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Amphetamine-sensitized rats show sugar-induced hyperactivity (cross-sensitization) and sugar hyperphagia

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Abstract

The goal was to determine the locomotor and consummatory effects of sugar in amphetamine-sensitized rats. Following a 30-min locomotor activity baseline using a photocell cage, male rats were administered either 3.0 mg/kg amphetamine or saline i.p. daily for 6 days. On the final day of injections, locomotor activity was measured again to affirm amphetamine sensitization. *Experiment 1*: Seven days later, half of each group was offered 10% sucrose or water for 1 min in the home cages, followed by a 30-min locomotor activity test to determine whether or not the animals had become hyperactive in response to sugar. Results showed that amphetamine-sensitized animals were hyperactive following a taste of sugar, but not water. *Experiment 2*: All subjects were then given access to 10% sucrose for 1 h daily for five consecutive days. Results showed that the amphetamine-sensitized group consumed more sucrose across the 5-day measurement period. These results suggest that sugar may be acting on the same system as amphetamine to trigger hyperactivity, and that alterations in this system caused by repeated doses of amphetamine can instigate an appetite for sugar that persists for at least a week.

Keywords: Cross-sensitization; Amphetamine; Sucrose; Sugar; Addiction

1. Introduction

Behavioral sensitization is defined as an increase in the locomotor-stimulating effect of a drug after repeated administration (Robinson and Becker, 1986; Stewart and Badiani, 1993). This phenomenon has been observed with several drugs of abuse, including cocaine, morphine and alcohol (Shuster et al., 1977; Hinson and Poulos, 1981; Cornish and Kalivas, 2001; Babbini and Davis, 1972; Brady and Holtzman, 1981; Powell and Holtzman, 2001; Hoshaw and Lewis, 2001; Lessov et al., 2001a; Fish et al., 2002). Drug-induced sensitization has also been associated with increased drug self-administration (Lessov et al., 2001b; White and Holtzman, 2001) and implicated as a factor contributing to drug addiction (Robinson and Berridge, 1993).

Animals sensitized to a particular drug will often show increased locomotor activity in response to a different drug of the same class. This phenomenon, known as cross-sensitization, has been demonstrated across several drugs of abuse, including amphetamine with cocaine or phencyclidine (PCP) (Pierce and Kalivas, 1995; Kalivas and Weber, 1988; Schenk et al., 1991; Greenberg and Segal, 1985), cocaine with alcohol (Itzhak et al., 1999; Itzhak and Martin, 1999) or MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) and heroin with cannabis (Pontieri et al., 2001).

In addition to hyperactivity, numerous clinical and animal studies have found that sensitization to one drug will lead to subsequent increased intake of another (Henningfiled et al., 1990; Liguori et al., 1997; Hubbell et al., 1993; Nichols et al., 1991; Volpicelli et al., 1991). In addition, sensitization to morphine injected into the nucleus accumbens (NAc) has been implicated in increasing the consumption of sweet, palatable foods (Bakshi and Kelley, 1994).

Ingestion of palatable foods releases opioids (Tanda and Di Chiara, 1998) and dopamine (DA) in the limbic system (Hernandez and Hoebel, 1988a,b; Radhakishun et al., 1988; Salamone et al., 1994). It is believed that enhanced mesolimbic dopaminergic neurotransmission plays a key role in the behavioral effects of cross-sensitization. Sugar has been shown to have behavioral and neural effects similar in some cases to drugs of abuse. Colantuoni et al. (2001)

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found that rats maintained on a diet of intermittent access to sugar and chow developed a pattern of excessive intake with bingeng during the first hour of daily access. Increased D_1 and mu-opioid binding and decreased D_2 receptor binding in the NAc were observed. In addition, somatic, behavioral and neurochemical evidence of withdrawal from sugar was seen in these animals (Colantuoni et al., 2002). Since the neurochemical and behavioral adaptations observed with sugar dependence are similar to those that occur during psychostimulant sensitization, it was hypothesized that amphetamine and sugar would cross-sensitize with each other. If so, this would lend further support to the theory that palatable foods such as sugar can have addictive properties.

2. Method

2.1. Experiment 1: Amphetamine–sugar cross-sensitization

2.1.1. Animals and equipment

Forty male Sprague–Dawley rats weighing 225–250 g were obtained from Taconic Farms (Germantown, NY) and housed individually on a reversed 12-h-light/12-h-dark cycle. Food and water were available ad libitum throughout the experiment. Locomotor activity was measured in a 43.2 × 43.2-cm open-field activity chamber (MED Associates, Georgia, VT) with 30.5 cm high acrylic sidewalls and 16 infrared photocells on each of the three axes. All procedures were approved by the Institutional Animal Care and Use Committee.

2.1.2. Locomotor activity measures

All locomotor activity tests were conducted during the fourth hour of the dark period. Baseline locomotor activity measurement was obtained on Day 1. Animals were allowed to habituate in the activity chamber for 15 min and then were administered an i.p. injection of saline. Fifteen minutes later, activity counts were measured for 30 min. Counts were quantified as the number of infrared beam breaks. Beginning on Day 2, subjects ($n = 20$/group) were administered saline or 3.0 mg/kg i.p. amphetamine sulfate in saline (Supreme Pharmaceutical) for six consecutive days to induce sensitization according to the technique of Wyvell and Berridge (2001). On the last day of injections (Day 7), animals were placed in the activity cage immediately after the injection, and 15 min later, locomotor activity was measured for 30 min. Seven days later, half of each group was offered 1-min access to 10% sucrose, and the other half received water, in their home cages. The experimenter would watch each subject and start and stop a timer while each animal was drinking. Once the animal began to drink, another timer would begin for 3 min, so that each animal could drink for a total of 1 min, but could take no longer than 3 min to do so. The amount of each animal's intake of sucrose was recorded. Subjects were immediately placed in the locomotor activity chamber, and 15 min later, activity counts were measured for 30 min.

2.2. Experiment 2: Subsequent consumption of sucrose

After the final activity measurement, all subjects (amphetamine-sensitized and saline-treated, $n = 20$/group) were returned to their home cages and were presented with free access to 10% sucrose in a bottle for 1 h during the sixth hour of the dark period for each of the next 5 days. Sucrose intake was recorded at the end of each 1-h access period.

2.3. Data analysis

2.3.1. Experiment 1

Locomotor activity counts were normalized to baseline (Day 1) for each rat. Locomotor activity data were analyzed with a two-way ANOVA (treatment × taste) and data for sugar and water taste consumption were analyzed with unpaired t tests.

2.3.2. Experiment 2

Sucrose intake data were analyzed using a two-way ANOVA (treatment × day). Post hoc Tukey HSD tests were used in both experiments when justified.

3. Results

3.1. Experiment 1: Amphetamine cross-sensitization shown as sugar-induced hyperactivity

After 6 days of amphetamine injections, Day 7 locomotor activity results found all amphetamine-sensitized animals were hyperactive compared to both baseline (Day 1) as well as saline-treated animals [$F(1,76) = 14.34$, $P < .01$]. There was no differences between the amphetamine-sensitized animals that would later receive a taste of

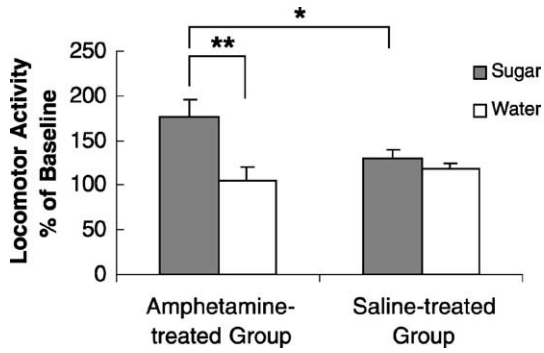

Fig. 1. Comparison of the taste of sucrose vs. the taste of water on locomotor activity 7 days after treatment with amphetamine or saline. Amphetamine-sensitized rats were more active after a taste of sugar than water ($P < .01$). Saline-treated rats did not show this effect.

water and the ones that would later taste sugar (P=.58). Additionally, there was also no difference between saline-treated animals that would later receive a taste of sugar or water (P=.57) or their activity levels compared to baseline (P=.84).

All rats in the experiment tasted the sugar or water, whichever was available. There was no difference between the groups that received amphetamine treatment and those that received saline treatment in the amount of sugar or water consumed during the 1 min of drinking during the 3-min access period [means: 2.6 ± 0.3 and 2.4 ± 0.5 ml of sucrose, respectively (P=.73); 1.3 ± 0.4 and 1.0 ± 0.3 ml of water, respectively (P=.55)].

The main effect was a significant interaction between drug treatment (amphetamine or saline) and fluid intake (sugar or water) during the final activity measurement 7 days after treatment had stopped [$F(1,36) = 5.5$, $P < .03$]. Amphetamine-sensitized rats showed an increased locomotor response to the taste of sugar as opposed to water ($P < .01$) (Fig. 1). The effect was also significant compared to saline-treated animals that received sugar ($P < .05$). Saline-treated animals showed a small increase in locomotor activity when challenged with sugar, but this was not significantly different than the effect of tasting water (P=.13).

3.2. Experiment 2: Amphetamine-sensitized animals consume more sugar than saline-treated animals

Animals treated with amphetamine a week earlier consumed more sugar in 1-h tests during the 5-day test period than animals previously treated with saline [$F(1,190) = 18$, $P < .01$] (Fig. 2). Both groups progressively increased their intake of sucrose over the 5-day period. Amphetamine-sensitized rats consumed more sucrose than saline-treated rats on the first, third and last day of testing (Day 1: $P < .05$; Day 3: $P < .05$; Day 5: $P < .05$).

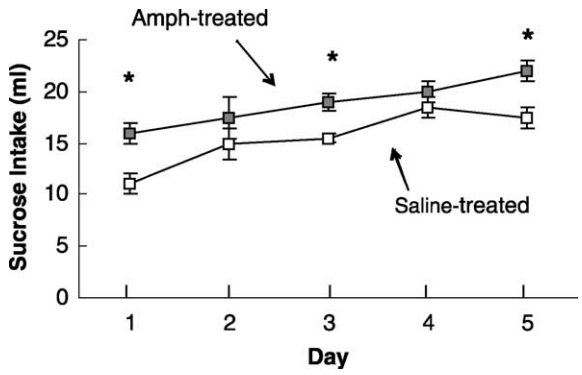

Fig. 2. Sucrose intake each day for 5 days during 1-h access periods subsequent to treatment with amphetamine or saline. Amphetamine-sensitized rats drank significantly more sucrose than saline-treated rats over the 5-day test period, specifically on Days 1, 3 and 5 ($P < .01$).

4. Discussion

Amphetamine-sensitized rats were more active than controls in response to drinking sugar for 1 min. Amphetamine-sensitized rats given access to a taste of water did not show this effect (Fig. 1). Thus, the results of the first experiment demonstrate that a taste of sugar can cause an increase in the locomotor activity of amphetamine-sensitized rats, indicative of cross-sensitization. These findings are similar to those observed when amphetamine cross-sensitizes with drugs of abuse (Pierce and Kalivas, 1995; Kalivas and Weber, 1988; Schenk et al., 1991; Greenberg and Segal, 1985).

Repeated treatment with morphine, cocaine, amphetamine or ethanol has been shown to induce long-lasting changes in NAc dopaminergic functions (Robinson et al., 1988; Kalivas and Duffy, 1993; Spanagel et al., 1993; Kalivas and Stewart, 1991). With stimulants, the terminal regions of the mesolimbic DA system adapt by increasing D_1 receptor binding, decreasing basal DA transmission and enhancing DA release in response to the drugs (Imperato et al., 1996; Vanderschuren and Kalivas, 2000). With opiates, there is a decrease in D_2 receptor sensitivity and increasing D_1 and mu-opioid receptor binding that may enhance the effects of an opiate drug (Unterwald, 2001; Unterwald et al., 2001). Sensitization of DA transmission in the NAc may be specific to the core region in both stimulant and opiate-induced sensitization (Cadoni and Di Chiara, 1999; Cadoni et al., 2000).

Repeated exposure to DA agonist drugs (amphetamine sensitization) produces a state of intermittent DA activation followed by periods of low basal DA transmission (Weiss et al., 1997; Imperato et al., 1996; Amano et al., 2002). Intermittent activation of the mesolimbic DA system, in the context of low DA transmission, may facilitate drug sensitization (Koob and Le Moal, 2001). Supersensitive D_1 receptors in the NAc are thought to be involved in the long-term persistence of the sensitized response (Henry and White, 1991, 1995). In the present study, a taste of sugar may be releasing DA in a manner that stimulates supersensitive D_1 receptors in amphetamine-sensitized animals, resulting in an increased locomotor response. It is interesting that taste-induced hyperactivity was observed a week after the last injection of amphetamine.

The results of the second experiment indicate that amphetamine-sensitized rats have an appetite for sugar when they taste it (Fig. 2). This finding is analogous to previous research which found that sensitization to one drug could increase voluntary intake of another drug of the same class (Lessov et al., 2001b; White and Holtzman, 2001; Henningfiled et al., 1990; Liguori et al., 1997; Hubbell et al., 1993; Nichols et al., 1991; Volpicelli et al., 1991). Other studies have found this effect with non-drug substances. Behavioral cross-sensitization between cocaine and stress has been demonstrated (Prasad et al., 1998; Covington and Miczek, 2001; Antelman and Caggiula, 1977). In addition,

increases in food intake (Bakshi and Kelley, 1994) and sexual behaviors (Fiorino and Phillips, 1999a,b; Nocjar and Panksepp, 2002) have been observed in animals with a history of drug sensitization. The present study found that amphetamine sensitization increased subsequent consumption of a palatable food, namely sugar, a week later.

The mechanism for this increase in appetite is probably the same as described above for cross-sensitization of sugar-induced locomotion. The taste of sugar may release DA that acts in a system with increased D_1 receptor binding in the mesolimbic DA system, decreased basal DA transmission and enhanced DA release (Imperato et al., 1996; Vanderschuren and Kalivas, 2000), thus producing an enhanced DA-mediated appetite. A similar process could be occurring in an opiate system.

The present results suggest that the neural changes caused by intermittent amphetamine occur in a system that subserves an animal's reaction to sugar, and perhaps, any very palatable food. To the extent that sugar and amphetamine act alike, one might surmise that intermittent sugar could lead to dependency. Recent work in this laboratory has found that intermittent sugar intake can up-regulate D_1 and mu-opioid receptors in the NAc core and shell regions much like amphetamine and cocaine (Colantuoni et al., 2001). Such animals show behavioral and neurochemical signs of opiate withdrawal when given naloxone (Colantuoni et al., 2002). It is suggested that prolonged intermittent exposure to sugar (e.g., 12 h each day for 30 days) leads to these neural changes such that bursts of sugar ingestion produce intense activation in the same systems as those which cause amphetamine sensitization and amphetamine dependency.

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References

Amano T, Matsubayashi H, Sasa M. Alteration of neuronal activities following repeated administration of stimulants. Nihon Arukoru, Yakubutsu Igakkai Zasshi 2002;37:31–40.

Antelman SM, Caggiula AR. Norepinephrine–dopamine interactions and behavior. Science 1977;195:646–53.

Babbini M, Davis WM. Time–dose relationships for locomotor activity effects of morphine after acute or repeated treatment. Br J Pharmacol 1972;46:213–24.

Bakshi VP, Kelley AE. Sensitization and conditioning of feeding following multiple morphine microinjections into the nucleus accumbens. Brain Res 1994;648:342–6.

Brady LS, Holtzman SG. Locomotor activity in morphine-dependent and post-dependent rats. Pharmacol Biochem Behav 1981;14:361–70.

Cadoni C, Di Chiara G. Reciprocal changes in dopamine responsiveness in the nucleus accumbens shell and core and in the dorsal caudate-putamen in rats sensitized to morphine. Neuroscience 1999;90:447–55.

Cadoni C, Solinas M, Di Chiara G. Psychostimulant sensitization: differential changes in accumbal shell and core dopamine. Eur J Pharmacol 2000;388:69–76.

Colantuoni C, Schwenker J, McCarthy J, Rada P, Ladenheim B, Cadet JL, et al. Excessive sugar intake alters binding to dopamine and mu-opioid receptors in the brain. NeuroReport 2001;12:3549–52.

Colantuoni C, Rada P, McCarthy J, Patten C, Avena NM, Chadeayne A, et al. Evidence that intermittent, excessive sugar intake causes endogenous opioid dependence. Obes Res 2002;10:478–88.

Cornish JL, Kalivas PW. Repeated cocaine administration into the rat ventral tegmental area produces behavioral sensitization to a systematic cocaine challenge. Behav Brain Res 2001;126:205–9.

Covington HE, Miczek KA. Repeated social-defeat, stress, cocaine or morphine. Effects on behavioral sensitization and intravenous cocaine self-administration "binges". Psychopharmacology (Berlin) 2001;158:388–98.

Fiorino DF, Phillips AG. Facilitation of sexual behavior and enhanced dopamine efflux in the nucleus accumbens of male rats after D-amphetamine-induced behavioral sensitization. J Neurosci 1999a;19:456–63.

Fiorino DF, Phillips AG. Facilitation of sexual behavior in male rats following D-amphetamine-induced behavioral sensitization. Psychopharmacology (Berlin) 1999b;142:200–8.

Fish EW, DeBold JF, Miczek KA. Repeated alcohol: behavioral sensitization and alcohol-heightened aggression in mice. Psychopharmacology (Berlin) 2002;160:39–48.

Greenberg BD, Segal DS. Acute and chronic behavioral interactions between phencyclidine (PCP) and amphetamine: evidence for a dopaminergic role in some PCP-induced behaviors. Pharmacol Biochem Behav 1985;23:99–105.

Henningfiled JE, Clayton R, Pollin W. Involvement of tobacco in alcoholism and illicit drug use. Br J Addict 1990;85:279–91.

Henry DJ, White FJ. Repeated cocaine administration causes persistent enhancement of D1 dopamine receptor sensitivity within the rat nucleus accumbens. J Pharmacol Exp Ther 1991;258:882–90.

Henry DJ, White FJ. The persistence of behavioral sensitization to cocaine parallels enhanced inhibition of nucleus accumbens neurons. J Neurosci 1995;15:6287–99.

Hernandez L, Hoebel BG. Feeding and hypothalamic stimulation increase dopamine turnover in the accumbens. Physiol Behav 1988a;44:599–606.

Hernandez L, Hoebel BG. Food reward and cocaine increase extracellular dopamine in the nucleus accumbens as measured by microdialysis. Life Sci 1988b;42:1705–12.

Hinson RE, Poulos CX. Sensitization to the behavioral effects of cocaine: modification of Pavlovian conditioning. Pharmacol Biochem Behav 1981;15:559–62.

Hoshaw BA, Lewis MJ. Behavioral sensitization to ethanol in rats: evidence from the Sprague–Dawley strain. Pharmacol Biochem Behav 2001;68:685–90.

Hubbell CL, Mankes RF, Reid LD. A small dose of morphine leads rats to drink more alcohol and achieve higher blood alcohol concentrations. Alcohol Clin Exp Res 1993;17:1040–3.

Imperato A, Obinu MC, Carta G, Mascia MS, Casu MA, Gessa GL. Reduction of dopamine release and synthesis by repeated amphetamine treatment: role in behavioral sensitization. Eur J Pharmacol 1996;317:231–7.

Itzhak Y, Martin JL. Effects of cocaine, nicotine, dizocipline and alcohol on mice locomotor activity: cocaine–alcohol cross-sensitization involves upregulation of striatal dopamine transporter binding sites. Brain Res 1999;818:201–11.

Itzhak Y, Martin JL, Black MD, Ali SF. Effect of dopaminergic neurotoxin MPTP on cocaine-induced locomotor sensitization. Pharmacol Biochem Behav 1999;73:101–7.

Kalivas PW, Duffy P. Time course of extracellular dopamine and behavioral sensitization to cocaine: I. Dopamine axon terminals. J Neurosci 1993;13:266–75.

Kalivas PW, Stewart J. Dopamine transmission in the initiation and expres-

sion of drug- and stress-induced sensitization of motor activity. Brain Res Brain Res Rev 1991;16:223–44.
Kalivas PW, Weber B. Amphetamine injection into the ventral mesencephalon sensitizes rats to peripheral amphetamine and cocaine. J Pharmacol Exp Ther 1988;245:1095–102.
Koob GF, Le Moal M. Drug addiction, dysregulation of reward, and allostasis. Neuropsychopharmacology 2001;24:97–129.
Lessov CN, Palmer AA, Quick EA, Phillips TJ. Voluntary ethanol drinking in C57/BL/6J and DBA/2J mice before and after sensitization to the locomotor stimulant effects of ethanol. Psychopharmacology (Berlin) 2001a;155:91–9.
Lessov CN, Risinger FO, Phillips TJ. Attenuation of ethanol-induced conditioned taste aversion in mice sensitized to the locomotor stimulant effects of ethanol. Behav Neurosci 2001b;115:146–53.
Liguori A, Hughes JR, Goldberg K, Callas P. Subjective effects of oral caffeine in formerly cocaine-dependent humans. Drug Alcohol Depend 1997;39:17–24.
Nichols ML, Hubbell CL, Kalsher NJ, Reid LD. Morphine increases intake of beer among rats. Alcohol 1991;8:237–40.
Nocjar C, Panksepp J. Chronic intermittent amphetamine pretreatment enhances future appetitive behavior for drug- and natural-reward: interaction with environmental variables. Behav Brain Res 2002;128:189–203.
Pierce RC, Kalivas PW. Amphetamine produces sensitized increases in locomotion and extracellular dopamine preferentially in the nucleus accumbens shell of rats administered repeated cocaine. J Pharmacol Exp Ther 1995;275:1019–29.
Pontieri FE, Monnazzi P, Scontrini A, Buttarelli FR, Patacchioli FR. Behavioral sensitization to heroin by cannabinoid pretreatment in the rat. Eur J Pharmacol 2001;421:R1–3.
Powell KR, Holtzman SG. Parametric evaluation of development of sensitization to the effects of morphine on locomotor activity. Drug Alcohol Depend 2001;62:83–90.
Prasad BM, Ulibarri C, Sorg BA. Stress-induced cross-sensitization to cocaine: effect of adrenalectomy and corticosterone after short- and long-term withdrawal. Psychopharmacology (Berlin) 1998;136:24–33.
Radhakishun FS, van Ree JM, Westerink BH. Scheduled eating increases dopamine release in the nucleus accumbens for food-deprived rats as assessed with on-line brain dialysis. Neurosci Lett 1988;85:351–6.
Robinson TE, Becker JB. Enduring changes in brain and behavior produced by chronic amphetamine administration: a review and evaluation of animal models of amphetamine psychosis. Brain Res 1986;396:157–98.
Robinson TE, Berridge KC. The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain Res Brain Res Rev 1993;18:247–91.
Robinson TE, Jurson PA, Bennett JA, Bentgen KM. Persistent sensitization to dopamine neurotransmission in ventral striatum (nucleus accumbens) produced by prior experience with (+)-amphetamine: a microdialysis study in freely moving rats. Brain Res 1988;462:211–22.
Salamone JD, Cousins MS, McCullough LD, Carriero DL, Berkowitz RJ. Nucleus accumbens dopamine release increases during instrumental level pressing for food but not free food consumption. Pharmacol Biochem Behav 1994;49:25–31.
Schenk S, Snow S, Horger BA. Pre-exposure to amphetamine but not nicotine sensitizes rats to the motor activating effects of cocaine. Psychopharmacology (Berlin) 1991;103:62–6.
Shuster L, Yu G, Bates A. Sensitization to cocaine stimulation in mice. Psychopharmacology (Berlin) 1977;52:185–90.
Spanagel R, Almeida OF, Shippenberg TS. Long lasting changes in morphine-induced mesolimbic dopamine release after chronic morphine exposure. Synapse 1993;14:243–5.
Stewart J, Badiani A. Tolerance and sensitization to the behavioral effects of drugs. Behav Pharmacol 1993;4:289–312.
Tanda G, Di Chiara G. A dopamine-mu1 opioid link in the rat ventral tegmentum shared by palatable food (Fonzies) and non-psychostimulant drugs of abuse. Eur J Neurosci 1998;10:1179–87.
Unterwald EM. Regulation of opioid receptors by cocaine. Ann NY Acad Sci 2001;937:74–92.
Unterwald EM, Kreek MJ, Cuntapay M. The frequency of cocaine administration impacts cocaine-induced receptor alterations. Brain Res 2001;900:103–9.
Vanderschuren LJ, Kalivas PW. Alterations in dopaminergic and glutamatergic transmission in the induction and expression of behavioral sensitization: a critical review of preclinical studies. Psychopharmacology (Berlin) 2000;151:99–120.
Volpicelli JR, Ulm RR, Hopson N. Alcohol drinking in rats during and following morphine injections. Alcohol 1991;8:289–92.
Weiss F, Imperato A, Casu MA, Mascia MS, Gessa GL. Opposite effects of stress on dopamine release in the limbic system of drug-naïve and chronically amphetamine-treated rats. Eur J Pharmacol 1997;337:219–22.
White DA, Holtzman SG. Acute opioid pretreatment potentiates naltrexone-induced drinking suppression in water-deprived rats. J Pharmacol Exp Ther 2001;298:156–64.
Wyvell CL, Berridge KC. Incentive sensitization by previous amphetamine exposure: increased cue-triggered "wanting" for sucrose reward. J Neurosci 2001;21:7831–40.