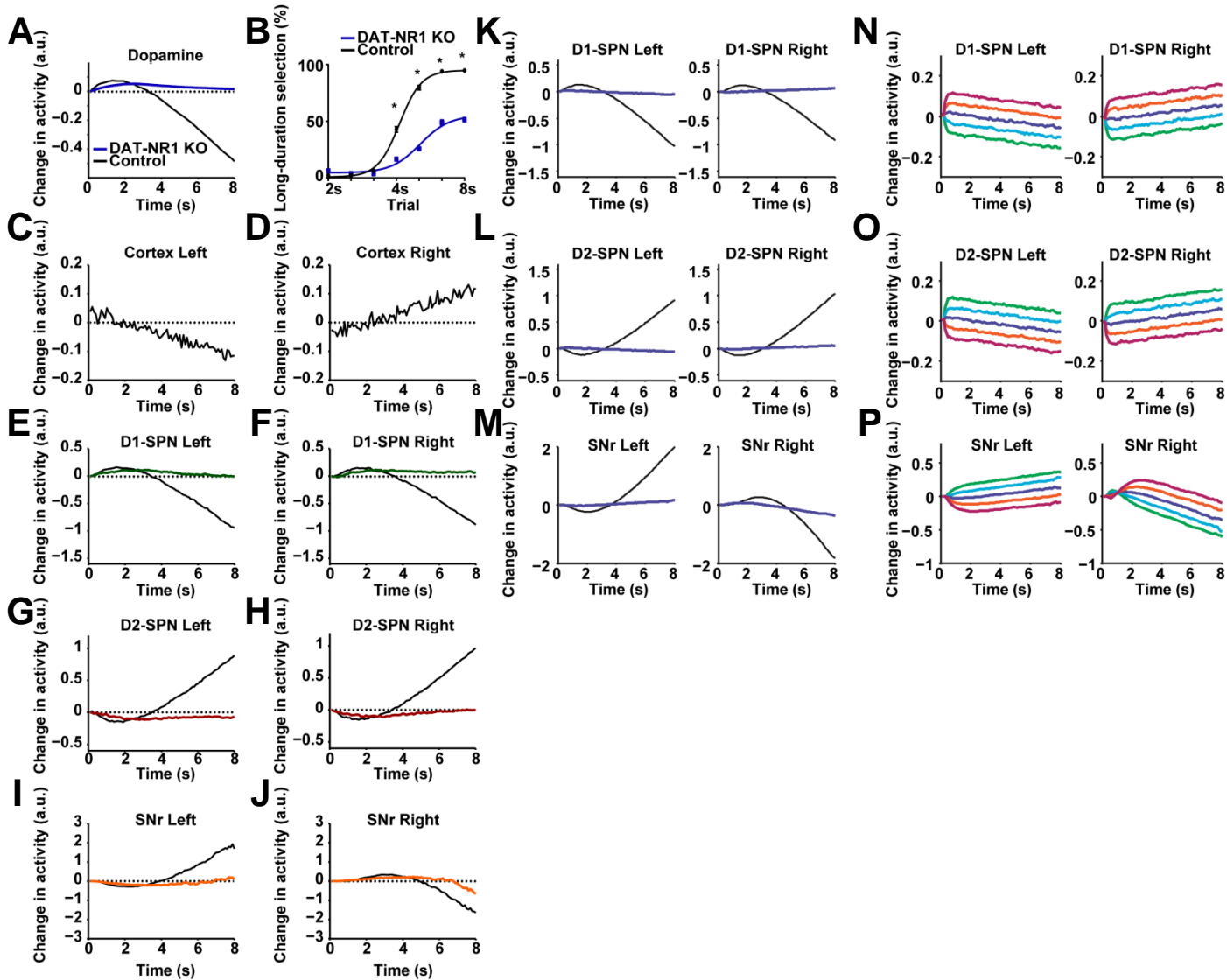


Figure S7. Modeled changes in basal ganglia circuitry. Related to Figures 7 and 8. (A) Modeled changes in dopamine concentration in DAT-NR1 KO (blue) and control mice (black). (B) Predicted changes in psychometric function based on SNr activity for DAT-NR1 KO (blue, $n = 10$) and control mice (black, $n = 10$) differ similarly to experimental data (two-way repeated measures ANOVA, significant effect of group, $F_{1, 18} = 557.8$, $P < 0.0001$, significant Fisher's LSD *post hoc* tests). (C-D) Modeled cortical inputs to striatal populations that encode left or right choice, respectively. For this and subsequent panels, 50 averaged trials from a single experiment are shown. (E-F) Modeled changes in D1 spiny projection neurons (SPNs) populations encoding either left or right choice. Traces from a DAT-NR1 KO mouse (green) are superimposed over a control mouse (black). (G-H) Modeled changes in D2 spiny projection neurons (SPNs) populations encoding either left or right choice. Traces from a DAT-NR1 KO mouse (red) are superimposed over a control mouse (black). (I-J) Modeled changes in SNr populations encoding either left or right choice. Traces from a DAT-NR1 KO mouse (orange) are superimposed over a control mouse (black). (K - M) Modeled changes in D1 spiny projection neurons (D1-SPNs) (K), D2-SPNs (L) and SNr neurons (M) encoding either left or right choice. Traces from a simulation with constant zero dopamine (zero change from baseline, blue lines) are superimposed over a control simulation with dynamic dopamine changes (black lines). (N - P) Modeled changes in D1-SPNs (N), D2-SPNs (O) and SNr neurons (P) with dopamine sustained at five constant levels (-0.05, -0.025, 0, 0.025, 0.05), and different levels are color coded by gradient.

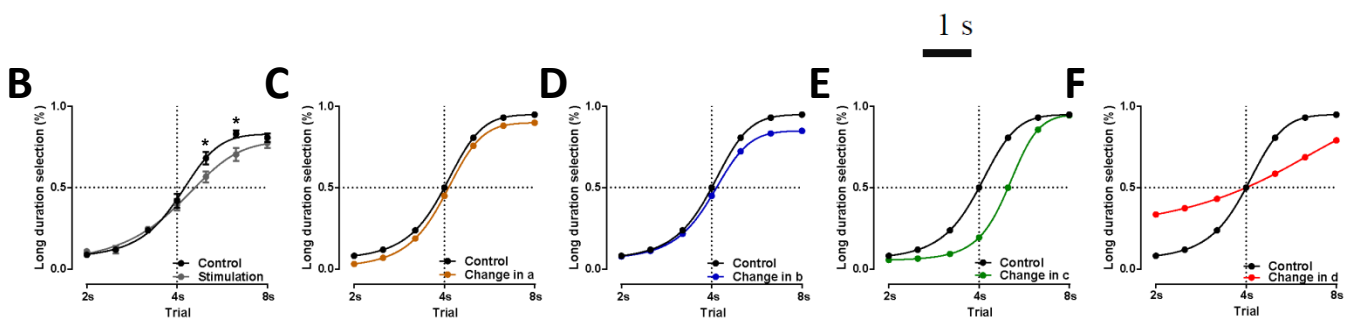
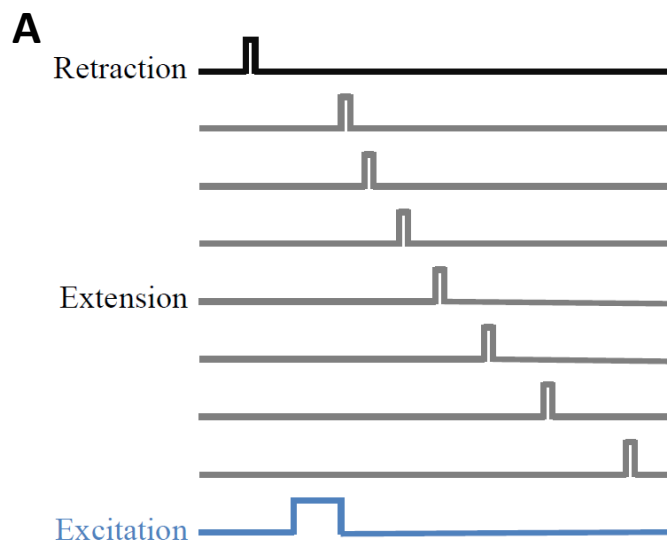


Figure S8. Optogenetic manipulation of dopamine alters psychometric curve. Related to Figure 6. (A) Schematic of the experiment investigating the effect of fixed-time optogenetic excitation on choice in different probe trials. (B) Mice were tested using retraction intervals of 2, 2.5, 3.2, 4, 5, 6.3, and 8 s to construct a psychometric curve (black dots and line). Stimulation of dopamine neurons occurred at half of trials selected randomly 1 s following lever retraction and lasting for 1 s (grey dots and line) (two-way repeated measures ANOVA, significant effect of group, $F_{6, 56} = 131.7$, $P < 0.0001$). (C-F) The modeled changes in overall choice (C), bias between short- and long-duration choice (D), changes in midpoint (E), and changes in slope or discrimination sensitivity (F) respectively (see Methods for model details).

Supplemental Video 1. Related to Figure 1. A typical example of behavior performance for a trained mouse during 8 s trial in the 2-8 s task.