Supplemental Methods

Behavioral procedure. Training and testing were conducted during the dark portion of the light/dark cycle. One week post-surgery rats were trained once a day to respond for electrical brain stimulation. After ICSS training and establishment of stable baseline ICSS thresholds, rats were prepared with a chronic intravenous catheter and 5 days later were food-restricted and trained for 4 days to press a lever to obtain food pellets. After food-training, rats were returned to ad libitum food. Two days later, 20 rats were tested for cocaine self-administration during two consecutive phases: a screening phase (1 day) and an escalation phase (12 days). Six other rats (drug naive controls) were exposed to the same experimental procedure, except that they were never exposed to cocaine. During the screening phase, the 20 rats tested for self-administration were allowed to self-administer cocaine during only one hour on a fixed-ratio 1 schedule (0.25 mg/injection in a volume of 0.1 ml delivered in 4 sec) after which two balanced groups with the same weight, cocaine intake and ICSS reward thresholds were formed. During the escalation phase, these two groups had differential access to cocaine self-administration (1 hour versus 6 hours). Starting 10 days before the beginning of the escalation phase, ICSS reward thresholds were measured two times a day to habituate the rats to the procedure before the start of the escalation phase. Each ICSS session lasted about 30 min. All thresholds were converted to percent change from each animal’s average baseline threshold measured during the baseline phase that occurred the day before the escalation phase.

Computation of slope coefficients. Since total intake increased continuously from session 3 to 11, individual slope coefficients were computed by fitting the data obtained over this time period with a linear function that accounted for more than 70% of the variance in 10 out of the
11 LgA rats tested (mean: 82%; range: 71-98%). One rat was excluded from the regression analysis because this function explained less than 10% of the variance in the data obtained in this rat. The same analysis was applied to ICSS data.