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Individual differences in sugar intake predict the locomotor response to acute and repeated amphetamine administration

Terrence L. Sills, F.J. Vaccarino

Psychology Department, University of Toronto, 100 St. George St., Toronto, Ontario M5S 1A1, Canada

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Abstract. Rats exhibit profound individual differences in their propensity to ingest sugar and in their locomotor response to AMP. Intrinsic variation in the responsiveness of mesolimbic dopamine mechanisms has been suggested to account for these individual differences. In light of this overlap, it might be expected that individual differences in one behavior would predict individual differences in the other. The present study determined whether individual differences in sugar intake would predict individual differences in the locomotor response to AMP. Male Wistar rats were divided into low and high feeders based on a median split of their sugar intake in response to saline administration and were subsequently tested for their locomotor response to either 1.0 or 1.75 mg/kg AMP in experiment 1. High sugar feeders exhibited significantly more locomotion than low sugar feeders in response to 1.75 mg/kg AMP. This difference was observed immediately after injection and continued for approximately 90 min. There was no difference between the two groups in their locomotor response to 1.0 mg/kg AMP. In experiment 2, rats receiving 1.0 mg/kg AMP in experiment 1 were tested for the development of behavioral sensitization with repeated AMP administrations. Rats were administered 1.0 mg/kg AMP across 5 test days, interspersed with days in which they received AMP treatment in their home cages to minimize conditioning effects. High sugar feeders exhibited greater behavioral sensitization than low sugar feeders with repeated AMP administration. Starting on test day 3, high sugar feeders exhibited significantly greater AMP-induced locomotor activity than low sugar feeders. Taken together, these findings support the notion that there is overlap in the neurobiological substrates regulating sugar intake and responsivity to the locomotor activating effect of AMP. Furthermore, these results establish that the propensity to ingest sugar is a predictor of the susceptibility to the locomotor enhancing properties of AMP.

Correspondence to: F.J. Vaccarino

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Amphetamine's (AMP) primary neurobiological action is to increase catecholaminergic transmission. Treatment with AMP has been shown to affect multiple behaviors, including locomotor activity and feeding, via its action on brain catecholaminergic systems. Investigations into AMP's loci of action show that there is considerable overlap in the neuroanatomical substrates mediating AMP's effects on locomotion and feeding. Specifically, stimulation of dopamine (DA) activity in the nucleus accumbens (Acc) is one mechanism through which AMP has been shown to affect both locomotion (Kelly et al. 1975; Pijnenburg et al. 1975; Joyce and Koob 1981; Vaccarino et al. 1986; Jones and Robbins 1992; Weissenborn and Winn 1992; Whishaw et al. 1992) and feeding (Carr and White 1986; Evans and Vaccarino 1986 and 1990; Colle and Wise 1988; Sills and Vaccarino 1991; Sills et al. 1993).

Recent evidence indicates that rats exhibit significant individual differences in response to AMP when either food intake or locomotion is the measure. For instance, Sills and Vaccarino (1991) and Sills et al. (1993) found that AMP stimulated sugar intake in rats with low baseline sugar intake levels and inhibited sugar intake in rats with high baseline sugar intake levels. Moreover, intra-Acc administration of alpha-flupenthixol, a DA receptor antagonist, reduced sugar intake in rats expressing AMP-facilitated intake as well as in rats with naturally elevated intake (Sills et al. 1993).

To account for their findings, Sills and Vaccarino (1991) and Sills et al. (1993) proposed that high sugar feeders express more Acc-DA activity than low sugar feeders. In light of the U-shaped response function relating DA activity and feeding (Heffner et al. 1977), it has been proposed that administration of a low dose of AMP to high sugar feeders induces a state of DA hyperstimu-

lation resulting in anorexia (Sills and Vaccarino 1991; Sills et al. 1993). In contrast, the same dose of AMP administered to low sugar feeders, on the other hand, produces a level of DAergic activation sufficient to stimulate feeding.

Individual differences in the locomotor response to AMP have been reported by a number of researchers. For example, Piazza et al. (1989) divided rats into two groups, a low responding (LR) group and a high responding (HR) group, based on a median split of their locomotor response to a novel environment. Piazza et al. subsequently examined the hyperlocomotion induced by a 1.5 mg/kg dose of AMP administered to these two groups of animals and found that HR rats exhibited a higher locomotor response to AMP than did LR rats. These findings have since been replicated by Hooks et al. (1991a) for both 0.5 and 1.0 mg/kg AMP. Moreover, Hooks et al. (1991a) found that HR rats, but not LR rats, exhibited significant sensitization to the locomotor activating effect of 1.0 mg/kg AMP with repeated treatments.

Piazza et al. (1990b 1991b) have provided direct evidence that intrinsic differences in the responsiveness of the mesolimbic DA system are associated with individual differences in responsivity to AMP treatment. Piazza et al. (1990b 1991b) have shown that HR animals exhibit a higher DOPAC/DA ratio in the Acc than LR animals under basal conditions, as well as in response to a novel environment. Similarly, Hooks et al. (1991b), utilizing in vivo microdialysis, have demonstrated that HR animals exhibit higher DA release in the Acc than LR animals under basal conditions, as well as in response to cocaine treatment. Thus, high AMP-responding animals exhibit greater Acc-DAergic activity than low AMP-responding animals under both basal and stimulated conditions.

In light of the overlap in the neural substrates regulating feeding and AMP locomotion, it might be expected that individual differences in one behavior would be predictive of individual differences in the other. The present experiment was developed to test this possibility. Specifically, the present experiment determined whether an animal's propensity to ingest sugar would be predictive of that animal's locomotor response to AMP treatment. Since both high sugar feeders and HR rats are thought to express higher levels of DA activity than low sugar feeders and LR rats, it was predicted that high sugar feeders would express more AMP-induced locomotion than low sugar feeders.

In a second experiment, the prospect that sugar intake level would also be a predictor of individual differences in the development of behavioral sensitization to repeated AMP administrations was assessed.

Experiment 1

To determine whether individual differences in sugar intake would predict the magnitude of the locomotor response to AMP, low and high sugar feeders were tested for their locomotor response to either 1.0 or 1.75 mg/kg AMP.

Method

Subjects. Sixty-six male Wistar rats (Charles River, Quebec) weighing approximately 250–300 g at the start of the experiment were housed in a temperature and light controlled environment, with lights on-off at 0700–1900 h. Rats had ad lib access to water and standard Purina lab chow pellets throughout the experiment, unless otherwise stated.

Procedure

Feeding phase. The experiment was divided into two phases. In the first phase, the feeding phase, animals' intake of powdered Purina lab chow and granulated sugar was determined. For 7 days, animals were presented with powdered lab chow and granulated sugar for 1 h (1500–1600) each day; for the remaining 23 h of each day, rats had ad lib access to standard Purina lab pellets. On day 8, animals were injected with 0.9% saline, in a volume of 1 ml/kg, immediately prior to presentation of the powdered lab chow and the granulated sugar. Intake was subsequently measured for 1 h. Animals were then divided into two groups based on a median split of their intake of sugar on day 8.

Locomotion phase. In the second phase of the experiment, animals were tested for their locomotor response to either 1.0 ($n = 32$) or 1.75 ($n = 34$) mg/kg AMP. Half of the animals in each drug condition were characterized as low sugar feeders and the other half as high sugar feeders.

Apparatus. To measure locomotion, eight photocell beam cages housed in another room were utilized. The cages measured 34 cm×33 cm, with two photocell beams placed 3 cm above the floor, with one beam located 11 cm from the front of the cage and the other beam located 11 cm from the back of the cage. The floor and back wall of the cages were constructed out of wire mesh, with the sides made of metal. The top and front of the cages were constructed out of Plexiglas. Each well measured 6 cm×6 cm and they were spaced 4 cm apart. The cages were interfaced with a computer located in another room that recorded photocell beam interruptions as counts.

Due to the number of available cages, a maximum of eight animals were tested at any one time; each group (low and high feeders) were represented equally on test days. On the first day of testing, animals were removed from their home cages and transported to the room housing the cages with the photocell beams. Animals were placed into the cages and locomotor activity recorded for a period of 3 h (1500–1800 hours). On the second test day, animals were again placed in the photocell beam cages for a 3-h adaptation period (1200–1500 hours). Subsequent to this adaptation period, animals were administered *d*-AMP at a dose of either 1.0 mg/ kg or 1.75 mg/kg and locomotor activity measured for another 3 h (1500–1800 hours).

Data were analysed with Student's *t*-test and analysis of variance (ANOVA) with post-hoc comparisons carried out with the Least Significant Difference test. In all cases the 0.05 level of significance was used.

Results

1.0 mg/kg AMP

Feeding phase. As in previous studies (Sills and Vaccarino 1991; Sills et al. 1993), rats ate mostly sugar and thus the results reported below are for sugar intake. A two-way ANOVA was carried out to examine the amount

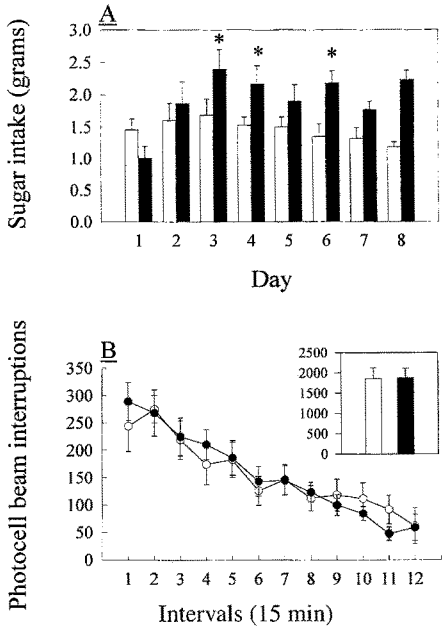

Fig. 1. A Sugar intake across the 7-day adaptation period exhibited by animals receiving 1.0 mg/kg amphetamine treatment. Animals were characterized as low (□) and high (■) sugar feeders based on a median split of their sugar intake in response to saline administration on day 8 (see text for further clarification). **B** Mean number of photocell beam interruptions across the 3-h test period in response to 1.0 mg/kg amphetamine exhibited by low (○) and high (●) sugar feeders (*inset*: total photocell beam interruptions). * Significantly higher than low sugar feeders

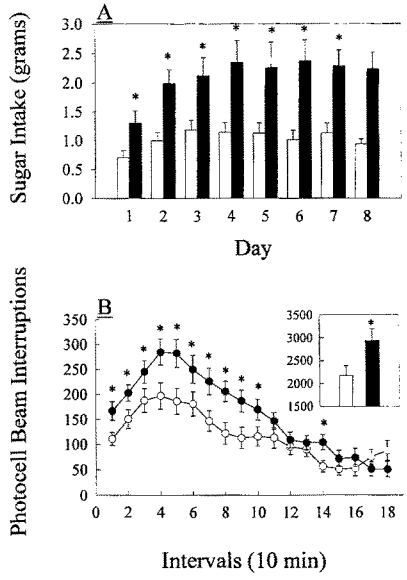

Fig. 2. A Sugar intake across the 7-day adaptation period exhibited by animals receiving 1.75 mg/kg amphetamine treatment. Animals were characterized as low (□) and high (■) sugar feeders based on a median split of their sugar intake in response to saline administration on day 8 (see text for further clarification). **B** Mean number of photocell beam interruptions across the 3-h test period in response to 1.75 mg/kg amphetamine exhibited by low (○) and high (●) sugar feeders (*inset*: total photocell beam interruptions). * Significantly higher than low sugar feeders

of sugar consumed on the previous seven days (adaptation period) in the two groups. The ANOVA revealed a significant group×day interaction, [$F(6, 180) = 3.194$]. As can be seen in Fig. 1a, starting on day 2, high sugar feeders consumed more sugar than low sugar feeders with this difference reaching statistical significance on days 3, 4, and 6.

Locomotion phase. Examination of the locomotor data revealed that low and high sugar feeders exhibited almost identical levels of total activity in response to 1.0 mg/kg AMP [$t(30) = 0.348$], (Fig. 1b). To examine the temporal aspects of the locomotor response to AMP administration, the 3-h test session was broken down into nine intervals of 20 min in duration. Once again, the ANOVA revealed no significant group effect [$F(1,29) < 1.0$] or group×interval interaction [$F(8,232) < 1.0$] (see Fig. 1b). There was a significant main effect of interval, [$F(8, 232) = 46.8$]. As can be seen in Fig. 1b, there was a steady decrease in locomotor activity across the three hour test period in both low and high sugar feeders.

1.75 mg/kg AMP

Feeding phase. A two-way analysis of variance (ANOVA) carried out to examine the amount of sugar consumed on the previous 7 days in the low and high sugar feeders revealed a significant main effect of group,[$F(1,32) = 13.9$] and also a main effect of days [$F(7,224) = 5.3$]. As can be seen in Fig. 2a, low feeders ate significantly less sugar than high feeders across all 7 days.

Locomotion phase. Results showed that there was a significant difference between low and high feeders in their locomotor response to AMP [$t(32) = 2.28$]. High feeders exhibited significantly more locomotion in response to AMP than did low feeders. To examine the temporal aspects of this difference, the 3-h test period was broken down into 18 intervals of 10 min in duration. Subsequently, a two-factor between-within ANOVA, with group and interval as the factors, was carried out. The ANOVA revealed that there was an interaction of group and interval [$F(17,544) = 2.89$]. Post-hoc analysis revealed that high feeders exhibited more locomotion than low feeders in response to AMP starting at the time of administration and lasting for approximately 100 min (see Fig. 2b).

Discussion

High sugar feeders exhibited significantly more locomotor activity in response to 1.75 mg/kg AMP treatment than did low sugar feeders. This difference in activity was observed beginning immediately after AMP administration and extending over the approximate period of AMP's action. These results establish that sugar intake level is a predictor of individual differences in the locomotor response to AMP administration. One implication

arising from this is that the mechanisms regulating sugar intake and AMP-induced locomotion overlap.

Increased Acc-DA activity has been shown to be critical to the locomotor stimulant effect of AMP (Kelly et al. 1975; Pijnenburg et al. 1975; Joyce and Koob 1981; Vaccarino et al. 1986; Jones and Robbins 1992; Weissenborn and Winn 1992; Whishaw et al. 1992) and feeding is accompanied by increased Acc-DA activity (Hernandez and Hoebel 1988a,b; Radhakishun et al. 1988). In a previous study, Mittleman et al. (1986) showed that rats with high levels of food intake elicited by electrical stimulation of the lateral hypothalamus, a procedure known to stimulate Acc-DA activity (Hernandez and Hoebel 1988a,b), exhibited a greater Acc-DA response to AMP treatment than rats with lower levels of food intake elicited by stimulation of the lateral hypothalamus. More recently, it has been shown that rats with a high locomotor response to AMP express more Acc-DA activity than rats with a low response (Piazza et al. 1990b, 1991b). Thus, the findings of the present experiment are consistent with the notion that high sugar feeders express more Acc-DA activity than low sugar feeders (Sills and Vaccarino 1991; Sills et al. 1993).

In the present experiment, low and high sugar feeders did not exhibit different levels of locomotor activity in response to 1.0 mg/kg AMP. One possible reason for the failure to observe differential levels of activation induced by 1.0 mg/kg AMP may be due to the fact that low and high sugar feeders receiving 1.0 mg/kg AMP were not as clearly dissociated as low and high sugar feeders receiving 1.75 mg/kg AMP. That is, low and high sugar feeders that received 1.0 mg/kg AMP did not exhibit as large, or as consistent, a difference in their sugar consumption as low and high feeders administered 1.75 mg/kg AMP. Perhaps if low and high sugar feeders were equally separable in the two conditions this discrepancy would not arise. Alternatively, the lack of difference between the low and high sugar feeders at the 1.0 mg/kg dose may reflect the limited resolution of our behavioral measure, which was only a gross index of general locomotor activity (i.e. the interruption of two photocell beams). This may have limited our ability to detect more subtle differences in activity patterns of low and high sugar feeders at the 1.0 mg/kg dose of AMP.

Another possible reason for the discrepancy in the locomotor effects of 1.0 and 1.75 mg/kg AMP in low and high sugar feeders may relate to differences in the amount of stimulation produced by these two doses of AMP. Indeed, the level of locomotor stimulation produced by the administration of 1.75 mg/kg AMP in both low and high sugar feeders was higher than that produced by 1.0 mg/kg AMP (compare Figs. 1b and 2b). Perhaps, then, low and high sugar feeders exhibit different levels of activation only when stimulated to a sufficient degree. It is known that feeding is accompanied by (relatively) low levels of Acc-DA activation (Hernandez and Hoebel 1988a,b; Radhakishun et al. 1988), while AMP administration, in doses that induce locomotor activation, results in significantly higher levels of DA activity (Hernandez and Hoebel 1988b; Kuczenski et al. 1991). Thus, the small differences in Acc-DA activity expressed by low and high sugar feeders under non-drug stimulated conditions (i.e. feeding) may need to be amplified to a sufficient degree in order to produce differences in locomotor activity. To this end, a more complete dose-response study would be of interest.

One manner in which to produce a sufficient degree of stimulation would be to chronically administer the 1.0 mg/kg dose of AMP. It is well established that repeated administrations of AMP results in the development of a sensitized response such that the same dose of AMP induces a higher degree of locomotor activation (Segal and Mandell 1974; Robinson and Becker 1986; Robinson et al. 1988; Vezina and Stewart 1989; Piazza et al. 1990a; Hooks et al. 1991a, 1992a,b). Moreover, there have been recent reports of individual differences in the development of sensitization to the locomotor activating effects of AMP (Segal and Kuczenski 1987; Hooks et al. 1992 a,b). Thus, it may be possible to produce different levels of locomotor activity in low and high sugar feeders with repeated administrations of 1.0 mg/kg AMP. The second experiment examined this possibility.

Experiment 2

Rats were given repeated administrations of 1.0 mg/kg AMP across 9 days to determine whether low and high sugar feeders would exhibit differences in the development of sensitization to the locomotor activating effect of 1.0 mg/kg AMP.

Methods and procedure

The procedure was identical to that of experiment 1 with the following exceptions: on test days, animals were adapted to the locomotor cages for 1.5 h prior to drug administration; between test days, animals received AMP injections in their home cages to minimize the effects of conditioning. Animals were tested for their locomotor response to AMP on days 1, 3, 5, 7, and 9, and were administered AMP in their home cages on days 2, 4, 6, and 8.

Results

Examination of the locomotor response to AMP in low and high sugar feeders across the five days of testing revealed a significant group × day interaction [$F(4, 108) = 2.645$]. As can be seen in Fig. 3, with repeated administrations of AMP, high sugar feeders exhibited a higher degree of sensitization than low sugar feeders. Starting on day 3, high sugar feeders exhibited significantly higher levels of locomotor activity than low sugar feeders. This difference between low and high feeders arise from the first 90 min of the test period (data not shown).

To examine the possibility that the pattern of results obtained were not confounded by conditioning effects, the data from the adaptation period of each of the 5 test days were analyzed. The ANOVA revealed no signifi-

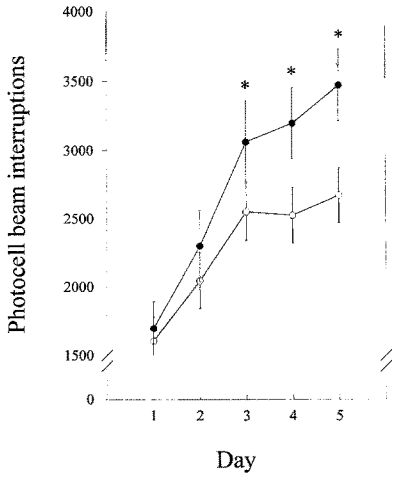

Fig. 3. Mean number of photocell beam interruptions in response to 1.0 mg/kg amphetamine administered across the 5 test days exhibited by low (○) and high (●) sugar feeders. * Significantly higher than low sugar feeders

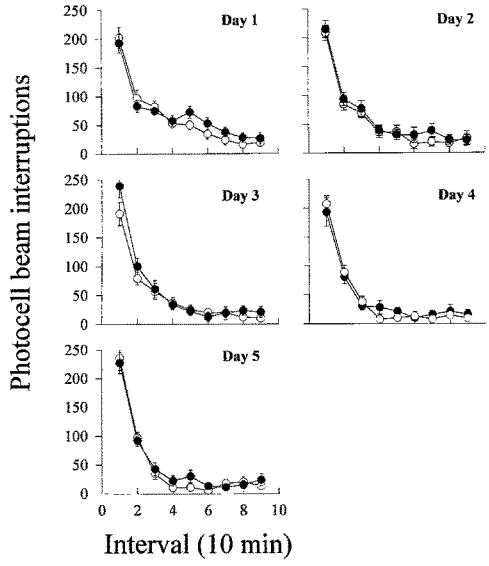

Fig. 4. Mean number of photocell beam interruptions measured across the 1.5-h adaptation period (see text for further clarification) on each of the 5 test days exhibited by low (○) and high (●) sugar feeders

cant effect of group [$F(1,22) = 1.912$], or group × day interaction [$F(4,88) < 1.0$], though there was a significant main effect of day [$F(4,88) = 8.769$]. As can be seen in Fig. 4, there was no difference between low and high sugar feeders in the amount of locomotion exhibited during the adaptation period. More importantly, there was no increase in activity across the 5 test days which indicates that there was no effect of conditioning in this paradigm.

Discussion

In experiment 1, low and high sugar feeders did not differ in their locomotor response to the acute administration of 1.0 mg/kg AMP. Experiment 2 showed that after repeated administrations of 1.0 mg/kg AMP, high sugar feeders exhibited significantly more locomotor activity than low sugar feeders. In other words, high sugar feeders exhibited a greater degree of behavioral sensitization to repeated AMP administrations than low sugar feeders. Thus, individual differences in sugar intake predict individual differences in the development of sensitization to the locomotor activating effect of AMP.

The present findings suggest that there is a critical level of AMP stimulation that is necessary for low and high sugar feeders to express differences in locomotor activity. This level of stimulation can be attained either with a high dose of AMP (e.g. 1.75 mg/kg) or with repeated administrations of lower doses (e.g. 1.0 mg/kg). Indeed, the level of locomotor activation attained with 1.75 mg/kg AMP was similar to that obtained after five administrations of 1.0 mg/kg AMP (compare insert of Fig. 2b with the day 5 results in Fig. 3).

Sensitization to AMP is thought to involve mesolimbic DA mechanisms. For instance, Eichler and Antelman (1979) showed that intra-cranial self-stimulation of the mesolimbic pathway sensitized rats to a subsequent administration of AMP. Segal et al. (1979) found that the development of sensitization to repeated AMP administrations was attenuated by 6-OHDA lesions of the Acc. More recently, Robinson et al. (1988), utilizing in vivo microdialysis in freely moving animals, found that the increased sensitivity to AMP administrations was accompanied by increased DA release in the Acc. Thus, sensitization to the motor stimulant effects of AMP may be a consequence of increased releasability of DA in the Acc.

One implication of the present findings is that following repeated administrations of 1.0 mg/kg AMP, high sugar feeders exhibit a higher level of Acc-DA activity in response to AMP treatment than low sugar feeders. This notion is in line with the hypothesis that low and high sugar feeders exhibit intrinsic differences in the activation of mesolimbic DA mechanisms (Sills and Vaccarino 1991; Sills et al. 1993).

One possible source of confound in the present experiment is that of conditioned locomotion. It is well established that the particular environment in which rats have been previously administered AMP will elicit locomotor activity in absence of the drug; this activity in AMP-pretreated rats is significantly greater than activity in non-pretreated rats or rats that had been pretreated with AMP in another environment (Gold et al. 1988; Martin-Iverson and McManus 1990; DiLullo and Martin-Iverson 1992). Thus, it is possible that a component of the sensitized response obtained in this experiment was due to a conditioning effect. There are three arguments against this possibility. First, the paradigm used in this study has been previously shown to minimize the effects of conditioning (Hooks et al. 1991a, 1992b). Second, if there was an obvious effect of conditioning, then the locomotor activity exhibited in the pre-drug, adaptation phase (Fig. 4) would be expected to increase across days. This was not the case; neither low nor high sugar feeders exhibited significantly different locomotor activity in this

period across the 5 test days. Third, if there was a conditioning component to the sensitization observed in the present study, it was no different between low and high feeders. This is evidenced by the fact that the locomotor response pattern during the non-drug, adaptation period was identical for low and high sugar feeders (Fig. 4). Therefore, a conditioning effect, if present, could not account for the differences in locomotor activity observed in low and high sugar feeders after repeated administrations of AMP.

General Discussion

The findings of the present experiments show that sugar intake level is a predictor of the locomotor response to AMP treatment, such that high sugar feeders are more sensitive to the locomotor stimulating effect of AMP than low sugar feeders. Piazza et al. (1989) have reported that the locomotor response to AMP is a predictor of susceptibility to the reinforcing properties of AMP. They showed that high AMP responders readily acquired self-administration of AMP, while low AMP responders did not acquire this behavior. The results of the present study add further to the profile of animals that may be vulnerable to the reinforcing properties of AMP. Specifically, these results suggest that high sugar feeders may be more vulnerable to the reinforcing effects of AMP than low sugar feeders. An attractive hypothesis that emerges is that rats with high liability to develop AMP self-administration may be more sensitive to natural reinforcers as well, at least those that access the mesolimbic DA system. This is an important consideration in developing animal models and theories of vulnerability to drug addiction.

Wise and Bozarth (1987) and Vaccarino et al. (1989) have argued that the stimulation of locomotor activity is a characteristic common to addictive drugs and appetitive behaviors. This notion is an extension of the theory advanced by Glickman and Schiff (1967), who posited that an elementary component of all positive reinforcers is the ability to elicit approach behavior. In the view of Wise and Bozarth (1987), drug-induced locomotor activity is an instance of approach behaviour in the absence of an orienting stimulus. Moreover, Wise and Bozarth (1987) propose that positive reinforcement and drug-induced locomotor activation are homologous. In other words, positive reinforcers (natural or otherwise) access the same neural mechanisms that promote approach behaviour. The mesolimbic DA system is thought to be one component of this mechanism (Wise and Bozarth 1987; Vaccarino et al. 1989). The findings of the present experiments, as well as those of Piazza et al. (1989, 1990b, 1991b) and Hooks et al. (1991a,b), fit well within this framework.

To be consistent with prior studies examining individual differences in sugar consumption and responsiveness to AMP treatment (Sills and Vaccarino 1991, 1993), animals were divided into low and high sugar feeders based on their consumption of sugar in response to saline injection. Prior to the saline injection, the animals were not handled; thus the injection could be construed as a mild stressor. It may be the case that the results obtained in this study reflect individual differences in sensitivity to stress. This is plausible in light of the fact that mild stressors stimulate feeding (Antelman and Szechtman 1975; Rowland and Antelman 1976; Wallach et al. 1977; Morley et al. 1983; Souquet and Rowland 1989). Moreover, the mechanisms regulating the response to stress and to AMP interact to some degree. For instance, it has been shown that intravenous administration of corticotrophin-releasing factor (CRF) antiserum attenuated the sensitized locomotor response obtained with repeated AMP administration (Cole et al. 1990a). A CRF antagonist delivered centrally has also been shown to block the sensitized locomotor response induced by restraint stress (Cole et al. 1990b). Moreover, CRF, in low doses, has been shown to facilitate AMP-induced stereotypy (Cole and Koob 1989) and repeated foot shock stress potentiates the locomotor activity induced by systemic (Herman et al. 1984) and intra-Acc (Leyton and Stewart 1990) AMP administration.

In a recent study, Piazza et al. (1991a) reported that animals expressing high levels (HR rats) of locomotor activity in response to a novel environment exhibited a longer duration of corticosterone secretion when exposed to the novel environment than low responding (LR) rats. The HR, but not LR, rats readily acquired AMP self administration (SA) and corticosterone administration to LR rats resulted in the acquisition of AMP-SA in these animals. Piazza et al. concluded that stress, and its consequences for the hypothalamic-pituitary-adrenal axis, may play an etiological role in the predisposition of rats to self-administer AMP. In support of this, Maccari et al. (1991) have reported that HR rats have lower affinities for both hippocampal type I and type II corticosteroid receptors relative to LR rats. This suggests that HR rats have an impairment in a negative feedback mechanism regulating corticosterone levels.

It has long been known that stress will alter Acc DAergic activity. For example, foot shock stress has been reported to increase DA utilization in the Acc, as well as the frontal cortex (Thierry et al. 1976; Robinson et al. 1987; Kalivas and Duffy 1989). Utilizing in vivo microdialysis, Abercrombie et al. (1989) and Imperato et al. (1989) have found that tail-shock stress increases extracellular DA in the Acc. Thus, individual differences in the responsiveness of the mesolimbic DA system to reinforcing stimuli may be a consequence of differences in the exposure of rats to stressful life events. In this regard, it is interesting to note that isolation rearing results in an increased sensitivity to AMP and other rewarding stimuli (Jones et al. 1990) and in an exaggerated Acc-DA response to AMP challenge (Jones et al. 1992).

In the present experiments, only the forward locomotor response to AMP was measured. It is well known that AMP will also produce stereotypy when administered in high doses (Kelly et al. 1975; Leith and Kuczenski 1982; Segal and Kuczenski; 1987; Patrick et al. 1991). Thus, it is possible that differences in AMP-induced stereotypy could have confounded the results in this study. This possibility appears unlikely for two rea-

sons. First, the doses of AMP that induce stereotypy (> 2.0 mg/kg) are generally higher than the doses used in the present study . Second, the profile of the locomotor activity generated by AMP administration to low and high feeders is not consonant with that of stereotypy. In both experiments it was shown that following the administration of AMP, there was a rapid rise in activity that peaked at around 40 min, with a steady decline thereafter in both low and high sugar feeders; the only difference between the two groups was that of magnitude of the locomotor response. The activity profile observed in the case of AMP-induced stereotypy, on the other hand, is multiphasic in nature. Following AMP treatment, there is an initial increase in locomotor activity, followed by a period of stereotyped responding when there is an almost complete cessation of forward locomotion, and then a final rise in locomotor activity (Leith and Kuczenski 1982; Robinson and Becker 1986). However, though it is unlikely, the present results do not completely rule out the possibility that low sugar feeders exhibited stereotypies as animals were not monitored for AMP-induced stereotypies.

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