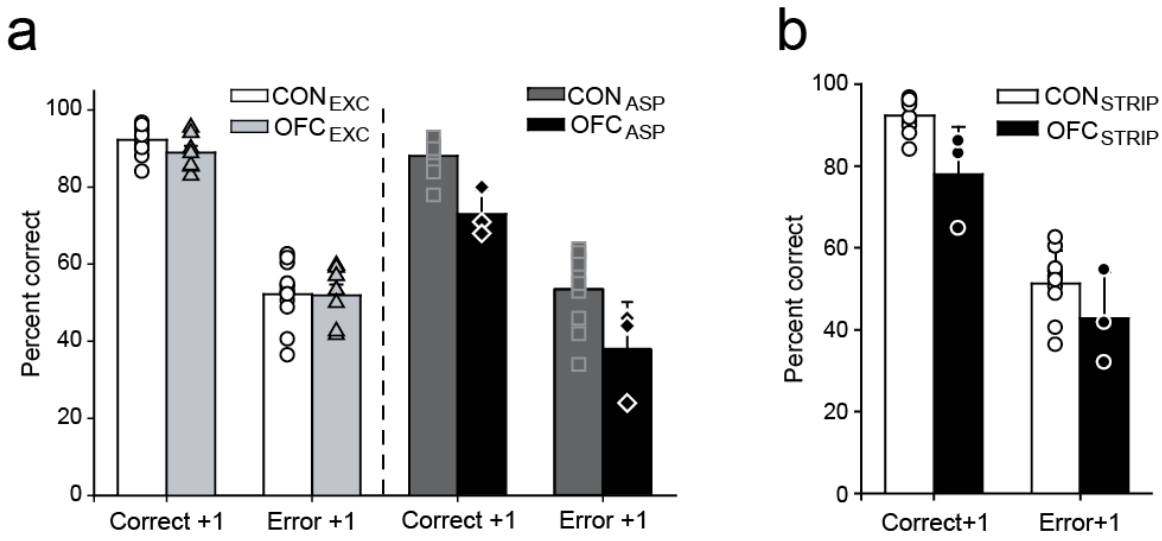
SUPPLEMENTARY INFORMATION:

Prefrontal mechanisms of behavioral flexibility, emotion regulation and value updating

Peter H. Rudebeck*, Richard C. Saunders, Anna T. Prescott, Lily S. Chau and Elisabeth A. Murray

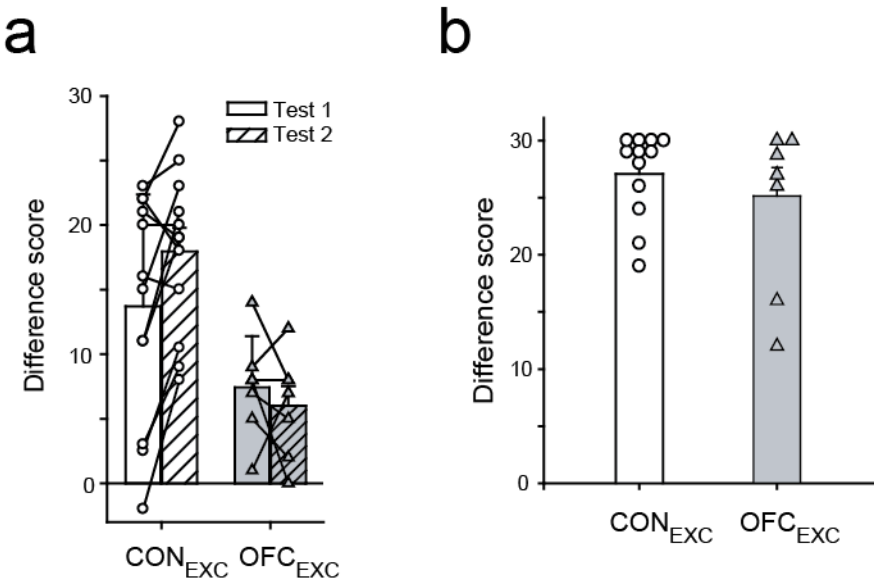
* To whom correspondence should be addressed.



Supplementary Figure S1: Trial-by-trial analyses of object reversal learning.

a) Performance (percent correct, ± SEM) during object reversal learning on trials following a correct response (Correct+1) or an error (Error+1) by control (white bars), monkeys with excitotoxic lesions of OFC (light grey bars). For comparison, the data from a previous study of monkeys with aspiration lesions of OFC (OFC_{ASP}, black bars) and their corresponding controls (CON_{ASP}, dark grey bars) are included. Data are collapsed across reversals. Symbols show scores of individual monkeys. Abbreviations: $CON_{EXC,}$ unoperated controls; OFC_{EXC}, monkeys with bilateral excitotoxic lesions of orbital

prefrontal cortex; CON_{ASP}, unoperated controls; $OFC_{ASP,}$ monkeys with bilateral aspiration lesions of orbital prefrontal cortex. Even more fine-grained analyses that determined the effect of multiple correct (EC analysis) or incorrect (EE analysis) choices on monkeys subsequent choices similarly failed to reveal any differences between monkeys with excitotoxic lesions of OFC and their controls (CON_{EXC} or CON_{ASP}; EC analysis, $p>0.1$, EE analyses, $p> 0.1$). b) Performance (percent correct, ± SEM) during object reversal learning on trials following a correct response (Correct+1) or an error (Error+1) by control (white bars) and monkeys with strip lesions of posterior OFC (black bars). Symbols show scores of individual monkeys. Abbreviations: $CON_{STRIP,}$ unoperated controls; OFC_{STRIP}, monkeys with bilateral strip lesions in posterior orbital prefrontal cortex.



Supplementary Figure S2: **Reinforcer devaluation tests.**

a) Mean ± SEM difference score for controls (CON_{EXC}) and monkeys with excitotoxic lesions of OFC (OFC_{EXC}) across for devaluation test 1 (plain bars) and test 2 (hatched bars). In test sessions that were preceded by selective satiation, unoperated controls adaptively shifted their object choices, selecting objects associated with the higher value (nonsated) food on a high proportion of trials. By contrast, monkeys with excitotoxic lesions of OFC failed to shift their object choices to the same degree as the controls (repeated measures ANOVA, effect of test $F(1,17)=1.44$, $p=0.25$; effect of group $(1,17)=10.01$, $p=0.006$). Differences between the groups could not be attributed to differences in learning the initial discriminations or the amount of food consumed prior to test sessions. Both OFC_{EXC} and CON_{EXC} groups of monkeys readily learned the object discrimination problems, taking a mean of 12 sessions (range: 5 to 32) to reach criterion (sessions to criterion, $F(1,17)=0.297$, $p>0.5$). An analysis of the mean errors to criterion across the CON_{EXC} and OFC_{EXC} groups did not reveal any differences; thus, the two

groups learned at a similar rate ($F(1,17)=0.651$, $p>0.4$). There was no difference in the amount of food that unoperated controls and monkeys with excitotoxic lesions of the OFC consumed during the selective satiation procedures prior to the choice tests (CON_{EXC}, Mean ± SEM =137.98g; OFC_{EXC}, Mean=154.1; $F(1,17)=0.4$, $p>0.5$). b) Mean ± SEM difference score for controls (CON_{EXC}) and monkeys with excitotoxic lesions of OFC (OFC_{EXC}). When monkeys with excitotoxic lesions of the OFC and their corresponding controls were tested for their preference between the two food items in the absence of objects, both groups chose the food that had not been sated (high value) on a high percentage of trials. A difference score was calculated for each monkey and comparison of these scores using a one-way ANOVA revealed no difference between groups ($F(1,17)=1.09$, $p > 0.3$). Symbols show scores of individual monkeys. Abbreviations: CON_{EXC}, unoperated controls; OFC_{EXC}, monkeys with bilateral excitotoxic lesions of the orbital prefrontal cortex.

Case #	Left	Right	Mean
Case 1	62.6	84.4	73.5
Case 2	83.8	44.8	64.3
Case 3	61.9	68.0	65.0
Case 4	82.0	78.2	80.1
Case 5	92.2	89.7	91.0
Case 6	81.2	60.7	71.0
Case 7	96.1	96.6	96.3
Mean	**80.0**	**74.6**	**77.3**

Supplementary Table S1: Estimated damage to OFC.

Estimated percent damage to OFC in monkeys (cases 1-7) that received bilateral injections of excitotoxins into orbital prefrontal cortex. Left, left hemisphere; Right, right hemisphere.