Behavioural Pharmacology 2000; **11**:447–454

The effects of amphetamine and raclopride on food transport: possible relation to defensive behavior in rats

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Received 28 February 2000; accepted as revised 3 May 2000

Recent work has shown that transport of food items from open, exposed food sources to a covered shelter is reduced by drugs thought to have anxiolytic properties in rodents and humans. We studied the effects of amphetamine and the dopamine $D_{2/3}$-receptor antagonist, raclopride, in this test of food transport that pits immediate food consumption against exposure in an open space. Rats traveled from a home cage along an elevated beam to obtain single food items of varying sizes located at one of 12 distances from the home cage. Large food items and items located close to the home cage were carried back and consumed inside the cage. Small items and items located farther from the cage were eaten immediately at the food source while sitting on the beam. Amphetamine sulfate (0.001–2.0 mg/kg, i.p.) decreased eating on the beam and increased carrying of food items to the home cage. Raclopride (0.005–0.2 mg/kg, i.p.) tended to reduce carrying of food to the home cage, but 0.05 mg/kg raclopride did not block the increase in food carrying seen with amphetamine treatment (2 mg/kg). The increased food carrying seen with amphetamine is opposite to the effect produced by anxiolytic drugs, raising the possibility that amphetamine promotes carrying by increasing defense or 'anxiety'. Consistent with this hypothesis, amphetamine (2 mg/kg; the maximally effective dose in the food-carrying experiment) decreased open-arm exploration in the elevated plus-maze, considered to be an anxiogenic effect. These results indicate that stimulation of monoaminergic neurotransmission increases food transport from exposed food sources to a shelter; $D_{2/3}$-receptor blockade tends to reduce it. The food-carrying test provides a rich, ethologically valid paradigm to assess the effects of psychoactive drugs on species-specific, defensive behaviors in rodents. © **2000 Lippincott Williams & Wilkins.**

Keywords: anxiety, dopamine, $D_{2/3}$ receptor, elevated plus-maze, food hoarding, rat

INTRODUCTION

Behavioral tests used to measure defensive behaviors and 'anxiety' in rodents often make use of the tendency of rats and mice to avoid open, exposed, or brightly lit environments. In tests such as the elevated plus-maze and the two-compartment black–white box, rats spend more time in the darker, enclosed parts, while less time is spent in the open, exposed parts of the apparatus (Treit and Menard, 1998). Recently, Whishaw and co-workers have devised a novel behavioral test to assess the tendency of rats to carry food items from an exposed food source back to an enclosed shelter for consumption (Whishaw *et al*., 1990). Rats are placed in a covered home cage with access to an exposed hoarding alley or beam that contains pieces of food. As is the case with other 'anxiety' tests, rats appear to prefer eating the food in the covered home cage, rather than out in the open alley. Thus, instead of eating it immediately at the food source, food is often carried back to the home cage for consumption, despite the time and effort necessary to travel back and forth between the cage and the food source.

Interestingly, the behavioral repertoire of laboratory rats exhibited in this foraging task is surprisingly complex. Thus, even though rats appear to prefer consuming food in the home cage, the 'decision' to carry food is modulated by a variety of factors. For example, larger food items are more readily carried, whereas small items that can be eaten quickly are unlikely to be brought back to the cage (Whishaw and Tomie, 1989). Further, the probability that a food item is carried back to the cage decreases with an increase in the travel dis-

tance between the cage and the place where food is encountered, or with increasing travel difficulty or effort (Whishaw and Dringenberg, 1991). Decreasing apparent exposure risk by lowering ambient illumination reduces food carrying so that even larger pellets, or pellets found close to the home cage, are now more likely to be eaten at the exposed food source (Whishaw and Dringenberg, 1991). Thus, far from performing a simple stimulus–response behavior, rats use a number of variables (e.g. travel distance, food size, exposure risk) and modulate their foraging responses accordingly.

Neuropharmacological evidence suggests that food carrying may be a sensitive measure to assess the effects of centrally active compounds on species-specific, defensive behavior in rodents. The classic anxiolytic, diazepam, and the putative anxiolytic serotonergic receptor agonist, buspirone, both produce a dose-dependent behavioral shift from carrying food to the home cage to consuming it at the exposed food source (McNamara and Whishaw, 1990; Dringenberg *et al*., 1994). The fact that rats continue to consume food, and only the locale where eating occurs is changed, suggests that non-specific effects on feeding, satiety, or the motoric abilities involved in eating or transporting food are probably not critically involved in the behavioral changes produced by these anxiolytic drugs.

The purpose of the present study was to investigate the role of dopaminergic neurotransmission in the control of food transport of rats using the test paradigm described above. Even though the role of dopamine (DA) in defensive or 'anxiety-related' behaviors has received less attention than that of other neurochemical systems, modulations of dopaminergic transmission are known to have pronounced effects in behavioral tests known to be sensitive to anxiolytic drugs. In the elevated plus-maze, stimulating dopaminergic transmission by systemic amphetamine administration can produce 'anxiogenic'-like effects, suggested by the decrease in the time rats and mice spend exploring the open, exposed arms of the maze (Pellow *et al*., 1985; Lapin, 1993; Lin *et al*., 1999; but see Dawson *et al*., 1995). Similarly, amphetamine suppresses exploration of the white, open half of a two-compartment light–dark box, also consistent with an increased defensive reaction and 'anxiogenic' effect (Hascoët and Bourin, 1998). Further, DA-receptor antagonists (e.g. the $D_{2/3}$ blocker, raclopride; Timothy *et al*., 1999) have been shown to modulate behavior in tests of rodent defense. In the present study, we examined whether amphetamine and raclopride, over a wide range of doses, modulate food-carrying behavior in a way consistent with an increased defensive response. An additional experiment re-examined the effects of amphetamine on behavior in a pharmacologically validated anxiety test, the elevated plus-maze.

METHODS

Subjects

All experimental procedures were conducted in accordance with guidelines published by the Canadian Council on Animal Care and approved by the Queen's University Animal Care Committee. Adult, male Long–Evans rats (300–450 g), housed as pairs in standard Plexiglas cages containing a 'play-object', were used. The colony room was kept under a 12 : 12 h light cycle (lights on at 07.00 hours) and all tests were conducted during the light phase of the cycle. Prior to training on the food-carrying task, rats were placed on a restricted feeding schedule and their body weight was maintained at about 85–90% of their initial body weight for the duration of the experiment. Rats used for the plus-maze experiment were not food restricted. All rats had free access to water.

Apparatus

For the hoarding experiments, a home cage was attached to one end of a wooden beam. The home cage was a $25 \times 25 \times 20$ cm wire-mesh cage, covered with dark cardboard except on one side, to allow observation of the rat inside the cage. The cardboard wall facing the hoarding beam had an opening (9×8 cm) to give rats access to the beam. The wooden hoarding beam attached to the cage was 480 cm long, 9 cm wide, and supported by legs at a height of 23 cm above the floor. The room was illuminated by 16 fluorescent tube light bulbs (34 W, 122 cm long).

Food items used for the initial experiments (not involving drug administration) consisted of Fruitloop cereal pieces (Kellogg Canada, Inc.) cut to one of three sizes (mean $\pm$ SEM): 51 ± 2 mg (*small*; approximate dimensions: $7 \times 4 \times 4$ mm), 87 ± 5 mg (*medium*; approximate dimensions: $13 \times 4 \times 4$ mm), and 153 ± 8 mg (*large*; $17 \times 7 \times 4$ mm). The composition of this cereal is as follows (per 1 g): protein, 43 mg; fat, 27 mg; carbohydrates, 900 mg; sodium, 4.2 mg; potassium, 1 mg; total of 3.83 calories. For the subsequent pharmacological experiments, only large pieces were used. The weight of the different food pieces was determined by weighing twenty randomly chosen pieces of each size.

The elevated plus-maze consisted of two opposing closed and two opposing open arms (50×10 cm), extending from a square central area (10×10 cm).

The two enclosed arms had walls (40 cm high) along the sides. The maze was supported by stands 50 cm above the floor. The room was illuminated by a 20 W fluorescent tube light bulb, and a video camera was mounted about 1.5 meters above the maze.

Procedure

For the food-carrying experiments, rats were habituated to the test apparatus for 1 week by placing them individually in the home cage and allowing them to explore the cage and attached hoarding beam for about 30 min/day. During this period, the rat could venture out onto the beam to retrieve food items that were scattered along the beam. Formal testing began when all rats reliably left the cage and traveled along the beam to retrieve food pellets.

In an initial experiment, food carrying of rats ($n = 12$) in the absence of any drug treatment was assessed. A rat was placed in the home cage and a single food piece was placed at one of 12 distances (40–480 cm in 40 cm intervals) away from the home cage. The rat left the home cage and searched for the food. After the food was encountered, the behavior of the rat was scored as either *Sit* or *Carry* by an observer sitting about 2 m away from the hoarding beam. A Sit was scored when the rat picked up the food with its mouth, stayed at the food source, transferred the food to the forepaws, and ate the food while sitting on the beam. A Carry was scored when the rat picked up the food piece with the mouth, turned around, and ran back to the home cage where the food was consumed. The next trial commenced after the rat had finished eating a food piece inside the cage, or had returned to the cage after eating a piece on the beam. A test session consisted of 12 trials, one trial for each of the 12 possible distances. The order of the distances where the food was located was randomized. Each rat underwent this test every second day for a total of three test sessions. On each test session, a different food size was used, and again, the order of sizes given to a rat was randomized across the three sessions.

For the pharmacological experiments, rats ($n = 23$) were habituated to the testing procedures as outlined above. However, for these experiments, only one food size (large) was used. Rats were tested every second day for a total of 6 days. On each of these days, one group of rats ($n = 12$) received one of the following amphetamine injections (mg/kg): 0.0 (i.e. saline), 0.001, 0.01, 0.1, 1.0, and 2.0. A second group of rats ($n = 11$) received each of the following doses (mg/kg) of raclopride: 0.0, 0.005, 0.01, 0.05, 0.1, and 0.2. The order of drug doses given to individual rats was arranged so that only 1–2 rats were given the same dose on a particular test day, that is, all drug doses used were represented on each test day. Each drug dose given to an individual rat was followed by the next higher dose on the subsequent test day, and the highest dose was followed by saline. This schedule was continued until all rats had been tested at each drug dose. The behavioral tests started 5 and 30 min after the administration of amphetamine and raclopride, respectively. Again, a rat was placed in the home cage and allowed to retrieve food pellets during 12 consecutive trials, one per travel distance, administered in random order.

A further experiment investigated the effects of combined treatment with raclopride and amphetamine on food carrying. Rats ($n = 9$; randomly chosen from the rats used for the raclopride experiment outlined above) were tested every second day for a total of three test days. On each of these days, rats received one of the following drug treatments: (a) saline–saline; (b) saline–amphetamine (2 mg/kg); or (c) raclopride (0.05 mg/kg)–amphetamine (2 mg/kg). Raclopride and amphetamine were administered 30 and 5 min before the behavioral test, respectively. The order of drug treatments given to each rat was randomized.

A final experiment examined the effects of amphetamine treatment on exploratory behavior in an elevated plus-maze. Rats were given (i.p.) either saline ($n = 6$) or amphetamine (2 mg/kg; $n = 6$). Five minutes after the injection, an individual rat was placed in the central area of the maze, the experimenter left the room, and the behavior of the rat was recorded with a video camera during a 5-minute period. Subsequently, the rat was removed and the maze was cleaned with a wet towel before the next animal was tested. The tapes were later viewed by an experimenter and the time a rat spent in the open and closed arms was determined. A rat was considered to be in the open part of the maze when all four paws had crossed the line into an open arm of the maze.

Drugs

D-amphetamine sulfate (Health Canada, Therapeutic Products Directorate, Ottawa) and raclopride tartrate (Astra Pharmaceuticals Wilmington, DE) were dissolved in saline and administered intraperitoneally at a volume of 1 ml/kg. The following doses (in mg/kg) were administered: amphetamine 0.0 (i.e. saline), 0.001, 0.01, 0.1, 1.0, and 2.0; raclopride 0.0, 0.005, 0.01, 0.05, 0.1, and 0.2.

Statistics

The data are presented as mean ± SEM. For statistical analyses, analyses of variance (ANOVA) and, where appropriate, simple effects tests and post-hoc *t*-tests (paired) were used. The plus-maze data were analyzed using an unpaired Student's *t* test. All statistics were computed with the software packages CLR Anova (Clear Lake Research Inc., Houston, TX) or StatWorks (Cricket Software Inc., Philadelphia, PA).

RESULTS

Food carrying in undrugged rats

Both the size of a food item and the travel distance between the cage and place where the food item was found had a strong influence on the likelihood that a pellet was carried back to the home cage for consumption (Figure 1). The incidence of carrying food items back to the cage was highest for the largest pieces; medium-sized pieces were carried less often, and small pieces were carried the least [$F(2,22) = 58.7$, $P < 0.001$]. Further, for all three food sizes, items located close to the home cage were more likely to be carried back to the cage than pellets found farther away from the cage [$F(11,121) = 11.4$, $P < 0.001$]. In addition, there was a significant interaction between food size and travel distance [$F(22,242) = 1.9$, $P < 0.02$]. It appeared that this interaction occurred because carrying of smaller food items declined and approached zero at shorter distances than carrying of large items (Figure 1).

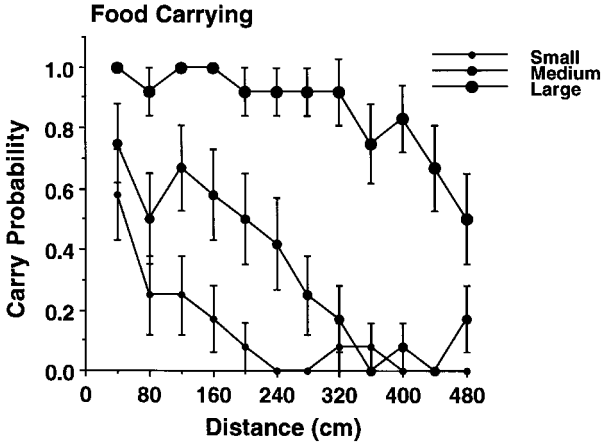

FIGURE 1. The effects of food size (small, medium, large) and travel distance on the probability to carry food to the home cage for consumption instead of eating it on the hoarding beam. Larger pellets were more likely to be carried back to the cage than smaller pellets (simple effect of size is $P < 0.005$, except for a distance of 40 cm, $P = 0.06$). Further, the probability of carrying pellets decreased with increasing travel distance between the cage and the food source (simple effect of distance is $P < 0.002$ for all three pellet sizes; see text for additional statistical details).

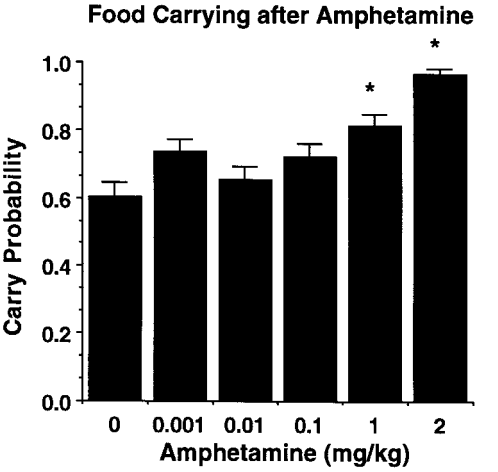

FIGURE 2. The effects of amphetamine (0.001–2.0 mg/kg, i.p.) on the probability of carrying food pellets back to the home cage for consumption. The carrying probabilities shown are averaged across all 12 travel distances. Amphetamine administration increased the likelihood that food was carried back to the home cage for consumption (* different from saline at $P < 0.05$, post-hoc *t*-test; see text for additional statistical details).

Effect of amphetamine on food carrying

Administration of amphetamine (0.001–2.0 mg/kg, i.p.) resulted in a dose-dependent increase in the probability that food was transported back to the home cage for consumption [$F(5,55) = 5.29$, $P < 0.001$]. When the likelihood of carrying a food item back to the home cage was averaged across all 12 distances, rats given saline had a probability of 0.6 ± 0.04 (mean ± SEM) to carry an item back to the cage. The two highest doses of amphetamine (1 and 2 mg/kg) increased this probability to 0.81 ± 0.03 and 0.97 ± 0.02, respectively (Figure 2). There also was a significant effect of travel distance [$F(11,121 = 17.3$, $P < 0.001$], and an interaction between distance and amphetamine treatment [$F(55,605) = 2.03$, $P < 0.001$]. The interaction occurred because amphetamine increased food carrying from distal food sources, but not from food sources located close to the home cage. Post-hoc analyses confirmed this observation: simple effects tests of treatment at each distance revealed that amphetamine increased carrying for distances between 320 and 480 cm ($P < 0.025$), but not for shorter distances ($P > 0.15$), with the exception of 200 cm ($P = 0.02$). An example of this effect is shown in Figure 3 for the maximally effective amphetamine dose (2 mg/kg). Amphetamine administration did not reduce feeding behavior during the test period. That is, all rats

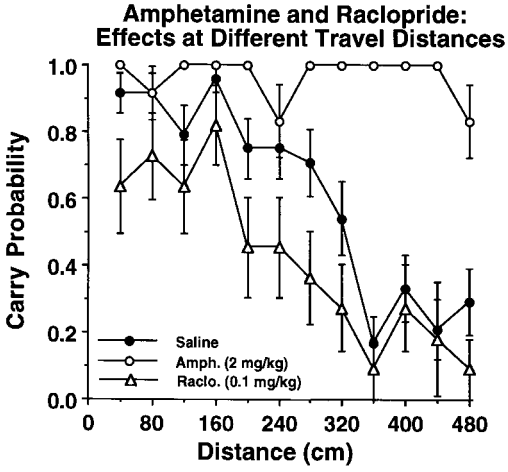

FIGURE 3. The effects of the maximally effective doses of amphetamine (Amph.; 2 mg/kg, i.p.) and raclopride (Raclo.; 0.1 mg/kg, i.p.) on the probability of carrying food for 12 different travel distances between the home cage and a food source. Saline-treated rats carried more food for shorter distances and showed little carrying for long travel distances. Amphetamine increased food carrying, especially by increasing carrying for long travel distances. Raclopride decreased carrying, especially for intermediate travel distances. The saline group shown represents the average of all saline-treated rats from both the amphetamine and raclopride experiments (saline-treated rats from these two experiments were not statistically different, [$F(1,21) = 0.007$, NS]).

continued to consume the food items, regardless of the drug treatment.

Effect of raclopride on food carrying

Administration of raclopride (0.005–0.2 mg/kg, i.p.) had a significant effect on carrying of food items back to the home cage (Figure 4) [$F(5,50) = 2.92$, $P < 0.025$]. At a dose of 0.1 mg/kg, raclopride suppressed food carrying relative to saline-treated rats (Figure 4). In addition, there was a significant effect of travel distance [$F(11,110) = 27.8$, $P < 0.001$], and a significant distance by drug interaction [$F(55,550) = 1.48$, $P < 0.02$]. Simple effects tests revealed that raclopride, across all doses tested, tended to be most effective in reducing carrying from intermediate distances (120, 200, 280, and 360 cm; $P < 0.025$), but did not produce a significant effect for the short (up to 80 cm; $P > 0.07$) or long distances (400–480 cm; $P > 0.5$). An example of this interaction is shown in Figure 3 for the maximally effective raclopride dose of 0.1 mg/kg.

Effect of concurrent raclopride–amphetamine treatment

In an additional experiment, the effects of treatment with saline–saline, saline–amphetamine (2 mg/kg), and raclopride (0.05 mg/kg)–amphetamine (2 mg/kg) on food carrying were evaluated. Consistent with the previous experiments, across all 12 distances, saline–saline treated rats had a carry probability of 0.62 ± 0.05. Treatment with saline followed by amphetamine increased carrying probability to 0.87 ± 0.03 ($P = 0.025$; data not shown). Treatment with raclopride followed by amphetamine, although slightly reducing carrying probability, did not result in a significant change relative to rats given saline and amphetamine (probability of 0.77 ± 0.04; NS; data not shown).

Effect of amphetamine on behavior in the elevated plus-maze

In a final experiment, the effects of amphetamine (2 mg/kg, the maximally effective dose in the food-carrying test) on exploratory behavior in the elevated plus-maze was investigated. During a 5-minute test period, rats given saline spent a mean ($\pm$ SEM) of 31.8 ± 12.3 s exploring the open arms of the maze; amphetamine reduced this time to 9.0 ± 4.2 s (unpaired t-test: $t(9) = 2.33$, $P < 0.05$).

DISCUSSION

The present experiments confirm previous results showing that several interacting variables guide foraging behavior of rats in a laboratory setting (Whishaw and Tomie, 1989; Whishaw and Dringenberg, 1991). First, rats use information regarding the distance between a food source and a shelter to determine whether food is transported to the shelter for consumption or eaten immediately at the food source. Food encountered close to a shelter is carried back for consumption, but the likelihood that

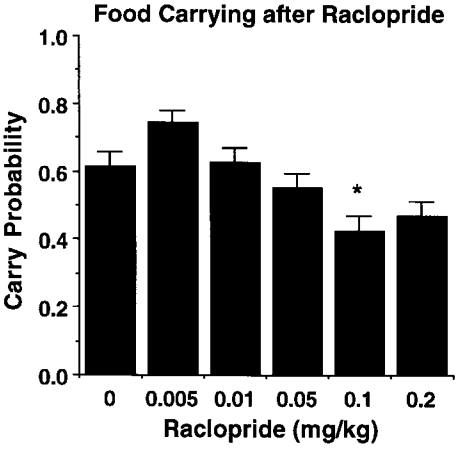

FIGURE 4. The effects of raclopride (0.005–0.2 mg/kg, i.p.) on the probability of carrying food pellets back to the home cage for consumption. The carrying probabilities shown are averaged across all 12 travel distances. Raclopride, at a dose of 0.1 mg/kg, produced a significant reduction in carrying relative to saline treatment (* different from saline at $P < 0.05$, post-hoc t-test; see text for additional statistical details).

food is carried decreases with an increase in travel distance. Secondly, the size of a food item influences the probability that it is carried back to a shelter; large food items are likely to be carried, whereas smaller pieces are less likely to be brought back and often are consumed immediately at the food source. Results of this kind have been interpreted within the framework of optimal foraging models that predict that foraging animals maximize food intake while, at the same time, minimizing energy expenditure and exposure to predators (Krebs and McCleery, 1984). Food size and travel distance to a shelter are known to influence foraging of animals (black-capped chickadees, gray squirrels, wild Norway rats) in natural settings (Lima, 1985; Lima *et al*., 1985; Whishaw and Whishaw, 1996), supporting the view that these variables contribute to adaptive, ecologically beneficial foraging behavior in a variety of species.

The principal novel finding of our experiments is that drugs known to interact with central monoaminergic (amphetamine) and dopaminergic (raclopride) transmission are effective in modulating food carrying in rats. In general, our results suggest that stimulating monoaminergic transmission with amphetamine enhances food transport from an exposed food source to a home cage; reducing dopaminergic transmission by blocking $D_{2/3}$ receptors with raclopride has a modest effect in the opposite direction. The increase in carrying seen with amphetamine administration was not affected significantly by pretreatment with a single dose of raclopride; before concluding that the effect of amphetamine does not depend on activation of dopamine $D_{2/3}$ receptors, further doses of raclopride and drug-naïve rats (to avoid potential tolerance to repeated raclopride treatment) will need to be tested.

Unlike our finding that raclopride reduced food carrying, Whishaw and Kornelsen (1993) have shown that neurotoxic ibotenic acid lesions of the nucleus accumbens, one of the main forebrain targets of dopaminergic fibers originating in the ventral tegmental area (Björklund and Lindvall, 1984), do not produce behavioral effects in rats tested in this foraging task. Lesioned rats carried food at the same level as non-lesioned rats, and they showed normal sensitivity to changes in food size and travel distance (Whishaw and Kornelsen, 1993). This result is consistent with a number of reports that nucleus accumbens injections of DA antagonists do not affect operant responding for food (Phillips *et al*., 1991b; Beninger and Ranaldi, 1993). Food-rewarded operant responding is well known to be reduced in a gradual extinction-like manner by systemic treatment with DA-receptor antagonists (Wise *et al*., 1978). Thus, the finding that systemic raclopride in the present study, but not nucleus accumbens lesions in the study of Whishaw and Kornelsen (1993), reduced carry probability in the hoarding alley can be seen as consistent with previous results. The data suggest that food reward is not mediated by the mesoaccumbens DA system. Studies of food-rewarded operant responding employing central injections of DA receptor antagonists have implicated the nigrostriatal DA system in food reward (Phillips *et al*., 1991b; Beninger and Ranaldi, 1993; Beninger *et al*., 1993).

Dopaminergic neurotransmission is thought to control a wide variety of motivated behaviors, including feeding. At least some drugs that act on dopaminergic receptors appear to modulate food intake, even though the precise nature of the dopaminergic involvement in feeding is controversial. Blackburn *et al*. (1992) conclude that, at least for DA-receptor antagonists, the available evidence indicates that they have little effect on general food intake, even though they may delay or impair the initiation of feeding. However, for food that appears to be particularly palatable to rats, DA antagonists can be effective in reducing consummatory behavior (Blackburn *et al*., 1992). Thus, it is possible that effects on general consummatory behavior play a role in the changes in food carrying produced by amphetamine or raclopride. While it is difficult to rule out this possibility, it is worth noting that, for the food-carrying test used here, different levels of food deprivation do not alter food carrying (Whishaw and Tomie, 1989). In other words, the level of hunger is not related to the probability that food is transported to a shelter, even though deprived rats eat food faster and initiate the next foraging trip more quickly than rats not kept on a deprivation schedule (Whishaw and Tomie, 1989). The fact the food carrying is relatively resistant to manipulations of consummatory motivation suggests that changes in carrying produced by dopaminergic (or other) drugs may not be related primarily to effects on internal states such as hunger and satiety. Other reports are consistent with this hypothesis: Phillips *et al*. (1991a) have shown that raclopride decreases operant responding for 1 and 10% sucrose solutions, but increases responding for, and consumption of, a 95% solution. Similarly, Salamone *et al*. (1991) demonstrated that the dopaminergic antagonist haloperidol decreases lever presses for preferred food, while, at the same time, increasing consumption of freely available non-preferred food. Both of these studies indicate that dopaminergic antagonists can influence food preference, but do not appear to

produce non-specific effects such as a generalized suppression of food intake (see also Martin-Iverson *et al*., 1987).

Previous work has shown that food carrying in rats is modulated by drugs used in the treatment of human anxiety disorders. The clinical anxiolytics diazepam and buspirone, a serotonergic partial 5-HT_{1A} receptor agonist (Baldessarini, 1996), both reduce the carrying of food from exposed food sources to a home cage (McNamara and Whishaw, 1990; Dringenberg *et al*., 1994). Whether this effect is related to a reduction in 'anxiety' is not known. Interestingly, a similar behavioral change is seen with decreases in the level of ambient illumination (Whishaw and Dringenberg, 1991), suggesting that there is a relation between the risk of exposure and predation and the likelihood of food being transported to covered shelters for consumption.

The effects of dopaminergic drugs on defensive behavior in rats are controversial. In the present study, amphetamine, at doses that can produce a several-fold increase in extracellular DA levels (Di Chiara *et al*., 1993), produced a dose-dependent increase of food carrying to the home cage, an effect opposite to that produced by anxiolytic drugs (see above). Amphetamine also increases the synaptic levels of serotonin and noradrenalin (norepinephrine) (Hoffman and Lefkowitz, 1996) and, at present, it is not known which of these effects is involved in the modulation of food carrying observed in the present study. Amphetamine, at the maximally effective dose in the food-carrying test, also decreased open-arm exploration in the elevated plus-maze, also an effect opposite to that of anxiolytics (see Treit and Menard, 1998). Together, these data raise the possibility that the increase in food carrying produced by amphetamine is related to an increase in the tendency to perform defensive behaviors and avoid open, exposed locales. Whether an increase in 'anxiety' by amphetamine is also involved in these behavioral effects cannot be assessed at present.

Even though there is no clear consensus regarding the effects of amphetamine in rodent tests known to be sensitive to anxiolytic drugs, several previous investigations are in good agreement with our results that amphetamine produces a decrease in open-arm exploration in the elevated plus-maze (Pellow *et al*., 1985; Lapin, 1993; Lin *et al*., 1999). A similar effect of amphetamine (decreased exploration of the white, illuminated compartment) has been shown for mice tested in a light–dark two-compartment test (Hascoët and Bourin, 1998). However, 'anxiolytic' responses to amphetamine in these and similar behavioral tests have also been reported (Dawson *et al*., 1995; Weiss *et al*., 1998). In humans, amphetamine can produce feelings of heightened anxiety, restlessness, nervousness, irritability, and panic, especially with high doses or a history of repeated drug administration (Reynolds, 1989; Hall *et al*., 1996; Williamson *et al*., 1997). Thus, in both rodents and primates, amphetamine appears to produce behavioral effects consistent with an increase in defensive behavioral responses and perhaps 'fear'; this tendency may be related to the increased transport of food from exposed food sources to a shelter in the food-carrying test used here.

The second drug we tested, the dopaminergic $D_{2/3}$-receptor antagonist, raclopride, had a modest effect on food carrying: at a dose of 0.1 mg/kg, raclopride significantly decreased food carrying. At a higher dose of 0.2 mg/kg, raclopride also suppressed carrying, even though this effect (and those of doses between 0.005 and 0.05 mg/kg) did not reach statistical significance. In the black–white two-compartment test, raclopride, at doses of 0.05 and 0.1 mg/kg, has been shown to decrease white-chamber exploration (Timothy *et al*., 1999), an effect not necessarily expected in the light of our results. These two sets of results highlight the fact that food carrying is a complex behavior; avoidance of exposed spaces, probably one of the critical features of the black–white box test, is only one of several interacting factors that determine whether food is carried or eaten immediately (see above). Thus, results obtained in the two-compartment box (e.g. avoidance of open spaces) cannot be expected always to map onto the food-carrying test we used.

In summary, the present experiments demonstrate that food carrying provides a rich paradigm to assess the effects of psychoactive drugs on defensive and food-hoarding behavior in rats. Previous work has shown that food transport to a shelter is reduced by drugs with anxiolytic properties in humans. Here, amphetamine, produced the opposite effect. The dopaminergic $D_{2/3}$-receptor antagonist raclopride tended to reduce food carrying. Together, these data confirm the hypothesis that dopaminergic mechanisms play a role in defensive behaviors in rodents (e.g. Blackburn *et al*., 1992; Weiss *et al*., 1998; Lin *et al*., 1999; Timothy *et al*., 1999) and suggest that enhancing monoaminergic neurotransmission with amphetamine can increase defensive responses, while blockade of $D_{2/3}$ receptors tends to reduce them.

Acknowledgements

This work was supported by grants from the Natural Sciences and Engineering Research Council of Canada to HCD and RJB.

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