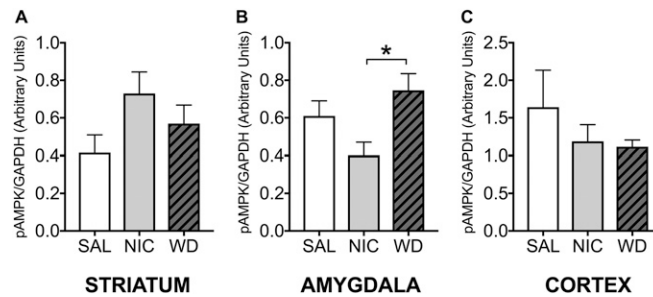
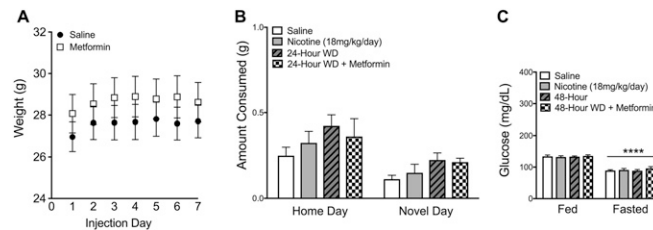


# Supporting Information

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**Fig. S1.** Relative to untreated conditions, chronic nicotine and nicotine withdrawal do not significantly alter pAMPK/GAPDH levels in the striatum, amygdala, or cortex. (A) Chronic nicotine use and nicotine withdrawal have no effect on levels of pAMPK in the striatum, as indicated by Western blot analysis ( $n = 7-8$ ). (B) Relative to chronic nicotine use, 24-h nicotine withdrawal significantly up-regulates pAMPK in the amygdala. Neither chronic nicotine use or nicotine withdrawal significantly alters pAMPK/GAPDH compared with untreated controls ( $n = 8$ ).  $*P < 0.05$ . (C) Chronic nicotine use and nicotine withdrawal have no effect on levels of pAMPK in the cortex ( $n = 8$ ).



**Fig. S2.** Systemically administered metformin has no effect on body weight, food consumption, or glucose levels under fed or fasted conditions. (A) Mice treated with seven daily i.p. injections of metformin show no differences in body weight compared with saline-injected mice ( $n = 8-9$ ). (B) Metformin treatment has no effect on the amount of a palatable food consumed in the home cage environment or in a novel environment. Chronic nicotine use and withdrawal also have no effect on consumption ( $n = 8$ ). (C) Metformin treatment has no effect on fed or fasted glucose levels in mice undergoing nicotine withdrawal. Chronic nicotine use and withdrawal also have no effect on glucose levels ( $n = 7-9$ ). Across conditions, glucose levels were lower under fasted conditions than under fed conditions. Bars represent mean latency  $\pm$  SEM.  $****P < 0.0001$ .