**Figure Legends**

**Figure 1** Summary of theexperimental time-line as a function of postnatal day (PND). Rats arrived at PND 22, and following a 6-day habituation period, underwent jugular catheterization surgery on PND 28. A 5-day self-administration training period began following recovery on PND 30 wherein rats had fixed ratio 1 access to 20 nicotine or saline infusions/day. A 10-day extended access period began on PND 35 wherein rats had access to an unlimited number of infusions for 23-hours/day. During the 10-day abstinence period that followed, rats had 2-hour/day access to an unlocked (exercise) or locked (sedentary) running wheel (PND 45–54). After the last exercise/sedentary session, rats were returned to their self-administration boxes. Nicotine-seeking was assessed the next day on PND 55 using a within-session extinction/cue-induced reinstatement procedure.

**Figure 2** Schematic of areas within the nucleus accumbens core (AcbC; green squares) and shell (AcbS; blue squares) analyzed at approximately Bregma 1.92 mm. The orange trapezoid represents the area from each coronal slice that used to make ultrathin sections. Modified from Paxinos and Watson 2006.

**Figure 3** An example electron micrograph of neuropil from which synapses were measured. In panel **A,** a dendritic spine that connects back to the dendritic shaft (dendrite) is highlighted in red, asymmetric synapses are highlighted in blue, symmetric synapse is highlighted in green with black arrow, and a myelinated axon is highlighted in orange. In panel **B**, red arrows mark dendritic spines, the black arrow marks a spine apparatus, and asterisk marks a postsynaptic dendrite. Panel **C** shows an enlarged image of a dendritic spine (red arrow) with asymmetric and symmetric synapses. Panel **D** shows an enlarged image of an asymmetric synapse onto a dendrite (asterisk) with a clearly defined synaptic cleft. Scale bar represents 0.5 m.

**Figure 4** Behavioral data (mean ± SEM) for extended access self-administration (A and B), distance run during abstinence (C and D), and active-lever responses during extinction (E) and reinstatement testing (F). In panel A, the number of infusions obtained is plotted for each of the groups and for each of the sessions during the 10-day extended access self-administration period. An asterisk indicate a significant difference between the saline and nicotine groups. In panel B, average daily nicotine intake is plotted for each animal in the nicotine sedentary and nicotine exercise groups. In panel C, the daily distance run in kilometers (km) is plotted for each exercise session during the 10-day abstinence period. In panel D, the average daily distance run is plotted for each animal in the saline exercise and nicotine exercise groups. The active-lever responses made during all extinction sessions (Panel E) and during the last extinction session versus the reinstatement test session (Panel F) is plotted for each animal in each of the groups. In panel E, an asterisk indicates a significant difference from the saline sedentary group, and a number signs indicates a significant difference from the nicotine sedentary group. n = 3 (saline, sedentary and exercise) or 4 (nicotine, sedentary and exercise). Exer, exercise; Nic, nicotine; Sal, saline; Sed, sedentary.

**Figure 5** Volumetric density (mean ± SEM) of asymmetric synapses onto dendrites (A and E), symmetric synapses onto dendrites (B and F), asymmetric synapses onto spines (C and G), and symmetric synapses onto spines (D and H) within the core (A-D) and shell (E-H). Data are based on average densities for each of the three regions within the core and shell for each of the rats in the saline (n = 3) and nicotine (n = 4) groups (data points are shown for each rat for each of the three regions). An asterisk indicates a significant difference from the saline sedentary group (Panel A), and a number signs indicates a significant difference from the nicotine sedentary group (Panels A and B). Exer, exercise; Nic, nicotine; Sal, saline; Sed, sedentary.

**Figure 6** Association between total active-lever responses during extinction and the density of asymmetric (A) and symettric (B) synpases onto dendrites averaged over the three regions of the nucleus accumbens core for each subject. n = 3 (saline, sedentary and exercise) or 4 (nicotine, sedentary and exercise). Exer, exercise; Nic, nicotine; Sal, saline; Sed, sedentary.

**Figure 7** Cumulative distribution (% of total) of asymmetric synapses onto spines by length in nucleus accumbens core for each of the groups up to 1.00 µm (A), and for a focused comparison of the saline and nicotine sedentary groups (B), the nicotine sedentary and exercise groups (C), and the saline sedentary and nicotine exercise groups up to to 0.40 µm. Asterisks indicate significant differences at a p < 0.05 (\*) or 0.001 level (\*\*\*). Exer, exercise; Nic, nicotine; Sal, saline; Sed, sedentary.

**Figure 8** Cumulative distribution (% of total) of asymmetric synapses onto spines by length in nucleus accumbens shell for each of the groups up to 1.00 µm (A), and for a focused comparison of the saline and nicotine sedentary groups (B), the nicotine sedentary and exercise groups (C), and the saline sedentary and nicotine exercise groups up to to 0.40 µm. Asterisks indicate significant differences at a p < 0.05 (\*) or 0.01 level (\*\*). Exer, exercise; Nic, nicotine; Sal, saline; Sed, sedentary.