Supporting Information (SI)

Fig. S1

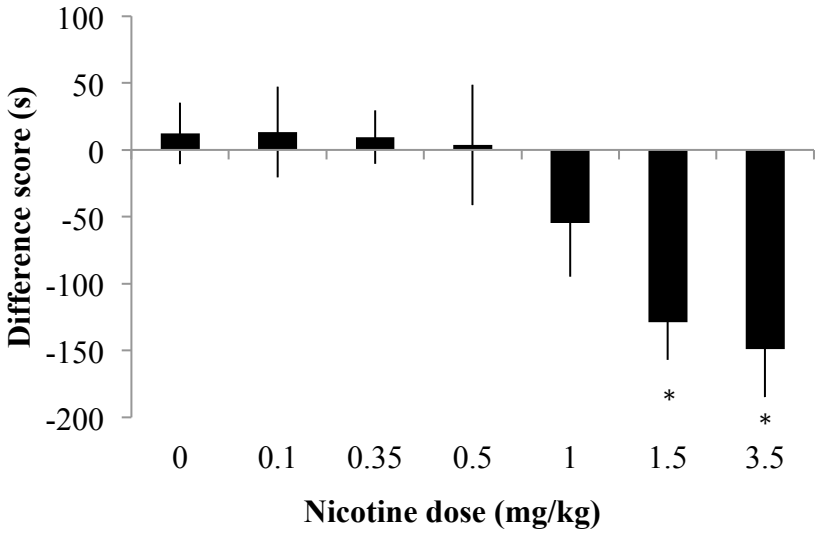

Fig. S1. The dose-response curve for acute nicotine in nondependent mice in our place conditioning paradigm. Only higher doses of acute nicotine (1.5 and 3.5 mg/kg) elicited a significant conditioned place aversion in groups of mice. Lower doses did not elicit a significant rewarding or aversive response. Data and error bars represent mean ± S.E.M. (**P* < 0.05).

Fig. S2

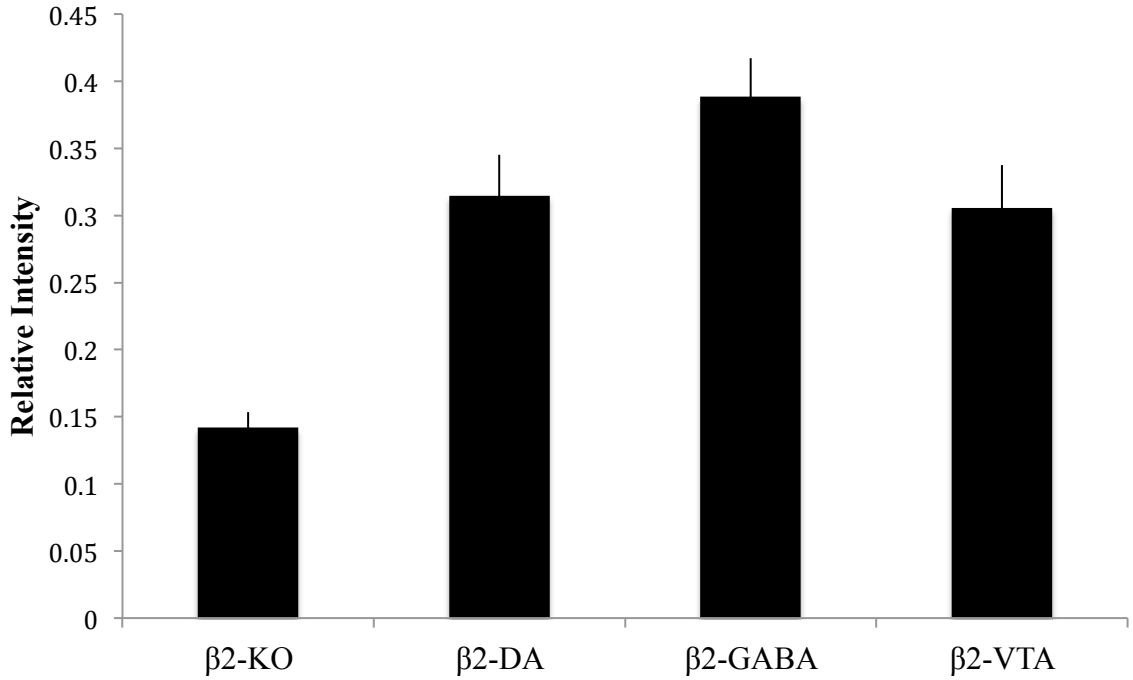

Fig. S2. [125I]-Epibatidine autoradiography binding quantification of lentiviral restoration of β2*-nAChRs in the VTA. Data show the mean inverse luminosity+SEM relative to β2-KO (*n*=2), β2-DA (*n*=2), β2-GABA (*n*=6) and β2-VTA (*n*=5), after subtraction of internal background and nicotine-resistant non-specific binding. Some subsisting background remains in β2-KO, probably due to the proximity of fasciculus retroflexus and interpeduncular nucleus which show high levels of [125I]-Epibatidine binding sites corresponding to non- β2 heteromeric nicotinic receptors (1, 2, 3).

Fig. S3

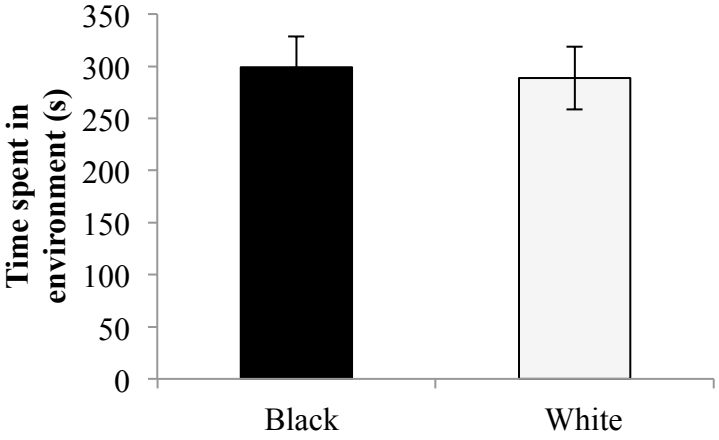

Fig. S3. Control groups of mice injected with saline in both the black and white environments showed no significant preference for either environment.

Fig. S4.

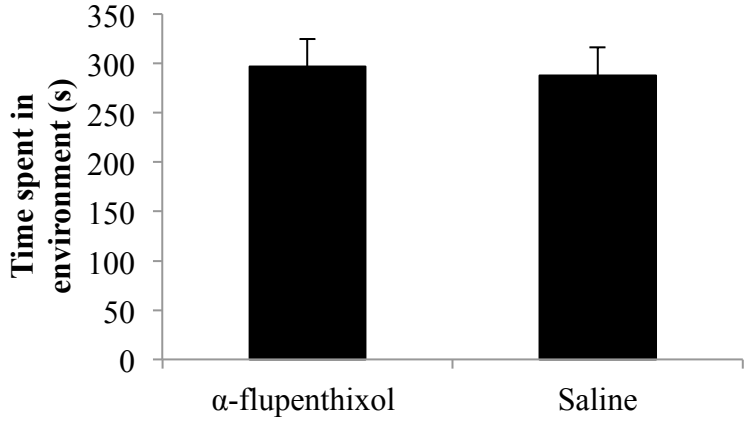

Fig. S4. α-flupenthixol has no motivational effects. A control group of C57Bl/6 mice given α-flupenthixol (0.8 mg/kg) in one environment and saline in the other showed no motivational preference for either environment. These results suggest that α-flupenthixol produces no motivational effects at the dose used in this study.

Fig. S5.

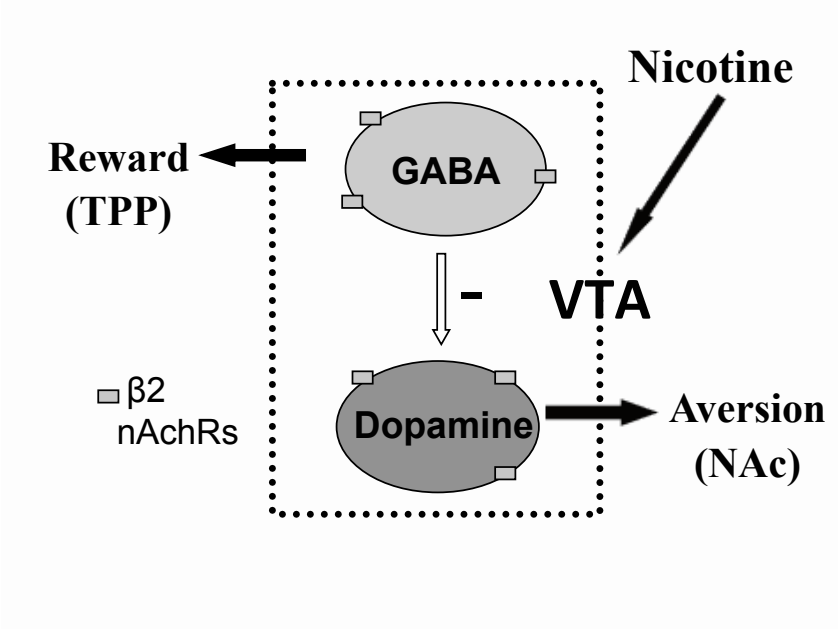

Fig. S5. Schematic summary of the VTA response to acute nicotine. Acute nicotine in nondependent mice acts on the ventral tegmental area (VTA) by activating β2 nAChRs located on the GABA and dopamine neurons. The acute nicotine reward signal is mediated by the tegmental pedunculopontine nucleus (TPP; 4), and the aversive signal by a specific pattern of dopaminergic activity at D1 receptors (5) to the nucleus accumbens (NAc). We show here that β2* nAChRs located on GABA neurons are necessary and sufficient to produce a CPP, and that the β2* nAChRs located on dopamine neurons are necessary and sufficient to produce CPA for acute nicotine.

References

1. Harrington L, Viñals X, Herrera-Solís A, Flores A, Morel C, Tolu S, Faure P, Maldonado R, Maskos U, Robledo P (2016) Role of β4* Nicotinic Acetylcholine Receptors in the Habenulo-Interpeduncular Pathway in Nicotine Reinforcement in Mice. *Neuropsychopharmacology* 41(7):1790-802.

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