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Home base behavior in amphetamine-treated tame wild rats (*Rattus norvegicus*)

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When a rat treated with amphetamine (0.5–5 mg/kg) locomotes in an unfamiliar environment, there are one or two places which it visits most often. In these one or two places the mean duration of a visit (stop) is the longest, and, compared to other places, the incidence of grooming and rearing are the highest. Since in intact rats these features of place characterize it as a 'home base', it is concluded that under amphetamine rats also establish one or two home bases. One home base was generally established by rats treated with low doses of amphetamine, while two bases were most evident in those treated with high doses. Since the paths of locomotion in amphetamine-treated rats were previously described to be stereotyped, it is suggested that home base location under this drug may be used as a reference point in the assessment of the organization of stereotyped locomotor behavior.

INTRODUCTION

In previous work we have documented that rats exposed to an unfamiliar open field show a preference for one or two places in this field[7]; these places were termed 'home bases'. The present experiments investigate the effects of amphetamine on rat home base behavior.

The existence of a key location – a home base – from which both wild and laboratory mammals proceed to explore the environment, and to which they return after exploratory excursions, has been noted by many[3,4,18,21,23,34]. In a novel environment, tame wild rats establish one or two home bases in which they spend the longest cumulative time, stop more than in any other place, perform the highest number of grooming bouts and of rearings, and crouch and arrest for extended periods[7].

The effects of amphetamine on rat open field behavior have been extensively documented[9,11,20,26,27,32]. These effects were reported to include changes in the frequency, rate, speed of performance, and completeness of components of general activity such as forward locomotion, turning, rearing, side to side head movements[1,2,24,28–31], and progression along fixed routes[6,19,22,33]. However, little is known regarding home base behavior under amphetamine. This may seem surprising considering that the home base phenomenon is perhaps the most conspicuous spatial regularity in intact rat open field behavior. Geyer[13,15] was the only one known to us to address the home base phenomenon under amphetamine, by reporting that under 1 mg/kg, laboratory rats "rarely exhibit a home area preference and make many seemingly random changes of direction". If there is under amphetamine a

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long-term organization of locomotor behavior in relation to specific reference places in the environment – long-term in the sense that the behavior is organized in reference to a place even when the rat is away from that place – then it should be possible to identify these places. If rats establish a home base under amphetamine, then such a home base would be a candidate for a natural reference place.

In the present study we show that under amphetamine rats do establish home bases, and we specify the changes induced by amphetamine on home base behavior. Like other aspects of spontaneous open field behavior, home base behavior may be used as a tool in pharmacological studies. Establishment of home base location under the drug may help in examining the rats' behavior when away from the home base but in reference to it. For instance, it has been suggested that rats infused with norepinephrine into the hippocampus exhibit "less tendency to return to the home even after they had started to run in the direction of the home area"[10], whereas under nicotine and caffeine, "rats exhibited – like controls – a preference for one corner and predictable excursions from that corner"[14]. In our own work, we have shown that compared to intact rats, amphetamine-treated rats exhibited a drastic increase in the number of excursions from home base, and a concurrent reduction in the number of stops per excursion[6,8]. These two effects highlight aspects of home base behavior which are less conspicuous in intact rats.

MATERIALS AND METHODS

The procedure of taming of the wild rats, the structure of the testing environment and the procedures of data acquisition and of data analysis were described in detail elsewhere[7]. Following are a brief summary of methods and some additional necessary detail.

Animals

Wild rats were used as subjects because, already in preliminary tests, their locomotor behavior under amphetamine appeared much more patterned and elaborate in relation to the environment than the behavior of their laboratory counterparts (see Discussion). Twenty male and 11 female tame wild rats (*Rattus norvegicus*), born to rats caught in the wild, or to first generation rats brought up in captivity, were kept singly in large cages (60 × 50 × 40 cm), on 14-h light/10-h dark cycle (lights on at 06.00 h). Recording sessions took place at the age of 4–12 months (rats weighed 250–400 g). Food and water were provided ad libitum.

Drug

(+)-Amphetamine was dissolved in saline and injected s.c. in the nape at concentrations of 0.5, 1, 2.5, and 5 mg/kg (n = 8 in all groups except the 1 mg/kg group in which n = 7; 5–6 males and 2–3 females in each group). Injection volumes were equivalent across doses (1 ml/kg).

Observation platform

The testing platform was a large glass table (160 × 160 cm and 100 cm high), without walls, placed 60 cm away from 4 walls, each of a different color and texture. A mirror, tilted at an angle of 4 degrees below glass allowed TV camera to capture simultaneously a bottom and side view of rat. The platform was divided into 25 rectangular places[7]. Videotaping of rats was performed under artificial lights, from behind a curtain. Only camera lens was visible to rats.

Procedure

Twenty-five rats were exposed to the testing platform for an hour, 4–6 weeks before testing under amphetamine[7]. Additional 6 rats were tested under drug without having previous experience on the platform. Since no difference was found between the behavior of rats injected during their first and second exposure to the platform, data are presented for all rats together; statistical support and further explanation are provided in the results section. Analysis of the behavior of the 25 intact rats during their first exposure to the platform was presented elsewhere[7]. Since we used as control the behavior of these intact rats, and not that of saline-treated rats, all the results should be taken to describe the compound effect of both injection and drug. Immediately after

injection, the rats were placed singly into the center of the open field and their behavior videotaped for 1 h. Videotaping took place during the daytime (08.00–17.00 h). All rats were tested under drug only once.

Behavioral analysis

In an open field a rat can be either locomoting or not. Periods of locomotion are referred to as periods of progression and periods of no locomotion as 'stops' or 'visits' to places. During forward progression rats do not perform large vertical movements, and do not groom. These movements are typically performed during stops. This spatio-temporal separation allowed us to describe behavior in terms of a sequence of visits to places and in terms of the movements performed in these places. Behavior was scored during regular and slow-motion playback of video records. For each rat, the entire 1-h period of observation was analyzed and coded into a computer by using custom programs. Behavioral scores included the sequence of different places visited by the rat, the arrival and departure time for each such visit (stop) to a place, and the performance of rearing and/or grooming during each visit. For each place data were added cumulatively, to obtain the total amount of time spent in each place during the 1-h session, and the incidence (total number per hour) of grooming, rearing, and stops per place. Grooming included face grooming alone, or both face and body grooming. Rearing consisted of a vertical movement of the whole trunk on the hindlegs, with release of foreleg contact with the substrate.

Statistics

Following a significant difference across groups in a one-way analysis of variance, Dunnett's test[5] was used to compare each of the amphetamine-treated groups to intact controls. Binomial distribution tests were used to assess the relationships between grooming, rearing, and time. The Kruskal–Wallis test was used to evaluate the effect of 1 or 2 exposures to the open field on the number of bases. Accepted level of significance was $P < 0.05$. Most calculations were performed using the statistical package MINITAB.

RESULTS

In normal rats, behavior at the home base typically included long intervals of crouching and arrest[6,7]. In contrast, amphetamine-treated rats did not crouch at all, and did not arrest for long intervals: they kept moving from one place to the next throughout the hour, alternating between progression and stopping. At all doses used, there was a large increase in the mean number of stops (Fig. 1 lower graph), and a reduction in the overall mean duration of staying in place (Fig. 1 upper graph). Rearing incidence was increased at the doses of 1 and 2.5 mg/kg, and grooming incidence remained unaffected at all doses (Fig. 1).

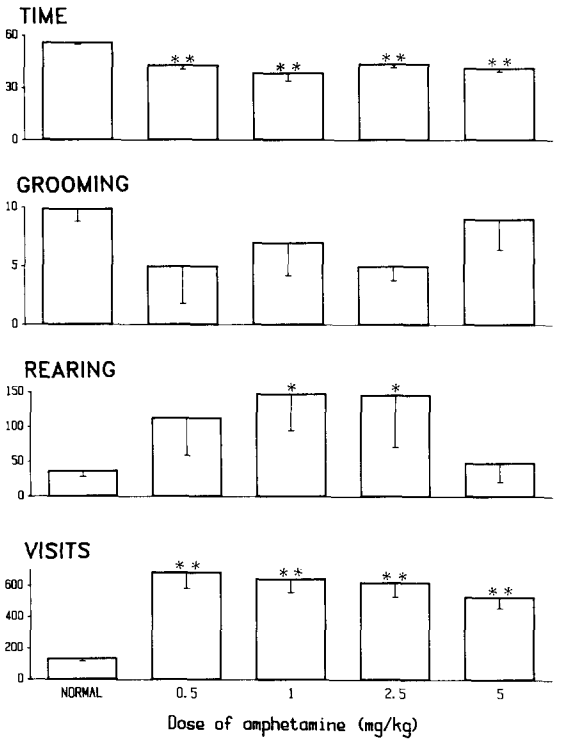

Fig. 1. The effect of amphetamine on several parameters of general activity (mean ± S.E.M.). The cumulative time of staying in place (non-locomotory period in minutes), decreased under all doses, compared to normal (one-way ANOVA, $F = 16.16$, $P = 0.000$); the incidence of grooming was not affected; the incidence of rearing and of visits (stops), increased (one-way ANOVA, $F = 2.60$ and $P = 0.048$ for rearing; $F = 22.75$ and $P = 0.000$ for visits). Results of comparing each dose-group to normal group (Dunnett's test) are indicated by asterisks ($*P < 0.05$; $**P < 0.01$).

Behavioral markers of home base location under amphetamine

The spatial distribution of stopping, staying in place, rearing, and grooming may tell us whether amphetamine-treated rats have a home base: if the performance of these behaviors is highest in one and the same location, then this preferred location may be legitimately described as the rat's home base. To assess the distribution of the cumulative time of staying in a place, we calculated for each rat the cumulative time it spent in each of the 25 places on the platform, and then sorted the places from highest to lowest, according to the cumulative time spent in each place. The rank order of places – as sorted according to the time spent in each place – was kept fixed for each rat in the following computations. Next, we computed for each of the doses, the cumulative time

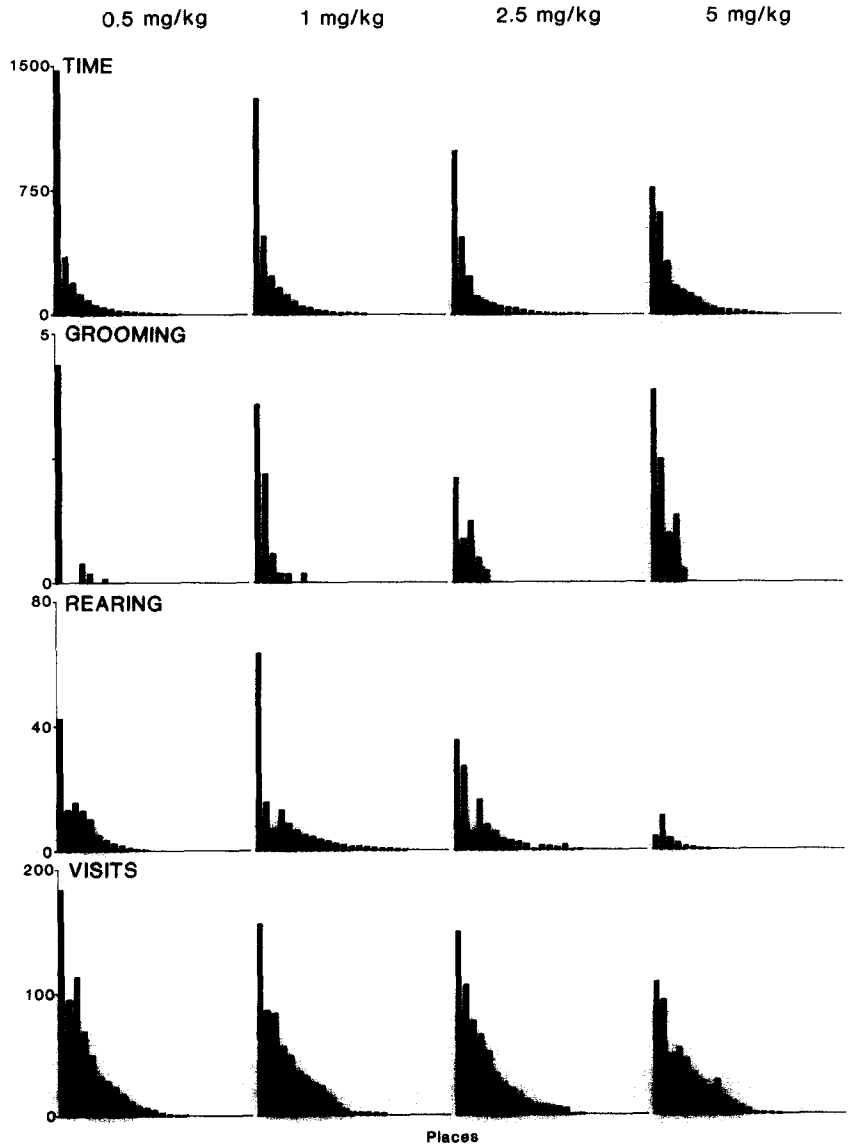

Fig. 2. The spatial convergence of several parameters of behavior to the place where the rat stayed for the longest time. For each rat, places were sorted from highest to lowest according to time spent in them during the 1-h session. Graphs on top row show, for each dose, cumulative Time for each rank ordered place (in seconds). The means of the incidence of Grooming, of Rearing, and of the number of Visits (stops per place), are presented for each rank ordered place by time, on the next 3 rows. The highest means for grooming, rearing and visits converge to the place in which the rats spent the highest cumulative time.

spent by all the rats together in each of the rank ordered places. The means of the cumulative time for each rank-ordered place are presented in Fig. 2 (top). The mean incidence of grooming, rearing, and stopping, for each rank-ordered place by time, were also computed for all rats in each of the doses (Fig. 2). As shown, in each of the doses, the highest incidence of grooming, rearing, and stopping, converge to the place in which the rats spent the longest duration of cumulative time, represented by the left bar. In other words, the place in which the rats stayed the most, was also the place with the highest incidence of grooming, rearing, and stopping. The only exception was the highest incidence of rearing, which was observed in the second rather than the first place, under 5 mg/kg. This exception is discussed in the section on home base behavior across time. Thus, the highest values of 4 behavioral variables typically converge under amphetamine to one place (which is located differently in different rats – see section on home base location).

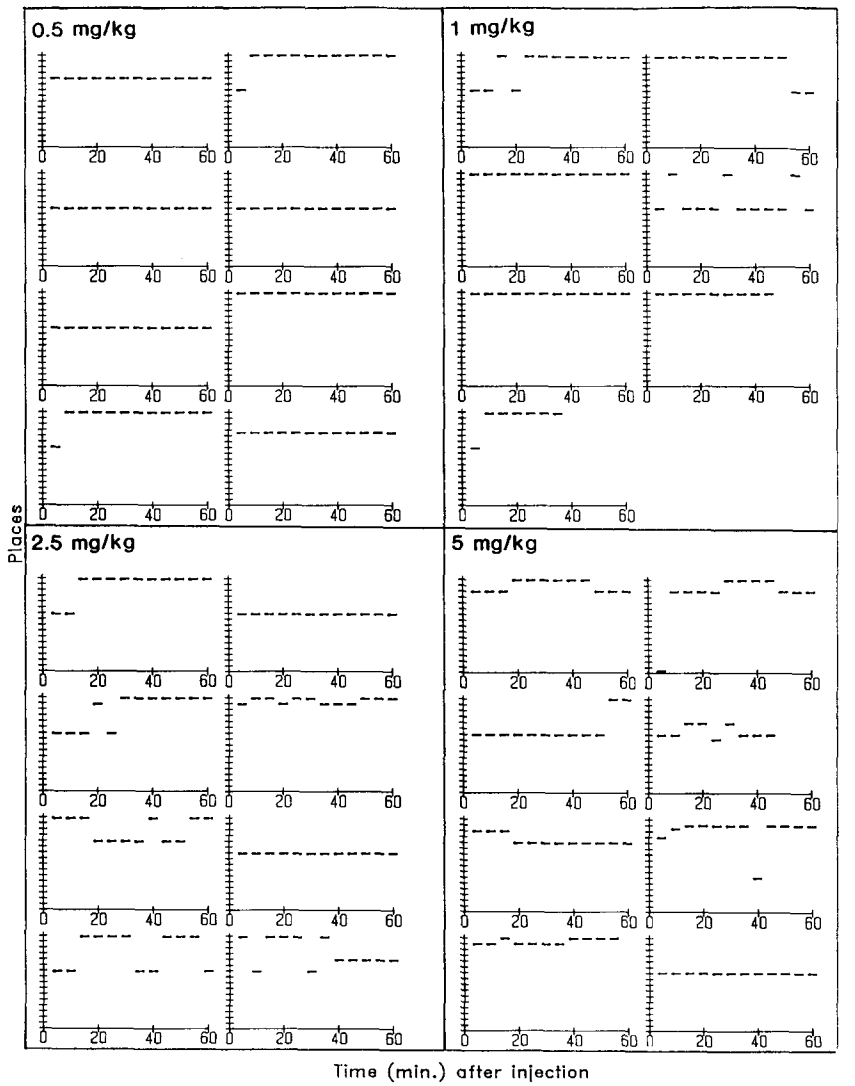

Fig. 3. Location of most preferred place (in terms of the cumulative time spent there), per 5-min intervals, across the session. Each inset graph represents an individual. In all inset graphs the x-axis represents time after injection in 5-min intervals; the y-axis represents, in a fixed order, the 25 places on the platform. Data points represent therefore the geographical location of the 5-min interval most preferred places. As shown, all rats have one or two most preferred places across the hour.

Most preferred location for staying in place across time

To examine staying in place across time, the time record of each rat was divided into successive 5-min intervals. In each such interval, there was a place where the rat spent the longest cumulative time. That place was marked on a graph as the rat's most preferred place for staying in place, for that interval. In following this procedure for all rats, it was found that in the course of the hour, the 5-min interval most preferred places were located in all rats in either one, or two, non-adjacent geographical locations. These locations were specific for each rat (Fig. 3).

Examination of the record of each of the 15 rats that had 2 such places revealed that the second most preferred place was also: (a) the second most preferred place in terms of the overall cumulative time of staying in place, (b) the second most preferred place in terms of the number of visits paid to it (exception: 3 rats visited a third place at the second highest incidence), and (c) one of the two most preferred places for grooming and rearing (exceptions: one rat groomed, and one reared at second highest incidence at a third place. Four rats groomed and 5 reared outside the main base, at an extremely low incidence which did not exceed 2 incidents per place). Based on these results, it was concluded that some of the rats had a second place to which the second highest values of the 4 behavioral variables tended to converge.

How independent are the 4 variables?

Cumulative time and number of visits. If the mean duration of a visit to any place would have been constant, then the highest values of cumulative time spent in the most visited places would merely reflect the number of visits to these places. That this is not the case is shown in Fig. 4, where the 10 most visited places are ranked, from highest to lowest, according to the number of visits paid to them. Data were calculated for each rat, and then pooled together for each dose group. As shown, the first and second places had the longest mean visit duration under 3 of the doses, and among the highest under the fourth dose (under 5 mg/kg, the distinction between the two most visited places

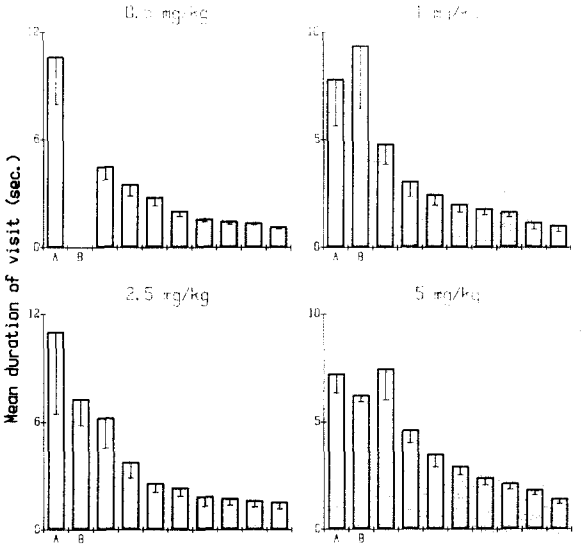

Fig. 4. Mean duration of a visit (± S.E.M.) to the 10 most visited places, rank ordered from left to right according to the number of visits paid to them.

and other places was lost, as other places were also visited repeatedly at a very high rate). In general, a place visited more was also visited for a longer mean interval.

Cumulative time and the incidence of grooming and rearing. The highest proportion of grooming and rearing at the one or two most preferred places might reflect the proportion of time spent there. These proportions would have been equal, had the performance of grooming and rearing been equiprobable in and away from the two most preferred places. As shown in Fig. 5, in 21 out of 26 rats who groomed, grooming was performed at the 2 most preferred places at a proportion higher than expected by the proportion of time spent there. The proportions of rearing were higher in only 11 out of the 27 rats that reared. Therefore, we cannot exclude the possibility that the incidence of rearing at these places merely reflected the time of staying there. Nevertheless, in rats that do rear, rearing is, like grooming, an extremely useful marker of the location of the 2 most preferred places.

It may thus be concluded that the highest values of 4 features of behavior, typically converge to one or two places under amphetamine. At least 3 of these features are not directly dependent on each other. Since these features also converge to

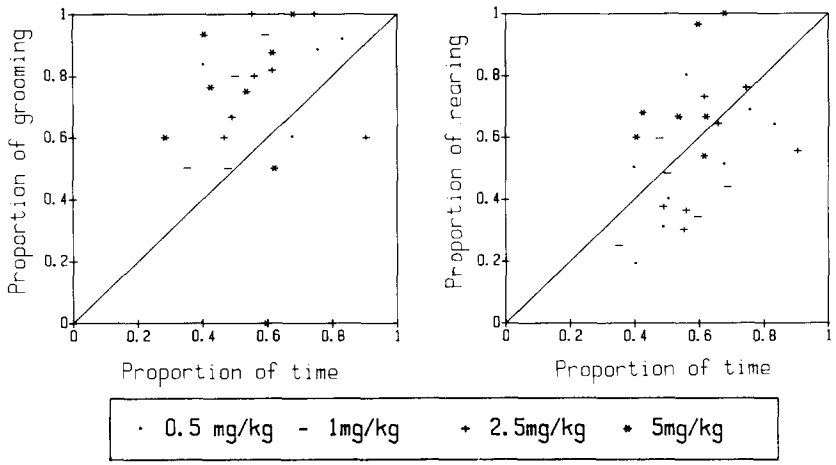

Fig. 5. Proportion of grooming and of rearing at home base in relation to proportion of time spent at base during the 1-h session. Each data point represents one rat. Proportion of grooming and rearing was obtained by dividing the incidence of performance at the home base(s), by total incidence. Proportion of time spent at home base was obtained by dividing the cumulative time spent at the home base(s) by the cumulative time spent in all 25 places on platform. Diagonal represents equal proportions. A binomial distribution test was used to compare the number of rats above and below the diagonal (significant for grooming, $P = 0.002$; non-significant for rearing, $P = 0.44$).

one or two places in normal rats, these places may be described, also under amphetamine, as the rat's home bases.

Is the number of bases dependent on dose?

While under the low doses rats tended to establish only one home base, under the higher doses they tended to establish two such bases in the course of the hour (Fig. 3). Since the 6 rats which had no previous experience on the platform were all injected with a low dose, their home base behavior parameters had to be compared to those of the experienced ones, to examine the homogeneity of the low dose groups. As shown in Table I, each of the low dose groups (0.5 and 1 mg/kg) was significantly different from the high dose groups. In contrast, a significant difference was not found between the experienced and inexperienced groups injected with a low dose. These results are consistent with our lack of ability to distinguish between the behavior of amphetamine-treated rats familiar or unfamiliar with the platform. Since rats injected with the low dose tended to establish 1 base regardless of previous experience, it appears that there might be an effect of dose on the number of bases a rat established.

A dose-dependent transition from 1 to 2 bases is also suggested by Fig. 2: the large difference between the first and second most preferred places under 0.5 mg/kg, decreases gradually across dose, becoming relatively small under 5 mg/kg. Calculation of the difference between the first and the second place (2 left hand columns in

TABLE I

Kruskal–Wallis test was used to compare rats injected with high doses of amphetamine (2.5 and 5 mg/kg; n = 16) on their second exposure to the open field, to rats injected with low doses (0.5 and 1 mg/kg) on their first (n = 6) and second exposure (n = 9) to the open field

The table indicates calculated H-values (critical value for significance is given in parentheses). Comparison does not include grooming and rearing because of the wide range of incidence of these behaviors in all groups (see Fig. 1). Statistical significance is indicated by asterisks (* $P < 0.05$; ** $P < 0.01$).

	2nd exposure low doses	*2nd exposure high doses*
1st Exposure low doses		
Time	ns 3.556 (3.84)	6.658 (6.64)**
Visits	ns 1.389 (3.84)	8.266 (6.64)**
2nd Exposure low doses		
Time	–	4.154 (3.84)*
Visits	–	4.154 (3.84)*

TABLE II

The number of bases in the 25 rats which were first observed as normal, and then under amphetamine

No significant change was found (McNemar's test; $\chi^2 = 1.56$, df = 1, $P = 0.211$).

		Normal	
		1 Base	*2 Bases*
Amphetamine	1 Base	5	5
	2 Bases	11	4

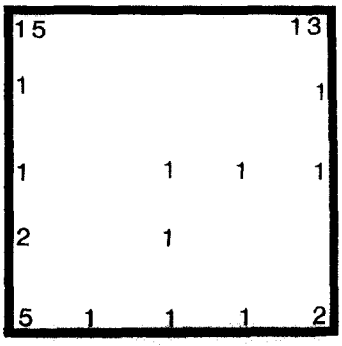

Fig. 6. Location of bases on the observation platform, in all 31 rats. The rectangle represents the platform. Numeral placing indicates location of bases on platform; values indicate the number of rats that established a base in that particular place.

each of the graphs of Fig. 2) and comparison of these differences across dose, shows that the difference for time and for number of visits is diminished significantly across increasing doses (one-way ANOVA; $F = 3.73$ and $P = 0.024$ for time; $F = 4.63$ and $P = 0.010$ for stops); no significant differences were found for grooming and for rearing.

During their first exposure to the platform, 60% of the 25 intact rats established one, and 40% established two home bases[7]. The number of bases a rat had before treatment had no effect on the number of bases it had after treatment (Table II).

Home base location on platform

Rats under amphetamine tended to establish a home base along the edge of the platform, preferentially at a corner. But rats that had two bases sometimes established one of them away from the edge (Fig. 6). The use of 17 out of the 25 available places on the platform for a home base, indicates that in this particular environment, home base location was not determined exclusively by the physical features of the testing environment. In other words, rats did exercise a certain amount of individual preference in the choice of home base location. Since all rats established at least one base in a corner, it could be argued that the term home base should be replaced by 'preferred corner'. However, on a circular platform, in the absence of corners, drugged rats also established 1 or 2 bases[6].

DISCUSSION

Our tests show that during locomotor behavior in a novel environment, amphetamine-treated rats (doses 0.5–5 mg/kg) manifest a strong preference for one or two places in the environment. The 4 constituents of this place preference are the highest number of stops, the highest mean duration of a visit, and the highest incidence of grooming and of rearing. These 4 constituents also characterize home base behavior in normal rats[7,23]. Therefore, the one or two most preferred places in rat open field behavior under amphetamine may also be legitimately described as the rats' home bases.

Unlike a normal rat, that sooner or later crouches at the home base for extended periods, an amphetamine-treated rat keeps moving throughout the session, persistently visiting the home base for brief intervals, without crouching at all. Amphetamine thus differentiates between organized locomotion, and sleep and the behaviors associated with it. The absence of arrested crouching at the home base under this drug, shows that the home base is not merely a place where a rat settles, grooms, and goes to sleep; it is an intrinsic component of active locomotor behavior in a novel environment.

While grooming and rearing are useful markers of home base location in drugged animals, their incidence is highly variable[17] (in the present study: 0–20 for grooming; 0–627 for rearing; one-

way ANOVA failed to find any difference between dose groups). In contrast, all rats, regardless of dose, spent significantly longer mean time intervals per visit at the one or two places which were also visited most throughout the session. Amphetamine thus detracts from the significance of crouching, grooming and rearing as behaviors which are intrinsic to the home base, and brings into relief the longer mean duration of a visit to the home base, and most importantly, the number of visits – a feature of home base behavior which is not as conspicuous in normal adult rats. Under amphetamine, the home base cannot be explained away any more as a mere resting place; rather, it appears as a key location in organized locomotor behavior.

Lat[19] and Schiorring[33], who describe patterns of progression of amphetamine-treated laboratory rats on a testing platform, do not mention the existence of a home base under this drug, and Geyer[13] notes that under 1 mg/kg amphetamine, laboratory rats exhibit a home area preference only rarely. The discrepancy between this statement and our results stems from the much stronger coupling between behavior and locale in wild rats under amphetamine (based on testing 15 hooded rats injected with 1–5 mg/kg amphetamine; Golani and Adani, unpublished observations).

The main significance of the establishment of the home base phenomenon under amphetamine lies in the potential use of home base location as a reference point in the examination of route stereotypies. Clearly, the mere performance of motor or even psychomotor components of exploratory behavior does not indicate, in and of itself, that an animal is engaged in exploration: a rat may perform all the psychomotor components of exploratory behavior and yet be completely disoriented in time and place, as has been documented in the recovery of exploratory behavior in rats after severe bilateral lateral hypothalamic damage[16]. Even progression along fixed routes does not necessarily reflect spatio-temporal orientation. For instance, under apomorphine rats may proceed along a fixed route by maintaining a fixed relationship between one side of their body, and the platform's edge. Such rats keep the platform on their right, for example, by walking along it in a counterclockwise direction. When the rat is placed along a cliff carved in the center of the platform, the sense of the route is reversed, and the rat proceeds along the new cliff clockwise, again keeping the edge on it's right[25]. To demonstrate orientation in time and place, it would be necessary to show that regardless of how fixed its routes along edges are, the rat is moving in reference to a particular place, even when it is away from the place[12,35]. Since the home base is the most plausible candidate for such a reference place, the demonstration of its existence under amphetamine provides a necessary step for showing that during performance of route stereotypies under this drug, rats are oriented in locale space.

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