Supplemental figure legends

Fig. S1. Extent of DA lesions following the infusion of 6-OHDA into the mVTA or SNc: two distinct patterns. (**A**) Representation of the mesencephalic and striatal subregions quantified in the selected coronal sections of the mesencephalon and striatum. (**B**) Mesencephalic and striatal TH-immunoreactivity quantification for the mVTA (green) and SNc (blue) 6-OHDA lesions. lSNc: lateral substantia nigra pars compacta, mSNc: medial substantia nigra pars compacta, mVTA: medial ventral tegmental area, NAc: nucleus accumbens, mTolf: medial olfactory tubercles, lTolf: lateral olfactory tubercles, DMS: dorsomedial striatum, DLS: dorsolateral striatum, *n* = 22-28. Note the segregation of the denervated striatal areas between the two lesions along a medioventral to dorsolateral gradient, as described by Voorn *et al*.[40], with a preferential loss of TH staining in the shell of the NAc and other parts of the ventral striatum (core of the NAc and olfactory tubercules) for mVTA lesions, and a selective loss of TH staining in the dorsal striatum, predominantly in its lateral part, for SNc lesions. (**C**) DA contents of the striatum and NAc, *n* = 8-12. Note that infusion of 6-OHDA into the mVTA lead to a preferential loss of DA in the NAc (69±1.2% DA loss in the NAc with respect to sham-operated animals vs. 24.7±1.8% in the striatum), whereas the opposite pattern was found for SNc 6-OHDA lesions (18.2±3.2% DA loss in the NAc with respect to sham-operated vs. 77.7±1.7% in the striatum). Two-way ANOVAs found significant effects of the lesions ($Fs > 34.86$, $Ps < 0.001$) and significant interactions between the lesion and the brain region considered ($Fs > 12.42$, $Ps < 0.01$). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, Sham-operated vs. Lesioned.

Fig. S2. Behavioral experiment schedules. (**A**) Evaluation of the behavioral effects of the mVTA and SNc DA lesions. (**B**) Evaluation of the effects of different pharmacological treatments on the behavioral deficits induced by SNc DA lesions. The behavioral studies began three weeks after surgery and tests were carried out in opposite orders for groups A

and B. CPP: conditioned place preference, FST: forced swim test, TBC: two-bottle choice procedure.

Fig. S3. SNc but not mVTA lesions reduced operant sucrose self-administration. (**A**) The number of sucrose deliveries along the 10 one-hour sucrose self-administration sessions was reduced in SNc-lesioned animals (effect of lesion: $F_{1,135} = 6.68$, $P < 0.05$ and significant lesion x session interaction: $F_{9,135} = 2.39$, $P < 0.02$), whereas similar performances were obtained for animals with mVTA lesions and control animals (no significant effect of lesion: $F_{1,108} = 1.66$, $P = 0.22$ and no lesion x session interaction: $F_{1,108} = 0.54$, $P = 0.84$). (**B**) Despite the small number of presses on the active, reinforced, lever for the SNc-lesioned animals, a two-way ANOVA nonetheless detected a significant effect of the lever ($F_{1,72} = 6.39$, $P < 0.05$), indicating that the animals pressed the active level significantly more frequently than the inactive level. (**C**) In a progressive ratio session, SNc (**$P < 0.01$), but no mVTA ($P = 0.12$) lesions significantly affected the breakpoint, corresponding to the last ratio completed (i.e., the last sequence of lever presses required to obtain a reward). n = 6-9. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, Sham-operated vs. Lesioned.

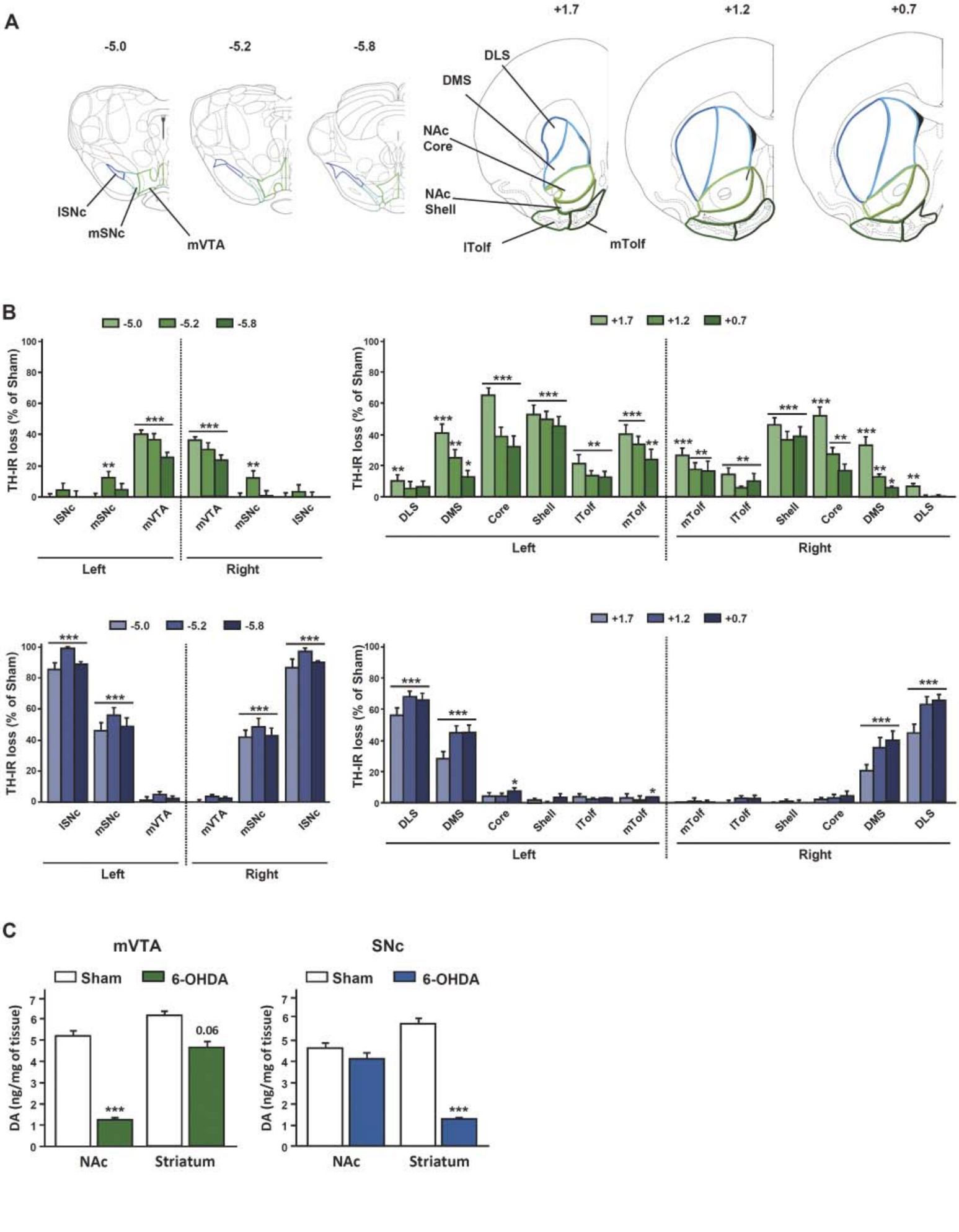
Fig. S4. 6-OHDA lesions do not alter sensitivity to rewarding sucrose and saccharin solutions. (**A**) The lesions had no significant effect on water (*Ps* > 0.05), 2% sucrose (*Ps* > 0.26) or total fluid intake (*Ps* > 0.27), in a two-bottle choice procedure, n = 12-19. (**B**) They also had no significant effect on the preference for a 0.002% saccharin solution (*Ps* > 0.32), or on water (*Ps* > 0.15) and saccharin (*Ps* > 0.20) intake, in a two-bottle choice procedure, n = 4-6. (**C**) The lesions had no significant effect on preference for a 0.02% over a 0.002% saccharin solution (*Ps* > 0.47), or on 0.002% saccharin (*Ps* > 0.15) and 0.02% saccharin (*Ps* > 0.51) intake, in a two-bottle choice procedure, n =4-6.

Fig. S5. SNc but not mVTA lesions induce depressive and anxiety-related behaviors. (**A**) SNc (effect of lesion: $F_{1,132} = 8.66$, $P < 0.01$ and no lesion x time interaction: $F_{4,132} = 1.32$,

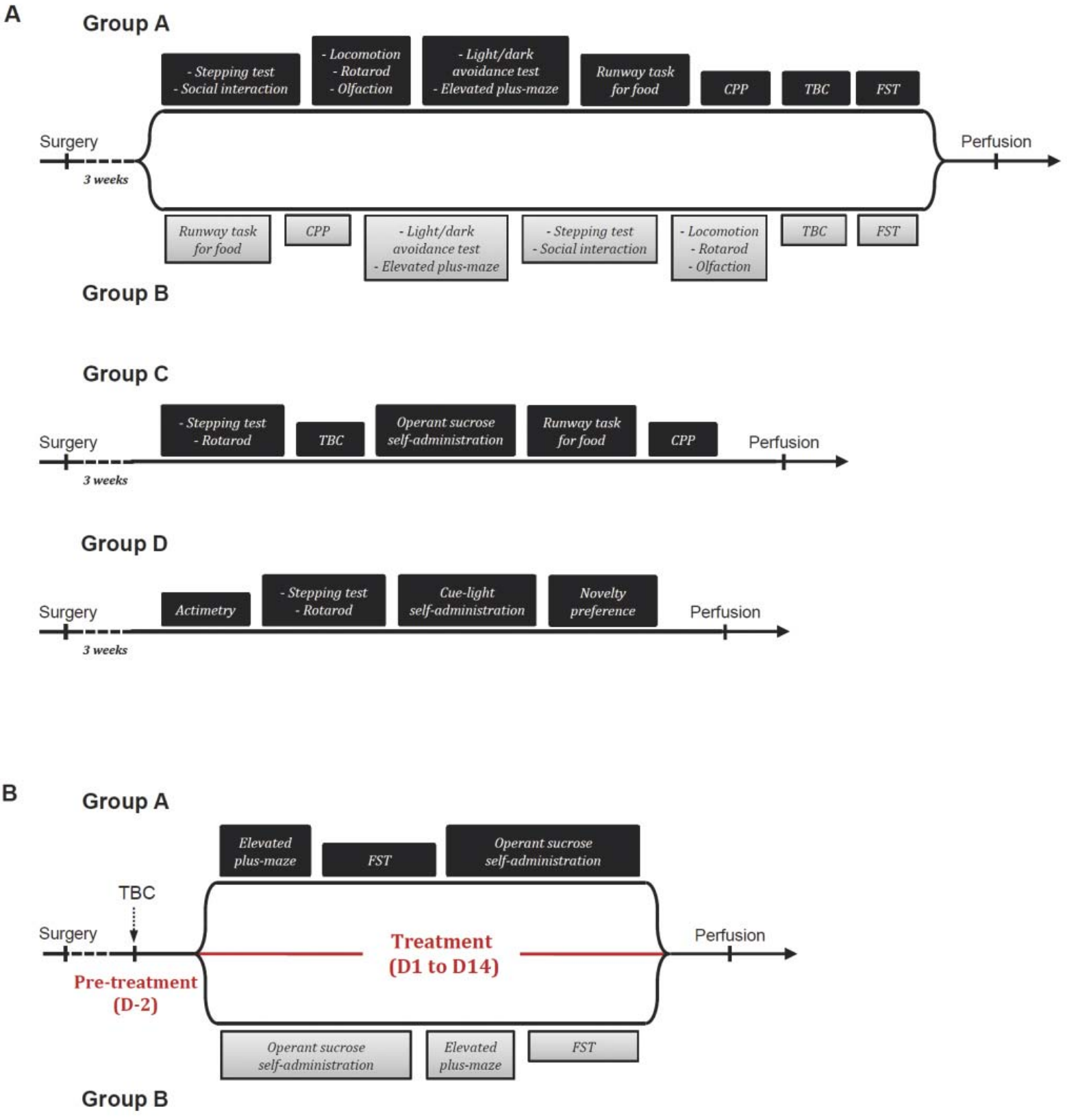
P = 0.27), but not mVTA (no effect of lesion: $F_{1,92}$ = 0.01, P = 0.98 and no interaction: $F_{4,92}$ = 0.77, P = 0.55) lesions decreased the time spent in activity along a 5 min forced-swim test, n = 11-19. (**B**) SNc lesions increased the time spent in the dark compartment during a 5-min light/dark avoidance test, whereas mVTA lesions did not, n = 12-19. (**C**) 6-OHDA lesions did not affect total arm entries (Ps > 0.14), indicating that general ambulatory activity in this test was not affected by the lesions, n = 15-22. *P < 0.05, **P < 0.01, Sham-operated vs. Lesioned.

Fig. S6. Effects of chronic intraperitoneal administration of L-dopa (12.5 mg/kg), ropinirole (1 mg/kg) and citalopram (10 mg/kg), on the depressive and anxiety-related behaviors and motivational deficits induced by SNc lesions. (**A**) L-Dopa and ropinirole, but not citalopram, reversed the decrease in the time spent in activity induced by the SNc lesions in a five-minute forced-swim test: an effect of the treatment was found for the lesion ($F_{3,120}$ = 25.88, P < 0.001), but not for the sham-operated ($F_{3,190}$ = 1.19, P = 0.33) condition. (**B**) No significant effect of lesion ($F_{1,60}$ = 0.76, P = 0.38) or of treatment ($F_{3,60}$ = 0.55, P = 0.65) and no interaction ($F_{3,60}$ = 0.12, P = 0.95) were found on the total number of arm entries in an elevated plus-maze test, indicating that general ambulatory activity during the test was affected by neither the lesion nor the treatment, n = 6-11. (**C**) A significant effect of lesions was found for all treatments (Fs > 5.49, Ps < 0.05), except for ropinirole (no effect of lesion: $F_{1,144}$ = 2.23, P = 0.16 and no lesion x session interaction: $F_{9,144}$ = 0.62, P = 0.78), on the number of sucrose deliveries over the 10 one-hour sucrose self-administration sessions. (**D**) A significant effect of lesion ($F_{1,65}$ = 5.15, P < 0.05) and treatment ($F_{3,65}$ = 3.22, P< 0.05), but no interaction ($F_{3,65}$ = 1.31, P = 0.28), were found on the breakpoint, which correspond to the last ratio completed (i.e., the last sequence of lever presses required to obtain a reward), during a progressive ratio session. n = 6-9. *P < 0.05, **P < 0.01, Sham-operated vs. Lesioned.

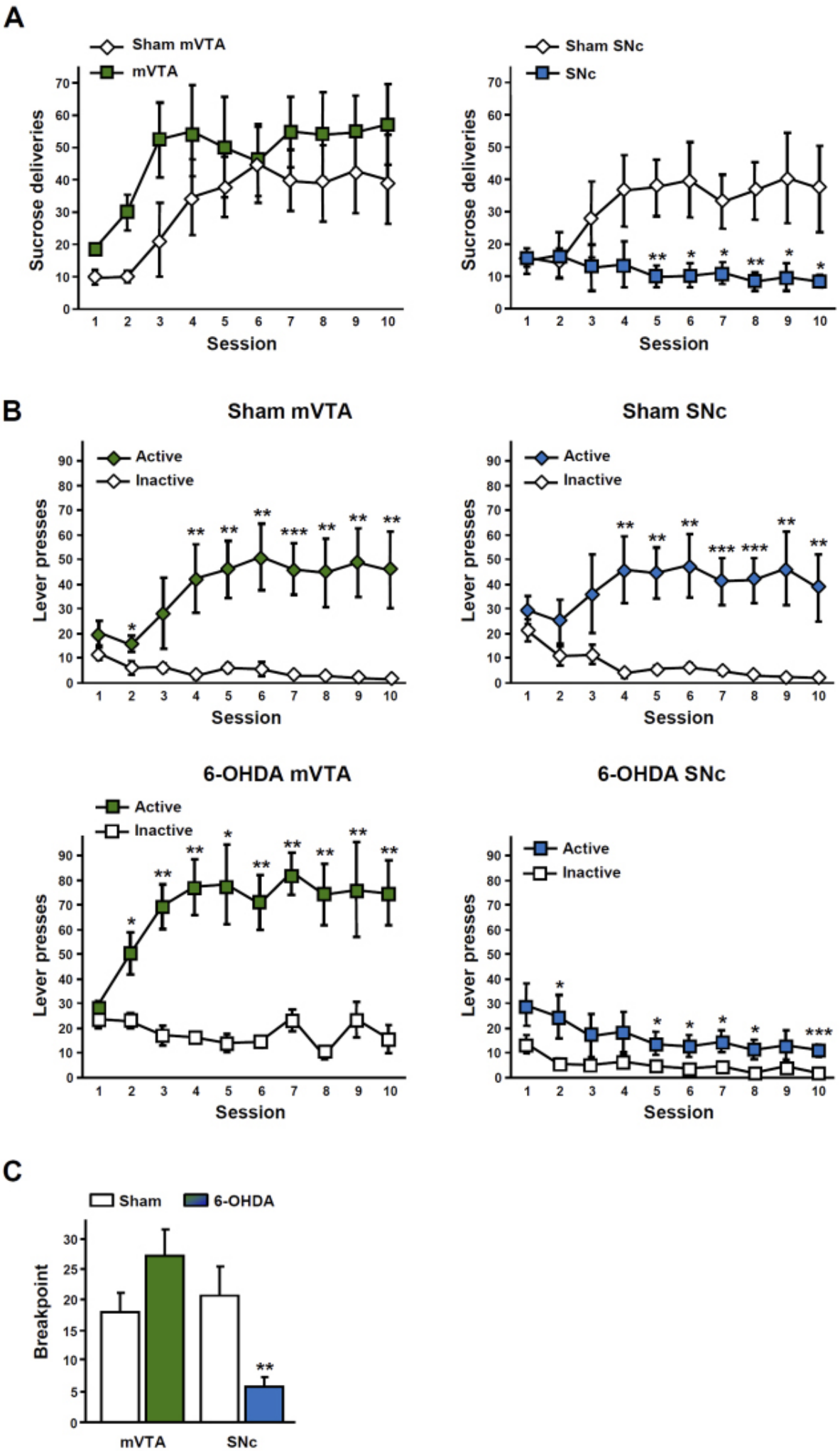
Drui et al., Figure S1



Drui et al., Figure S2



Drui et al., Figure S3



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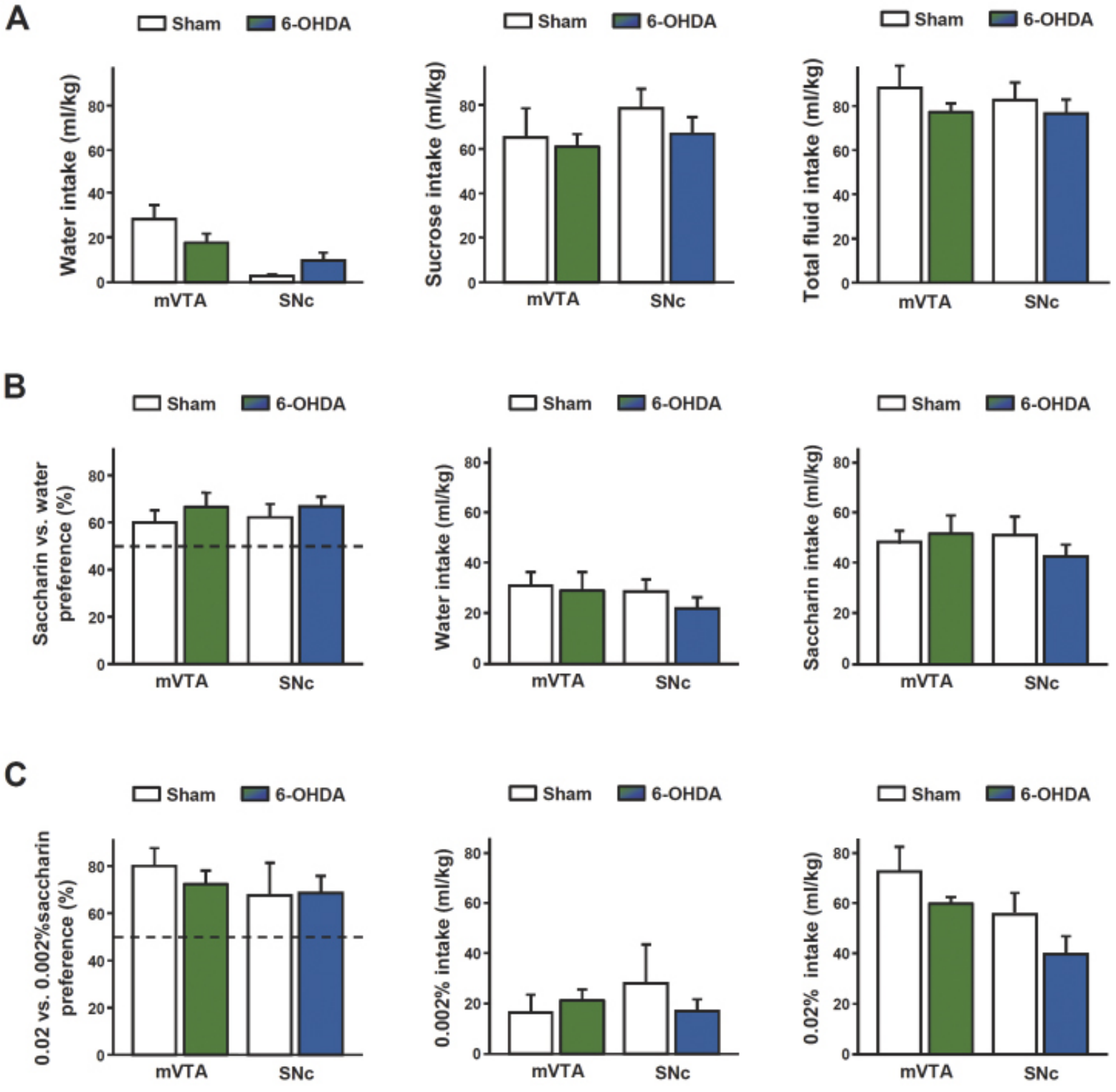
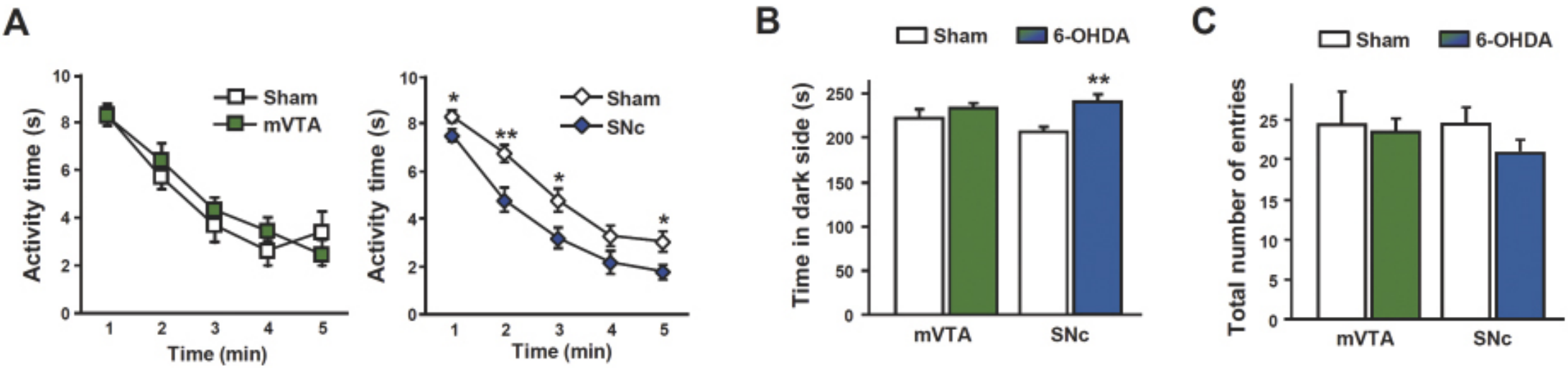


Drui et al., Figure S5



Drui et al., Figure S6