Supplementary Material

Selective serotonin reuptake inhibitor treatment retunes emotional valence in primate ventral striatum

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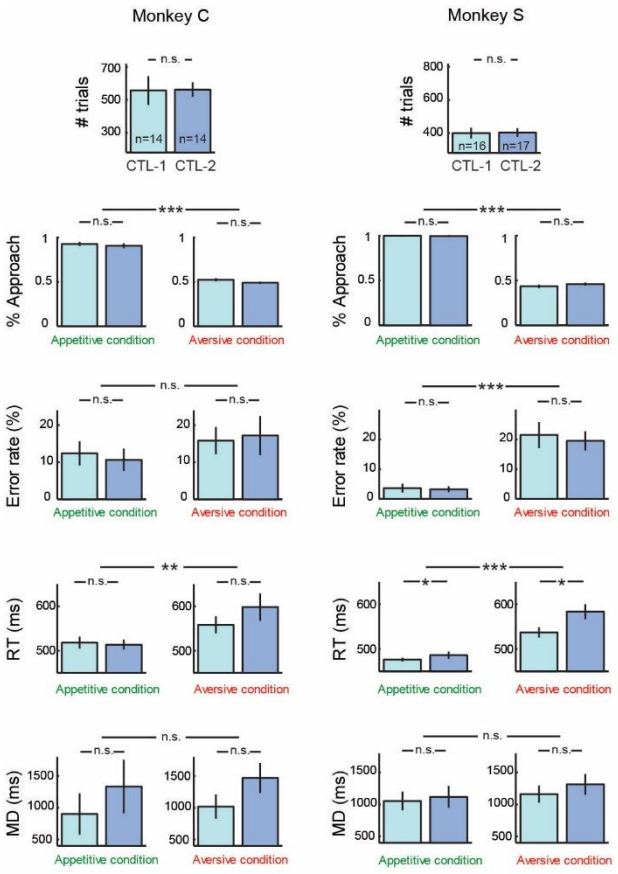
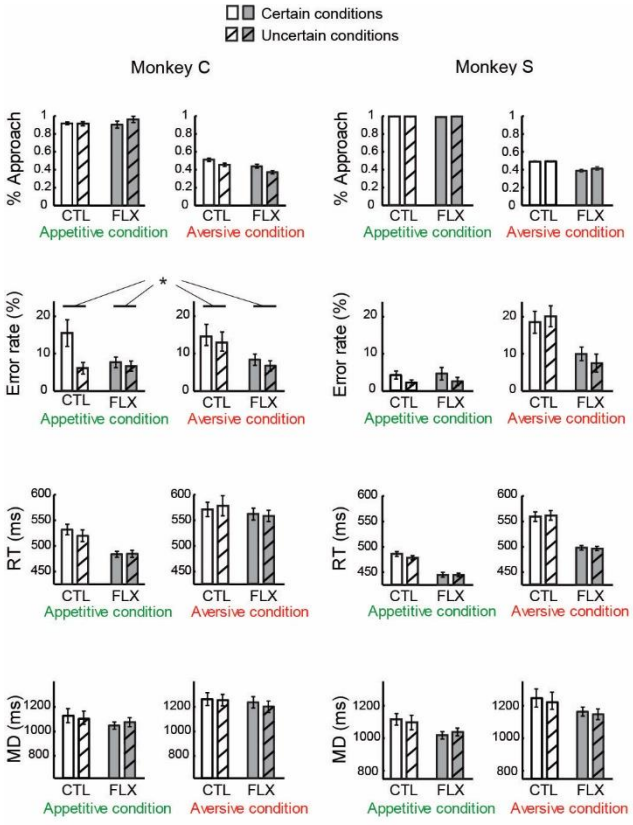
Contents:



	Monkey C	Monkey S
# trials	CTL-1 vs. CTL-2 $t(26)=0.055$ $p=0.956$	CTL-1 vs. CTL-2 $t(31)=0.064$ $p=0.949$
% Approach	CTL-1 vs. CTL-2 $F(1,26)=1.59$ $p=0.212$ Appetitive vs. Aversive $F(1,26)=366$ $p<0.001$*** Interaction $F(1,26)=0.13$ $p=0.723$	CTL-1 vs. CTL-2 $F(1,31)=0.71$ $p=0.402$ Appetitive vs. Aversive $F(1,31)=1609$ $p<0.001$*** Interaction $F(1,31)=1.03$ $p=0.315$
Error rate	CTL-1 vs. CTL-2 $F(1,26)=0$ $p=0.965$ Appetitive vs. Aversive $F(1,26)=1.63$ $p=0.207$ Interaction $F(1,26)=0.16$ $p=0.690$	CTL-1 vs. CTL-2 $F(1,31)=0.17$ $p=0.678$ Appetitive vs. Aversive $F(1,31)=36.37$ $p<0.001$*** Interaction $F(1,31)=0.08$ $p=0.776$
RT	CTL-1 vs. CTL-2 $F(1,26)=0.77$ $p=0.383$ Appetitive vs. Aversive $F(1,26)=9.63$ $p=0.003$** Interaction $F(1,26)=1.22$ $p=0.274$	CTL-1 vs. CTL-2 $F(1,31)=6.04$ $p=0.016$* Appetitive vs. Aversive $F(1,31)=47.58$ $p<0.001$*** Interaction $F(1,31)=2.54$ $p=0.116$
MD	CTL-1 vs. CTL-2 $F(1,26)=2.05$ $p=0.157$ Appetitive vs. Aversive $F(1,26)=0.17$ $p=0.684$ Interaction $F(1,26)=0$ $p=0.976$	CTL-1 vs. CTL-2 $F(1,31)=0.49$ $p=0.486$ Appetitive vs. Aversive $F(1,31)=0.95$ $p<0.332$ Interaction $F(1,31)=0.08$ $p=0.774$

Figure S1. Stability of the animals' performance during the control sessions. Behavioral measures (mean ± SEM) were compared between two groups of control sessions collected without drug administration. Rates of approach (selection of the ipsilateral target), reaction times (RT), movement durations (MD) and error rates were tested across control periods [early period (CTL-1) vs. late period (CTL-2)] and types of trials (positive vs. negative valence) using two-way ANOVAs. Statistical data are detailed in the right column. Except an increase of RTs for monkey S, no significant behavioral changes were found across control periods.



	Monkey C	Monkey S
% Approach	Certainty F(1,45)=2.03 p=0.162 Certainty x Valence F(1,45)=1.45 p=0.230 Certainty x Drug F(1,45)=0.82 p=0.367	Certainty F(1,48)=1.14 p=0.288 Certainty x Valence F(1,48)=0.52 p=0.474 Certainty x Drug F(1,48)=0.88 p=0.349
Error rate	Certainty F(1,45)=6.24 p=0.013* Certainty x Valence F(1,45)=3.63 p=0.058 Certainty x Drug F(1,45)=3.42 p=0.066	Certainty F(1,48)=2.98 p=0.086 Certainty x Valence F(1,48)=0.01 p=0.933 Certainty x Drug F(1,48)=0.96 p=0.329
RT	Certainty F(1,45)=0.01 p=0.912 Certainty x Valence F(1,45)=0.05 p=0.823 Certainty x Drug F(1,45)=0.01 p=0.935	Certainty F(1,48)=0.16 p=0.687 Certainty x Valence F(1,48)=0.21 p=0.646 Certainty x Drug F(1,48)=0.05 p=0.819
MD	Certainty F(1,45)=0.05 p=0.817 Certainty x Valence F(1,45)=0.15 p=0.699 Certainty x Drug F(1,45)=0.01 p=0.912	Certainty F(1,48)=0.29 p=0.589 Certainty x Valence F(1,48)=1.15 p=0.285 Certainty x Drug F(1,48)=0.12 p=0.733

Three-way ANOVA

Figure S2. Effects of certainty levels on task performance. Rates of approach, reaction times (RT), movement durations (MD) and error rates were tested across certainty levels (certain vs. uncertain trials), valence conditions (positive vs. negative valence) and drug conditions (ON vs. OFF) using three-way ANOVAs. Statistical data concerning the effects of certainty on behavior and its interactions with other parameters are detailed in the right column. Except an increase of error rates in certain condition for monkey C, no significant behavioral changes were found across certainty levels. This increase in error rates could result from a difference in attentional processes recruited during the task execution, suggesting a lower level of attention when the monkey C could predict the upcoming task condition.

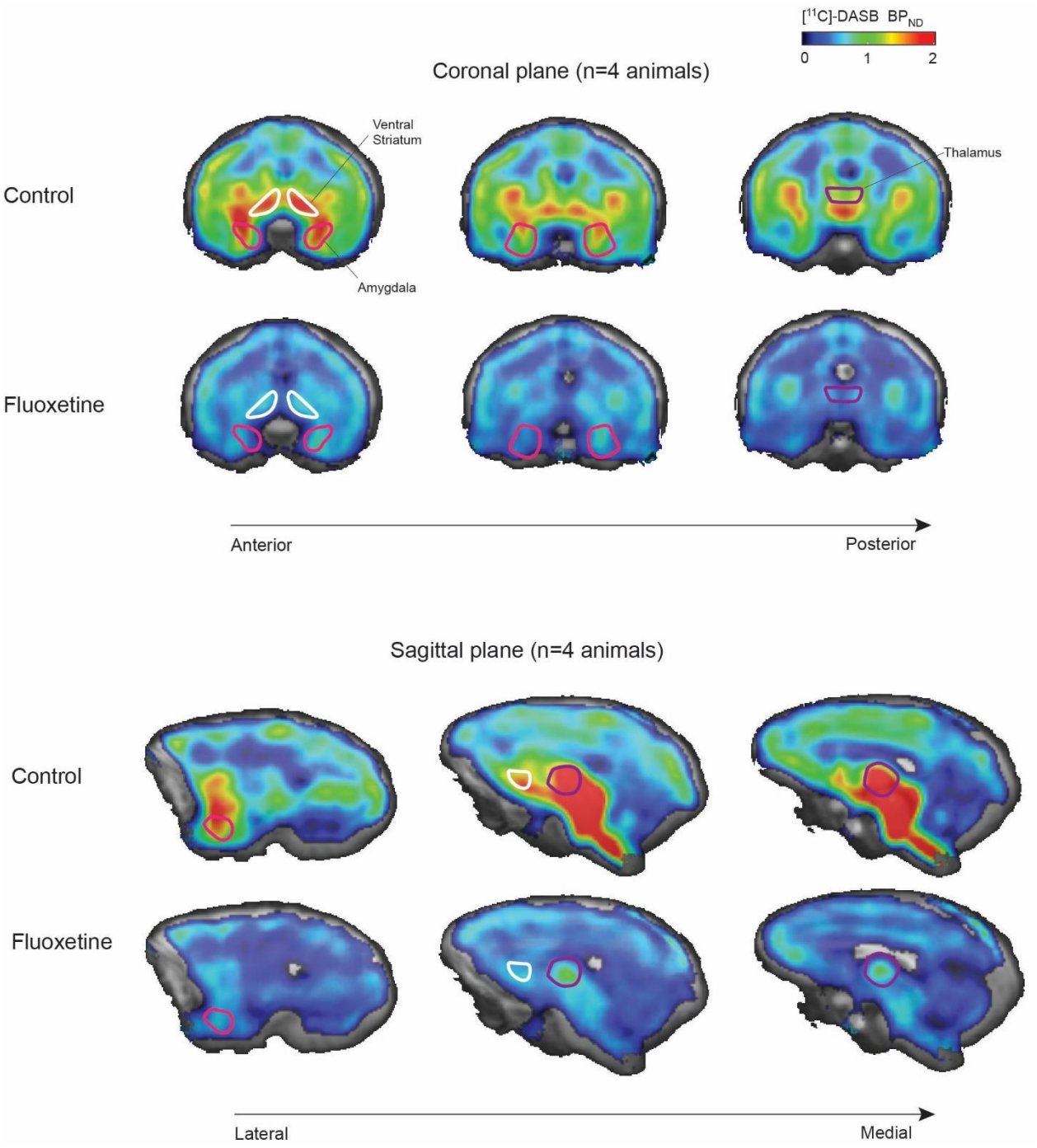


Figure S3. Fluoxetine binding in the primate brain. Population-averaged [^{11}C]-DASB PET images superimposed on an MRI template (n=4 animals). The ventral striatum (white), the amygdala (pink) and the thalamus (purple) are delineated by lines.

Table S1. Effects of fluoxetine on task-related neurons. The prevalence of striatal neurons encoding task parameters (and interactions) was determined using a regression analysis ($P < 0.05$, corrected for 150 time bins). A unit was considered as encoding a regressor if a significant effect was detected in a 3-s test window around the event. *P<0.05, **P<0.01 (χ^2 test).

Encoding	Treatment	Cue	Outcome	Task
Valence	Control	28 (24%)	51(43%)	59 (50%)
	Fluoxetine	22 (27%)	50 (62%)*	55 (68%)*
Location	Control	6 (5%)	10 (8%)	15 (13%)
	Fluoxetine	7 (9%)	8 (10%)	15 (19%)
Certainty	Control	9 (8%)	3 (3%)	12 (10%)
	Fluoxetine	10 (12%)	10 (12%)**	17 (21%)*
Valence x Location	Control	4 (3%)	14 (12%)	17 (14%)
	Fluoxetine	5 (6%)	7 (9%)	12 (15%)
Valence x Certainty	Control	6 (5%)	18 (15%)	21 (18%)
	Fluoxetine	5 (6%)	17 (21 %)	20 (25%)

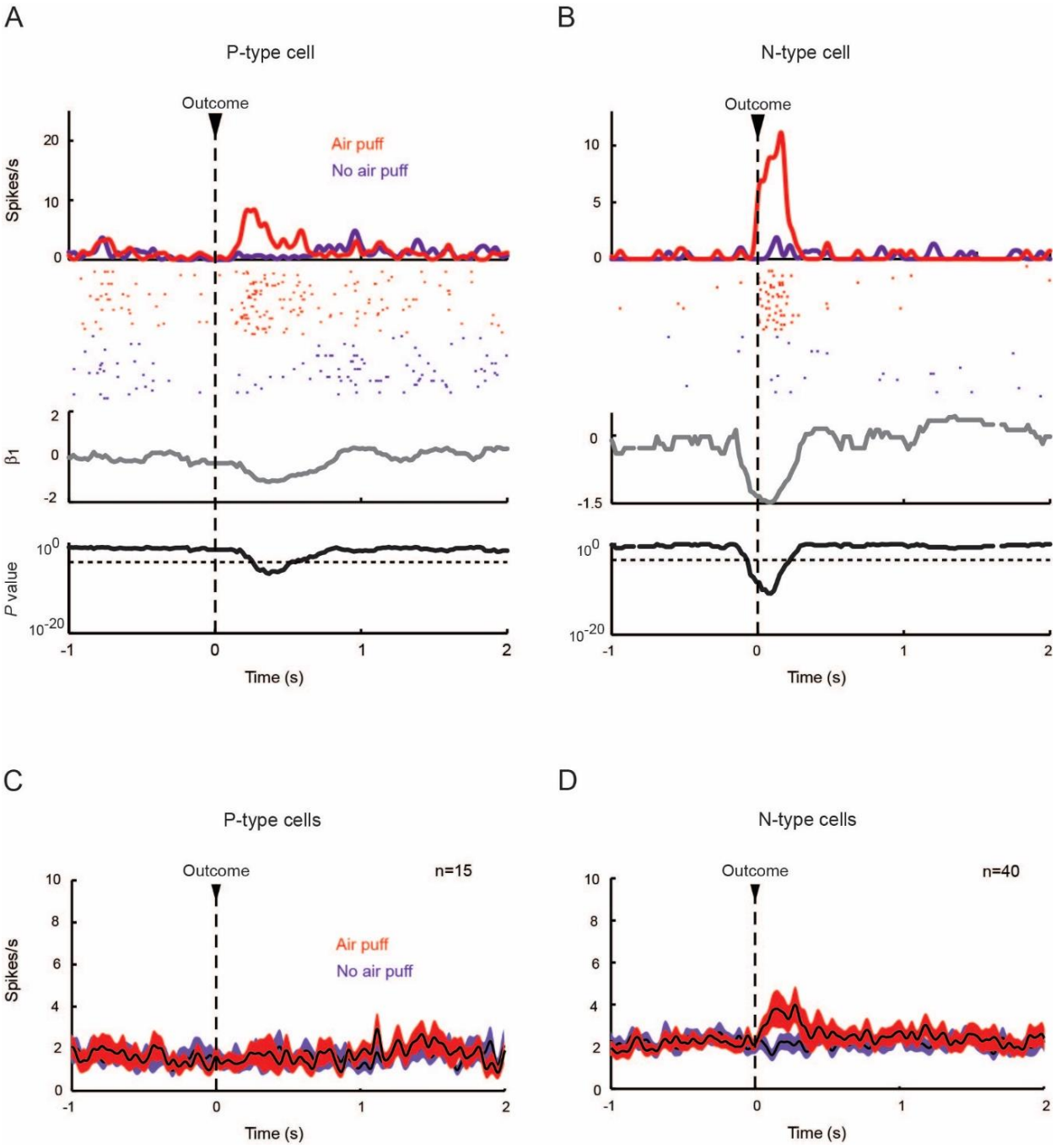


Figure S4. N-type neurons selectively responded to airpuff delivery. (**A**-**B**) The activity of the two exemplar neurons shown in Fig. 3 classified as (**A**) P-type cell and (**B**) N-type cell. Spike density functions and raster plots illustrate activity around the occurrence of both types of outcomes in aversive trials, i.e., airpuff and no airpuff (when the animal selected the contralateral target). To compare the firing rate between trials, we used the same regression analysis ($P < 0.05$ corrected for 150 time bins). These figures follow the conventions of Fig. 3. (**C**-**D**) Population-averaged activities of (**C**) P-type cells and (**D**) N-type cells aligned around the time of outcomes in aversive trials. The width of the lines indicates the population SEM. N refers to the number of cells in each population. Note that N-type cells only responded to airpuff, and P-type cells did not respond when the animal successfully prevented a punishment.

Table S2. Effects of fluoxetine treatment duration on striatal neurons. To test the effects of treatment duration on our findings, we compared data collected during the first days of fluoxetine administration (early period, i.e., the first half of neurons) with data collected at the end of the treatment (late period, i.e., the second half of neurons). We found that the mean (± SEM) spontaneous firing rate of striatal neurons increased between the two periods (* 2-tailed *t*-test, t=2.35 P=0.019), but no effect on the prevalence of cells was measured (χ^2 test, P>0.05). Notably, the ratio between P-type and N-type neurons remained unchanged during the full treatment period (χ^2=0.74 P=0.39).

	Early period	Late period
Number of cells	101	101
Firing rate (spikes/s)	2.23 ± 0.25	3.34 ± 0.4*
Coefficient of variation	1.72 ± 0.1	1.83 ± 0.08
Task-related cells	43/101 (43%)	38/101 (38%)
Valence encoding	28/43 (65%)	27/38 (71%)
Location encoding	9/43 (21%)	6/38 (16%)
Certainty encoding	12/43 (28%)	5/38 (13%)
P-type / N-type cells — Cue	5 / 11	4 / 8
P-type / N-type cells — Outcome	14 / 15	15 / 10

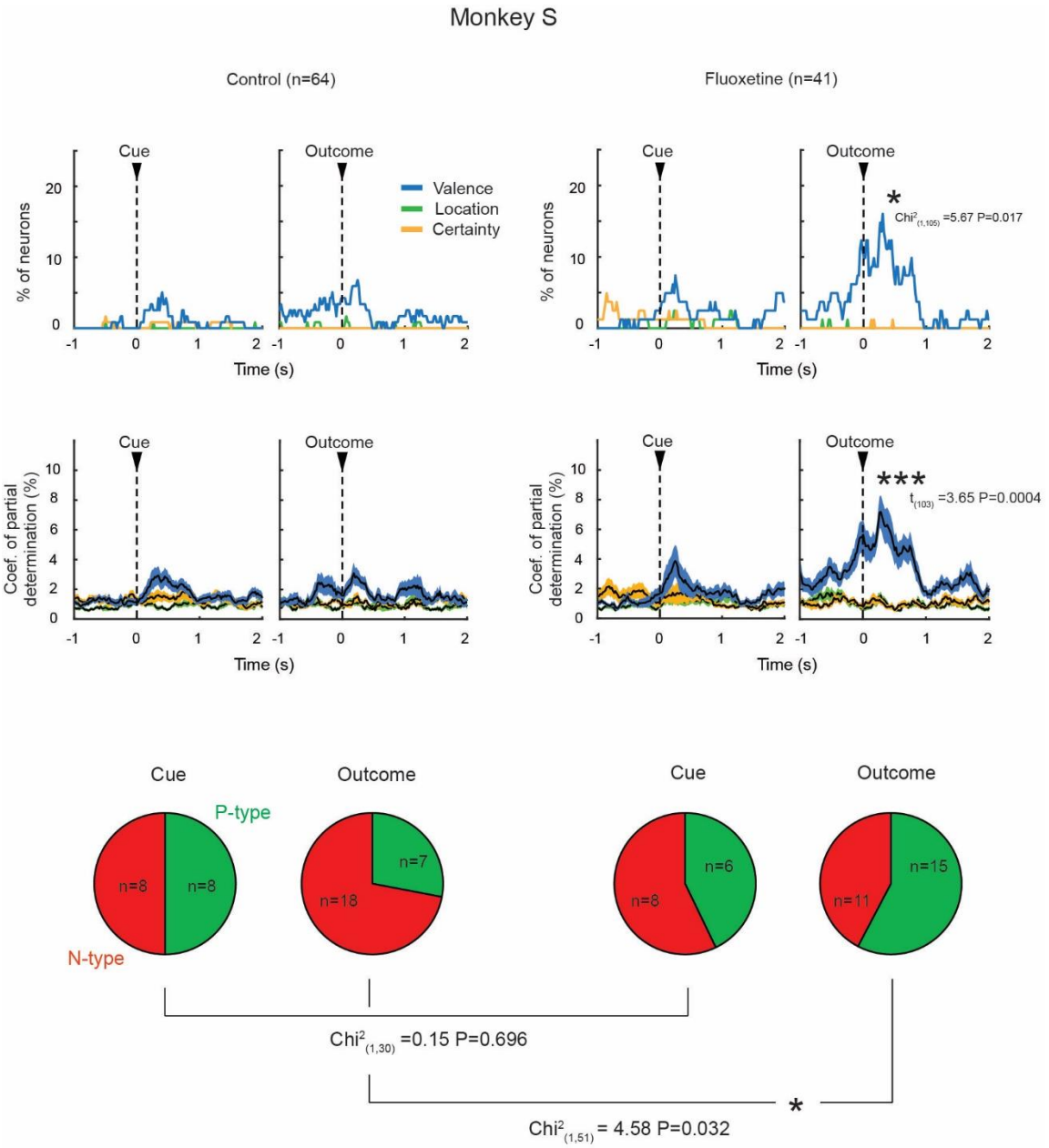


Figure S5. Fluoxetine effects on valence-encoding cells in monkey S. (*Top*) Fraction of neurons showing a change in activity to different task parameters such as valence, location and certainty ($P<0.05$, corrected for 150 time bins). The faction of neurons encoding valence around the time of outcome was larger during fluoxetine administration (Chi^2 test, $^*P<0.05$). (*Middle*) Population averages (± SEM) of the coefficient of partial determination for the same regressors. The proportion of variance accounted for by valence increased with fluoxetine (2-tailed *t*-test, $^{***}P<0.01$). (*Bottom*) The ratio of P-type cells to N-type cells was affected by fluoxetine around the time of the trial outcome (Chi^2 test, $^*P<0.05$). During fluoxetine administration, the striatal neurons processed punishments less often and rewards more often than during the control condition.

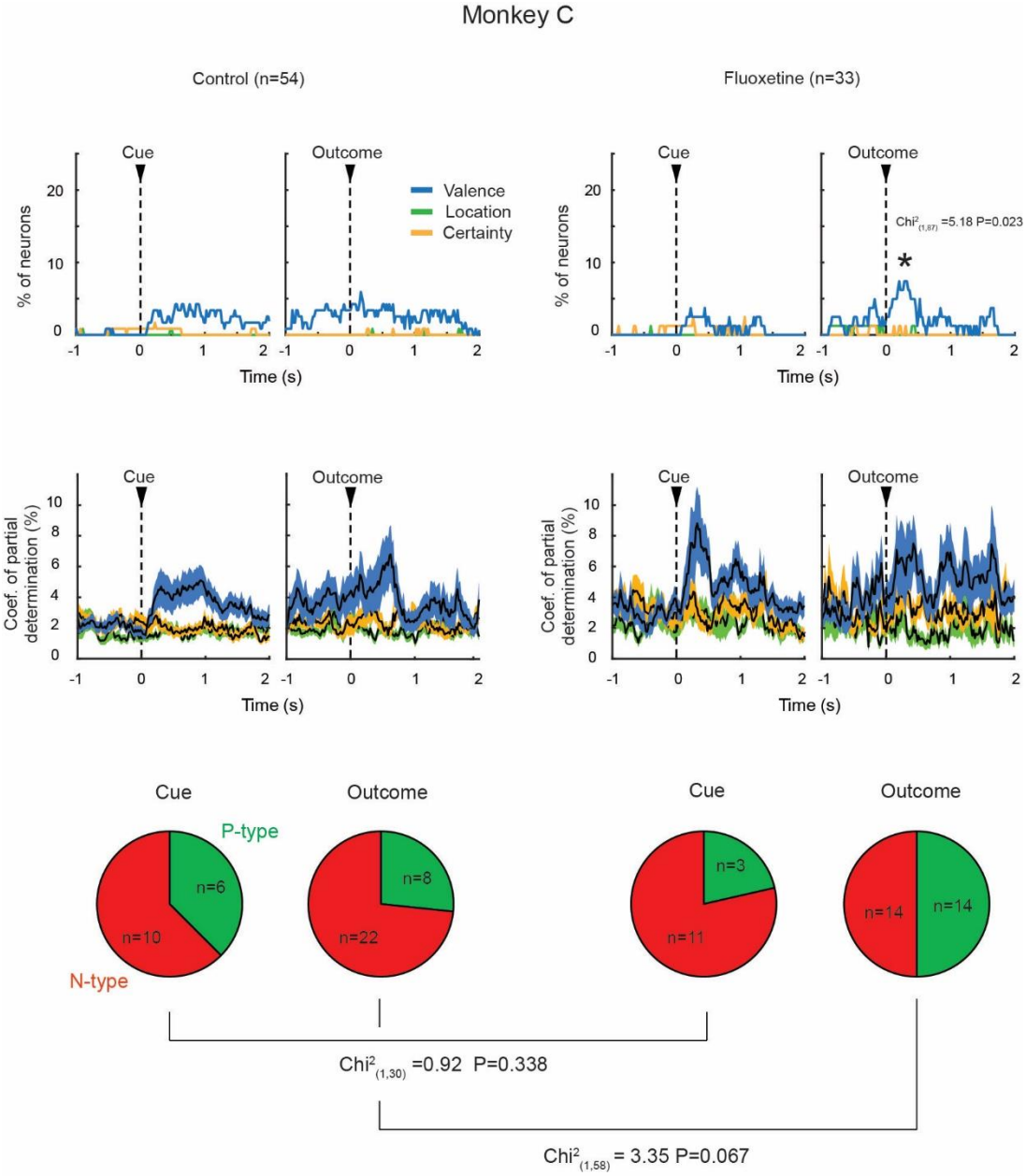


Figure S6. Fluoxetine effects on valence-encoding cells in monkey S. (*Top*) Fraction of neurons showing a change in activity to different task parameters such as valence, location and certainty (*P*<0.05, corrected for 150 time bins). The faction of neurons encoding valence around the time of outcome was larger during fluoxetine administration (Chi² test, **P*<0.05). (*Middle*) Population averages (± SEM) of the coefficient of partial determination for the same regressors. (*Bottom*) The ratio of P-type cells to N-type cells was not significantly affected by fluoxetine around the time of the trial outcome (Chi² test, **P*<0.05). However, during fluoxetine administration, the striatal neurons tend to process rewards more often (x2.75).