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A comparison of motor behaviours in groups of rats distinguished by their climbing response to apomorphine

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1 Administration of apomorphine hydrochloride (0.5 mg kg^{-1} s.c.) to adult male or female Wistar rats previously acclimatized to the test environment induced climbing behaviour in approximately 50% of animals examined. The proportion of animals climbing was related to age, being maximal at 8–9 weeks.

2 Those animals showing an initial climbing response to apomorphine (0.5 mg kg^{-1} s.c.), climbed when challenged with this dose of apomorphine on subsequent occasions. In 'climbing' animals the intensity of response was related to the dose of apomorphine administered; no dose-response relationship was observed in 'non-climbing' animals.

3 No overall differences in the spontaneous motor behaviour of 'climbing' and 'non-climbing' animals were apparent as assessed by measurement of spontaneous climbing behaviour, by holeboard activity, and by locomotor activity measured in either photocell cages or in a treadwheel.

4 There was no overall difference in the ability of apomorphine to induce locomotor activity or stereotyped behaviour in 'climbing' and 'non-climbing' animals. However, the administration of apomorphine induced rearing and treadwheel activity only in those animals classified as 'climbers'.

5 There was no difference between the number (B_{max}) of specific [^{3}H]-spiperone binding sites or the dissociation constant (K_D) in striatal or mesolimbic tissue preparations for 'climbing' and 'non-climbing' rats.

6. The ability of an animal to climb in response to apomorphine appears to be dependent on an ability to orient vertically, since this is a component of behaviour common to climbing, rearing, and treadwheel activity. The ability to climb does not appear to be related to differences in dopamine receptor numbers in brain or to the penetration of apomorphine into brain.

Introduction

Mice placed in an enclosed area with mesh sides will climb either spontaneously (Costall *et al.*, 1982) or in response to the administration of dopamine receptor agonist drugs (Von Voigtlander *et al.*, 1975; Protais *et al.*, 1976; Marcais *et al.*, 1978; Gianutsos & Palmeri, 1983). Drug-induced climbing behaviour has been employed extensively to study interactions with brain dopamine systems (Lassen, 1979; Kovacs *et al.*, 1981; Quock & Lucas, 1981), and to detect antipsychotic molecules (Costall *et al.*, 1978; Peuch *et al.*, 1978). Climbing behaviour has advantages in that it detects atypical neuroleptic drugs. Thus sulpiride, which does not produce catalepsy or readily inhibit apomorphine-induced stereotyped behaviour, potently inhibits apomorphine-induced climbing behaviour (Costall & Naylor, 1975; Peuch *et al.*, 1976; Costall *et al.*, 1978; Jenner *et al.*, 1978). This has led to the idea that the dopamine receptors involved in climbing may be distinct from those involved in other behaviours initiated by dopamine agonists.

Recently, it has been demonstrated that rats also exhibit a climbing response to the administration of apomorphine (Sokoloff *et al.*, 1982; Davis *et al.*, 1983; Protais *et al.*, 1984). Schwartz and colleagues have suggested that, as in mice, climbing in the rat is more sensitive to atypical neuroleptics than other motor paradigms, and that this may be related to differences in the receptor populations involved. However, pre-screening of rats is required to select those showing a climbing response.

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Nothing is known as to why some rats exhibit climbing behaviour while others do not. In the present paper we have attempted to establish optimal conditions for studying climbing behaviour in rats and to determine those components of motor behaviour which distinguish rats which climb in response to apomorphine from those which do not.

Methods

Female Wistar rats (Bantin & Kingman Ltd) weighing 180–220 g were employed in most experiments. The age-dependence of climbing ability was investigated in animals whose weight ranged from 100–250 g. In some experiments, male Wistar rats (Bantin & Kingman Ltd) weighing 180–220 g were utilized. Animals were housed in groups of 6–7 and maintained at 22 ± 2°C on a 12 h light/dark cycle. Animals had free access to food and water. All experiments were performed between 9 h 00 min and 18 h 00 min.

Climbing selection procedure

Animals were placed in individual climbing cages with 1 cm diameter wire mesh sides (30 cm long, 20 cm wide, 40 cm high). Following a short habituation period (10–15 min), each animal was removed and 0.5 mg kg^{-1} apomorphine hydrochloride (Sigma Chemical Co.; dissolved in 0.1% sodium metabisulphite solution) was administered subcutaneously in a volume of 0.5 ml per 100 g body weight. The animals were then returned to the cages and the ability to climb was assessed at 5 min intervals from 5–30 min following apomorphine administration. The following scoring system was employed:- 0 = all paws on cage floor; 1 = two paws placed on the side of the cage; 2 = all paws off floor. The scores achieved by individual animals were summed so that each animal obtained a final score between 0 and 12. Animals scoring a total of 2 or less were classed as 'non-climbers' whilst those scoring above 2 were classed as 'climbers'.

In all subsequent experiments the animals employed were initially selected using this procedure. At least 4 days, but not more than 3 weeks, were allowed to elapse before further experiments were performed.

Routine measurement of the climbing response

Animals were again placed in individual climbing cages, and allowed a 1 h acclimatisation period. Animals were then removed from the cages, a range of doses of apomorphine hydrochloride (0.03–1.0 mg kg^{-1} s.c.) or vehicle (0.05 ml 100 g^{-1} body weight; 0.1% sodium metabisulphite) administered and the animals returned to their cages.

In initial experiments to establish the time course of the climbing response, animals were scored at 2 min intervals (using the scoring system described above) until the effect of the apomorphine had disappeared. In all other experiments the animals were scored at 2 min intervals between 10–20 min following apomorphine administration. This was determined to be the period of maximum drug effect. The final score obtained by each animal was taken as the mean of the 6 scores achieved during this 10 min observation period.

Spontaneous climbing

Spontaneous climbing, without apomorphine provocation, cannot be assessed accurately using a scoring system due to its erratic nature. Consequently, spontaneous climbing was assessed in non-acclimatised animals by measurement of the total time in which each animal climbed during 5 min periods up to 30 min following introduction to the wire mesh cages.

Measurement of rearing behaviour

Animals were placed in individual opaque plastic boxes (30 cm long, 23 cm wide, 18 cm deep) and allowed a 1 h acclimatisation period after which time apomorphine hydrochloride (0.03–1.0 mg kg^{-1} s.c.) or vehicle was administered. The rearing response to apomorphine was scored at 1 min intervals on an 'all or none' basis (0 = no rearing; 1 = rearing present). The final score attained by each animal was the sum of the scores attributed during the peak time of drug effect (10–20 min following apomorphine administration).

Measurement of locomotor activity

Locomotor activity was assessed in Perspex activity cages (38 cm long, 25 cm wide, 23 cm high), each fitted with 2 photocell units such that light beams were parallel and traversed the base at equal distances (6.5 cm) either side of the mid-line. A Commodore PET 4032 computer was used to scan each photocell unit for interruptions of the light beams at intervals of 0.2 s. This apparatus was designed and built in the department by Mr H. Bertoya, and was able to collect data from 32 activity cages simultaneously.

Monitoring was commenced immediately following the introduction of animals into individual activity cages. The total number of light beam interruptions occurring during each 5 min period was recorded. This spontaneous behaviour was monitored for 1 h after which the animals were removed, apomorphine hydrochloride (0.03–0.5 mg kg^{-1} s.c.) or vehicle administered, and activity measurement then continued for a further 30 min.

Measurement of treadwheel behaviour

Animals were placed individually in a unidirectional Perspex treadwheel (25 cm diameter, 8 cm wide) attached to a digital rotometer. During an acclimatisation period of 1 h, spontaneous activity was measured as the number of complete rotations recorded during each 5 min period. Animals were then removed and apomorphine hydrochloride (0.12–1.0 mg kg^{-1} s.c.) or vehicle administered. Animals were then returned to the apparatus and the number of complete rotations recorded during the 10–20 min period following drug administration (the time of peak drug response).

Measurement of stereotyped behaviour

Apomorphine-induced stereotyped behaviour was assessed simultaneously with climbing behaviour. As described above, pre-acclimatised animals were assessed at 2 min intervals from 10–20 min following the administration of apomorphine hydrochloride (0.03–1.0 mg kg^{-1} s.c.). Stereotyped behaviour was assessed using the following scoring system:- 0 = animals indistinguishable from controls; 1 = discontinuous sniffing and locomotor activity; 2 = continuous sniffing; 3 = continuous sniffing and discontinuous biting; 4 = continuous compulsive biting, licking or gnawing. The final score given to each animal was the mean of the scores attributed during the 10 min observation period.

Measurement of hole-board activity

Animals were observed individually in a hole-board apparatus (48 cm × 48 cm, 13 cm deep), with the base of the box divided into 9 equal areas, and perforated with 25 evenly distributed holes (3.5 cm in diameter). Behaviour was recorded during the 3 min period immediately following the introduction of the animals into the apparatus. The number of times an animal crossed from one of the 9 areas into another was recorded as a 'cross'; the number of times an animal raised its forelegs onto the side of the box was scored as a 'rear'; and the number of times a rat pushed its head completely through one of the holes was recorded as a 'head dip'. This apparatus was used only to record spontaneous behaviour.

Determination of specific [^{3}H]-spiperone binding

Female Wistar rats 180–200 g designated as 'climbers' or 'non-climbers', as defined above, were stunned and decapitated. The brains were removed, and the striatum and mesolimbic areas (nucleus accumbens and tuberculum olfactorium) dissected out and placed separately in ice-cold 50 mM Tris HCl buffer (pH 7.6). Pooled striatal or mesolimbic tissue from 2 animals was homogenised in 200 volumes of 50 mM Tris HCl buffer (pH 7.6), containing 120 mM NaCl, using a Polytron homogeniser (setting 6). The tissue homogenate was centrifuged for 10 min at 18,500 r.p.m. using a Sorvall RC5B centrifuge. The resulting pellet was resuspended by homogenising in a further 200 volumes of Tris HCl buffer. The homogenate was centrifuged again and the pellet finally resuspended in 540 volumes of Tris HCl buffer and kept on ice until required.

Standard incubations contained the following: 0.9 ml of the final membrane preparation (equivalent to 1.67 mg of original tissue), 50 µl of a solution of [^{3}H]-spiperone (16 Ci $mmol^{-1}$; Amersham International), and either 50 µl of distilled water (for total binding) or 50 µl of a solution of 2×10^{-4}M (±)-sulpiride (giving a final concentration of 10^{-5}M for determining non-specific binding). Samples were incubated to equilibrium at 37°C in a shaking water bath for 15 min. The incubation was stopped by rapid filtration under vacuum through Whatman GF/C glass fibre filters. The filters were rapidly washed twice with 5 ml ice-cold 50 mM HCl Tris buffer and transferred to scintillation vials.

The specific binding of [^{3}H]-spiperone to the membranes was determined as the difference between the amount of radioactivity bound in the presence and absence of (±)-sulpiride, and it was determined at six ligand concentrations between 0.03–1.0 nM. Each ligand concentration was examined in triplicate on 5 separate occasions using different tissue pools. The K_D and B_{max} values for the specific binding of [^{3}H]-spiperone were calculated using a curve-fitting programme.

Statistical analysis

Spontaneous and drug-induced locomotor activity measured using the photocell technique was analysed using a Student's t test. For all other forms of behaviour studied, a comparison between the response of the 'climbing' and 'non-climbing' animals was made using the non-parametric Mann-Whitney U-test.

Analysis of ligand binding data obtained from 'climbers' and 'non-climbers' was carried out using a two-tailed Student's t test.

Results

Screening of rats for climbing activity

In an initial experiment, a group of 72 female rats received one of a range of doses of apomorphine hydrochloride (0.125–0.5 mg kg^{-1} s.c.) or vehicle, on separate occasions. In this group apomorphine hydrochloride (0.5 mg kg^{-1} s.c.) induced a continuous clim-

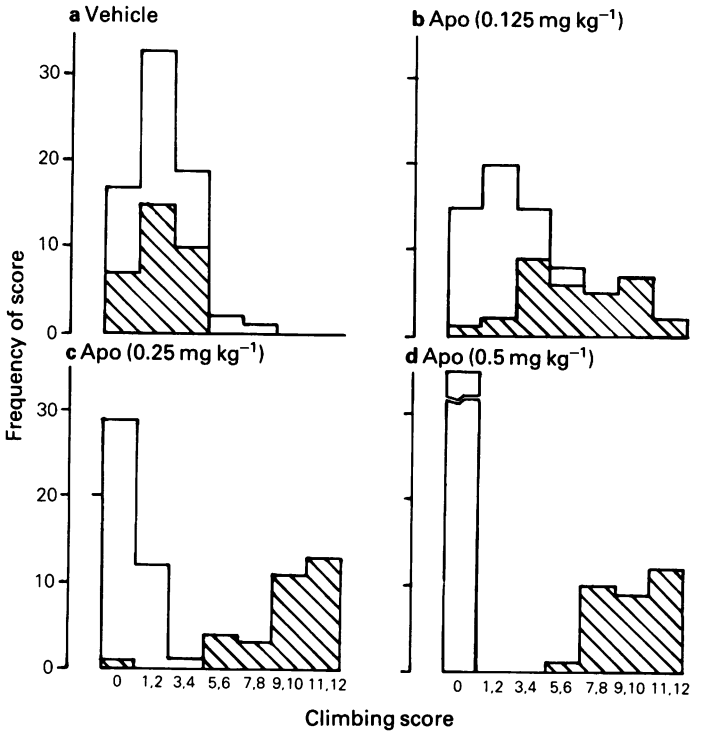

Figure 1 Frequency distribution of the climbing scores obtained for a typical group of 72 rats following subcutaneous administration of apomorphine hydrochloride (Apo) 0.125, 0.25 and 0.5 mg kg^{-1} s.c. or vehicle on different occasions. Animals demonstrating a climbing response at 0.5 mg kg^{-1} apomorphine (s.c.) are indicated by the shaded area, while those showing no response at this dose are indicated by the unshaded area.

bing response in 32 of the 72 animals (Figure 1). At this dose of apomorphine no climbing behaviour was evident in the remaining 40 animals. On administration of vehicle both groups of animals showed a low intensity but indistinguishable frequency of climbing. As the dose of apomorphine was increased from 0.125 to 0.5 mg kg^{-1} s.c. 'climbing' animals showed a more intense climbing response, whereas the slight climbing response to vehicle seen in the other group disappeared. Increasing the dose of apomorphine above 0.5 mg kg^{-1} s.c. did not increase the proportion of animals exhibiting a climbing response.

A subsequent group of 129 female rats was examined for their climbing response to apomorphine hydrochloride (0.5 mg kg^{-1} s.c.) on two occasions separated by a 14 day drug-free period. On the first occasion 79 animals were classified as 'climbers', all these animals showed a climbing response to apomorphine when examined on the second occasion, and 50 animals were classified as 'non-climbers'. On the second occasion 42 of the latter 50 animals did not climb in response to administration of apomorphine, but 8 showed a climbing response.

Age-dependence of climbing response to apomorphine

The proportion of female animals exhibiting a climbing response to the selected dose of apomorphine hydrochloride (0.5 mg kg^{-1} s.c.) varied according to age (Figure 2). When 4 weeks old only 10% of rats showed a climbing response to apomorphine. The proportion increased linearly to 50–60% at the age of 8–9 weeks. At this stage the weight range was 180–250 g. The proportion of animals climbing in response to apomorphine did not increase further with increasing age. Consequently, animals were not routinely employed in these studies until 8 or more weeks old.

Time and dose-dependence of apomorphine-induced climbing

Administration of low doses of apomorphine hydrochloride (0.03 and 0.06 mg kg^{-1} s.c.) to susceptible animals produced a minimal climbing response which did not differ from that observed in vehicle-injected animals (Figure 3).

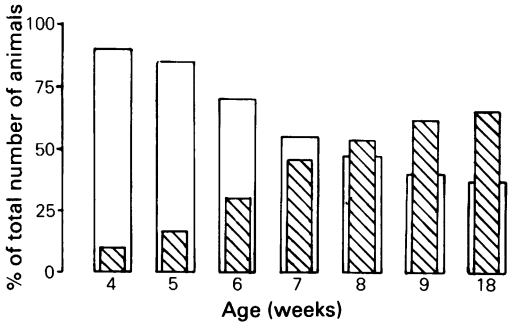

Figure 2 Age-dependence of the climbing response to apomorphine. The hatched columns represent the percentage of animals exhibiting climbing behaviour in response to subcutaneous administration of apomorphine (0.5 mg kg^{-1} s.c.). The open columns represent those animals that did not show this response. The ability to climb was assessed in naive rats during a 30 min period following treatment with apomorphine. At least 60 animals were tested in each age group.

Apomorphine (0.12 mg kg^{-1} s.c.) produced a moderate climbing response which lasted for some 30 min. Higher doses of apomorphine (0.25 and 1.0 mg kg^{-1} s.c.) produced a period of intense climbing which lasted for 40 and 80 min respectively. Accordingly, in subsequent experiments climbing was assessed between 10–20 min when a maximum response to apomorphine was apparent.

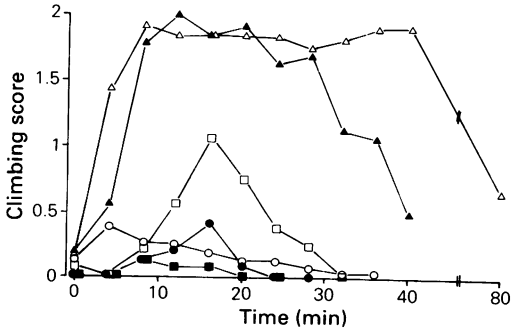

Figure 3 Time course of the climbing response to a range of doses of apomorphine hydrochloride (0.03–1.0 mg kg^{-1} s.c.) in pre-selected climbing rats. Apomorphine hydrochloride 0.03 (○), 0.06 (■), 0.12 (□), 0.25 (▲), 1.0 (△) mg kg^{-1} or vehicle (●) was administered subcutaneously and climbing assessed at 2 min intervals until it was no longer observed. To aid clarity, standard error bars have been omitted and the data are presented as the mean responses over each 4 min period. S.e.means were less than 15% of the mean values.

Assessment of climbing during the period of maximal effect to a range of doses of apomorphine revealed a sigmoid dose-response relationship (Figure 4a). In 'non-climbers' no continuous climbing response to the range of doses of apomorphine was observed at any time interval.

The climbing response to apomorphine in male rats

Administration of the screening dose of apomorphine hydrochloride (0.5 mg kg^{-1} s.c.) to male rats ($n = 90$), induced a climbing response in exactly 50% of the animals tested. Administration of a range of doses of apomorphine hydrochloride (0.03–1.0 mg kg^{-1} s.c.) induced a dose-dependent climbing response in prescreened 'climbing' male rats (Figure 4b). In 'non-climbers', no climbing response to the range of doses of apomorphine was observed.

Spontaneous motor behaviours

The duration of spontaneous climbing in female animals prescreened into 'climbing' and 'non-climbing' groups (on the basis of their response to apomorphine) did not differ when assessed over a 30 min period immediately following their introduction into the climbing cages (Figure 5a).

Assessment of spontaneous locomotor activity using the treadwheel technique showed no difference in the number of rotations recorded for the 30 min test period for 'climbing' and 'non-climbing' rats (Figure 5b). However, spontaneous locomotor activity measured using the photocell technique was higher in 'non-climbing' rats in the first 15 min after introduction into the apparatus than in 'climbing' animals (Figure 5c).

Measurement of spontaneous behaviour in the hole-board apparatus demonstrated no differences in the number of crosses, dips or rears recorded by 'climbing' and 'non-climbing' animals (Figure 5d).

Apomorphine-induced motor behaviour in 'climbing' and 'non-climbing' rats

Rearing behaviour was induced in a dose-dependent manner following administration of apomorphine (0.03–1.0 mg kg^{-1} s.c.) to those female animals pre-selected as 'climbers' (Figure 6a). Administration of apomorphine did not induce rearing behaviour in 'non-climbing animals. Any spontaneous rearing observed in these animals was abolished by apomorphine treatment.

Apomorphine hydrochloride (0.12–1.0 mg kg^{-1} s.c.) induced locomotor activity in the treadwheel in animals pre-selected as 'climbers', but not in 'non-climbing' rats.

Using the photocell technique, administration of

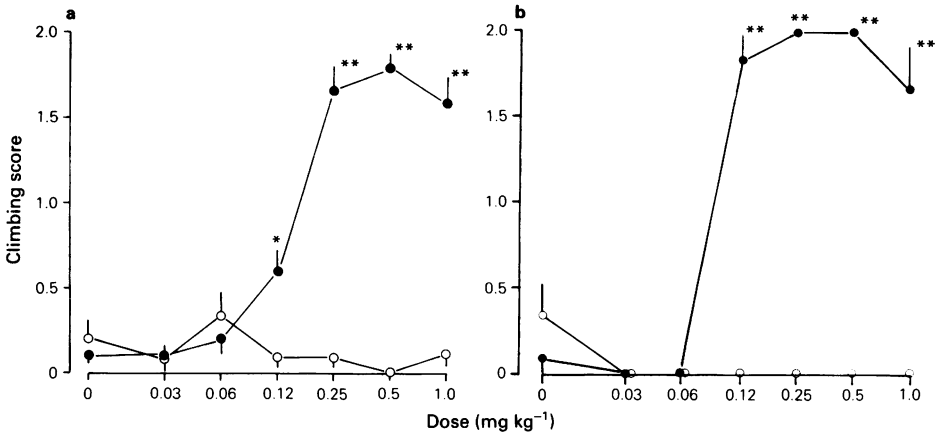

Figure 4 The relationship between a range of doses of apomorphine hydrochloride (0.03–1.0 mg kg s.c.) and the climbing response in (a) female animals and (b) male animals pre-selected as 'climbers' (●) and 'non-climbers' (○). Each point represents the mean, with vertical lines showing s.e.mean, of 6–10 animals. $*P < 0.05$, $**P < 0.001$, responses of 'climbers' compared to those of 'non-climbers' using the Mann-Whitney U-test.

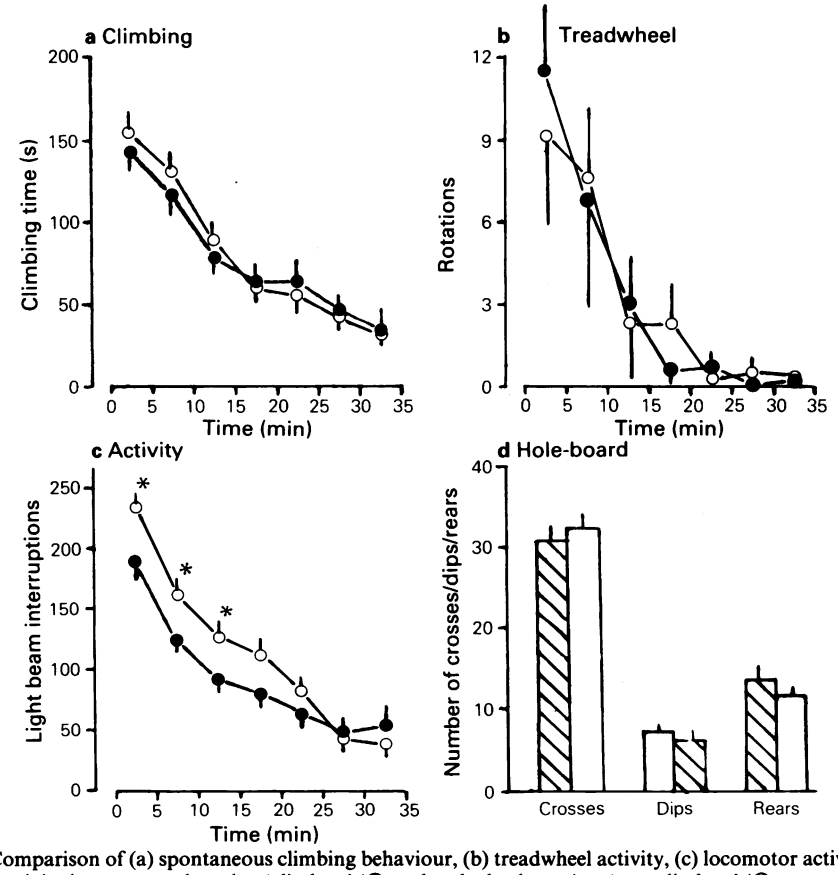

Figure 5 Comparison of (a) spontaneous climbing behaviour, (b) treadwheel activity, (c) locomotor activity, and (d) hole-board activity in rats pre-selected as 'climbers' (●, or hatched columns) or 'non-climbers' (○, or open columns). In the climbing and activity experiments ($n = 25–30$) 'climbing' and 'non-climbing' groups were compared using a Student's t test. In the hole-board and treadwheel experiments ($n = 6–15$) the groups were compared using the Mann-Whitney U-test. $*P < 0.05$.

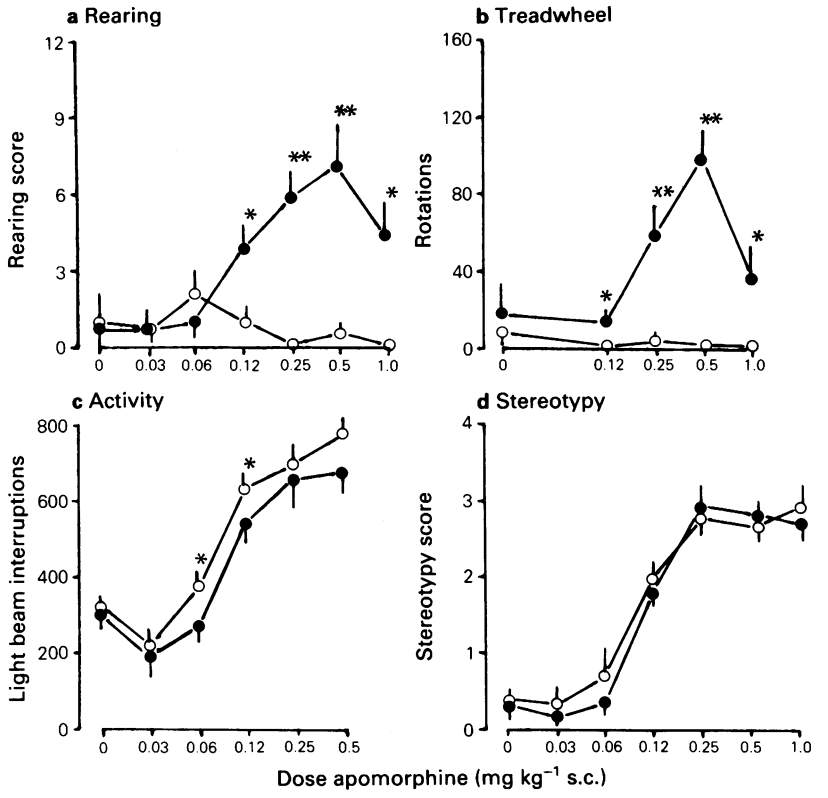

Figure 6 A comparison of apomorphine (0.03–1.0 mg kg^{-1} s.c.)-induced (a) rearing behaviour, (b) treadwheel activity, (c) locomotor activity and (d) stereotypy in rats previously selected as 'climbers' (●) or 'non-climbers' (○). Each point represents the mean, with vertical lines showing s.e.mean, of 6–15 animals (25–30 animals for locomotor activity). $P<0.05$, $^{**}P<0.01$, responses of 'climbers' compared to those of 'non-climbers'. The Mann-Whitney U-test was used to compare rearing behaviour, treadwheel activity and stereotypy. Locomotor activity was compared using Student's *t* test.

apomorphine hydrochloride (0.03–0.5 mg kg^{-1} s.c.) induced a dose-related increase in locomotor activity in both 'climbing' and 'non-climbing' animals (Figure 6c). 'Non-climbers' showed an apparently greater response to apomorphine than 'climbers', but visual observation suggested that this difference was an artefact due to the development of rearing in the 'climbing' group.

Administration of apomorphine (0.03–1.0 mg kg^{-1} s.c.) induced a dose-related increase in stereotyped behaviour that was identical in animals of both 'climbing' and 'non-climbing' groups.

Striatal and mesolimbic binding of [^{3}H]-spiperone in 'climbing' and 'non-climbing' female rats

There was no difference in the number of sites (B_{max}) or dissociation constant (K_D) for the specific binding of [^{3}H]-spiperone (0.03–1.0 nM; defined using 10^{-5}M (±)-sulpiride) to striatal tissue from 'climbing' (B_{max} 18.3 ± 1.9 pmol g^{-1} tissue; K_D 0.16 ± 0.02 nM) compared to that from 'non-climbing' (B_{max} 19.2 ± 1.9 pmol g^{-1} tissue; K_D 0.19 ± 0.02 nM) female rats.

Similarly, there was no difference in B_{max} or K_D values for specific [^{3}H]-spiperone binding to mesolimbic tissue preparations from 'climbers' (B_{max} 5.6 ± 0.7 pmol g^{-1} tissue; K_D 0.16 ± 0.01 nM) compared to those from 'non-climbers' (B_{max} 6.7 ± 0.7 pmol g^{-1} tissue; K_D 0.16 ± 0.02 nM).

Discussion

Climbing behaviour has been extensively studied using mice but it was thought to be inconsistently produced by the administration of apomorphine to rats. The results of this investigation show that under controlled

conditions apomorphine-induced climbing behaviour can be consistently and reproducibly obtained using female or male Wistar rats.

Using animals of the Wistar strain it was apparent that within a given group the administration of increasing doses of apomorphine led to a differentiation into those animals which showed a climbing response and those animals which did not. Once distinguished in this manner climbing animals consistently showed the same behavioural response on repeated exposure to apomorphine. Overall, in our investigations approximately 50% of rats were designated as 'climbers'. While this manuscript was in preparation Protais and colleagues (1984) have also, similarly, described a consistent climbing response to apomorphine in pre-screened rats. This was most prevalent in Wistar rats, where some 65% of animals exhibited drug-induced climbing, but was less marked in Long-Evans and Sprague-Dawley strains.

The differentiation of animals from the same strain into 'climbers' and 'non-climbers' is difficult to explain. Such animals are highly inbred and it might be expected that their spontaneous behaviour and response to drug administration would be very sumilar. It might be argued that the differentiation into 'climbers' and 'non-climbers' was artefactual and merely related to the dose of apomorphine. However, the climbing response in 'climbers' increased with increasing doses of apomorphine whereas there was no such trend in the 'non-climbing' group. This might suggest that it is some pharmacodynamic difference in the response to apomorphine which differentiates these groups of animals.

The proportion of animals exhibiting a climbing response to apomorphine increased with age, becoming maximal at 8–9 weeks and remaining constant thereafter. Age-related changes in behavioural response to apomorphine in rats have been found previously. For example, the stereotypy and locomotor responses to apomorphine become maximal 3 weeks postnatal, while the sedative effects of low doses of apomorphine, purported to be due to autoreceptor activation, do not develop until weeks 4 or 5 (Shalaby & Spear, 1980). Such changes probably reflect the maturation of brain dopamine systems which occurs during the first 4 postnatal weeks (Loizou, 1972). However, climbing behaviour becomes maximal at later times so another explanation should be sought. Perhaps some change linked to puberty is responsible but no difference has been found in the development of apomorphine-induced climbing behaviour between male and female rats. At the optimal age for climbing, the proportion of male rats exhibiting climbing behaviour, and the sensitivity of this response to apomorphine was similar to that of females.

Is the behavioural difference between 'climbers' and 'non-climbers' reflected in their spontaneous behaviour or in other apomorphine-initiated behaviours? In non-acclimatised female animals there was no difference in spontaneous climbing behaviour between the groups, or in the extent or repertoire of exploratory behaviours as assessed in a hole-board or using a treadwheel. However, using a photocell technique to assess total exploratory activity, a smaller but consistent difference was observed with non-climbing rats showing greater overall activity. However, no differences in spontaneous behaviour were observed which would have accounted for the differentiation of animals into 'climbers' and 'non-climbers' following apomorphine administration.

Following administration of a range of doses of apomorphine there was no variation in the intensity of stereotyped behaviour, and little difference in the degree of enhancement of locomotor activity between the 'climbing' and 'non-climbing' groups. In contrast, examination of the ability of apomorphine to induce rearing and to increase activity in a treadwheel revealed clear differences between the 'climbing' and 'non-climbing' groups. Rearing in 'climbing' animals increased after the administration of apomorphine whereas in 'non-climbing' animals rearing was not produced and any spontaneous rearing was inhibited. When examined in this manner it becomes clear that the rearing response is an integral initiator of climbing with the increase in locomotor activity common to both groups acting to drive the animals to climb actively. In this light the reason for the difference between the response of 'climbers' and 'non-climbers' in the treadwheel becomes more apparent. Thus, the rearing of the animals when placed in the treadwheel initiates its rotation which is then maintained by the enhanced locomotor response of the animals. So, rearing would appear to be the key behavioural response in initiating climbing behaviour but does not explain why it occurs.

Two explanations are immediately apparent to account for the difference in response to apomorphine between 'climbing' and 'non-climbing' animals. There may be a difference in the penetration of apomorphine into the area of brain responsible for initiating climbing behaviour. However, although we have not directly measured apomorphine concentrations, this appears unlikely since increasing the dose of apomorphine over a wide range did not initiate climbing in 'non-climbing' animals. Also, other motor behaviours initiated by apomorphine were identical in 'climbing' and 'non-climbing' rats. The alternative explanation is that some pharmacodynamic difference exists between the groups. From the experiments undertaken in this study it does not appear that this is related to differences in the number or affinity of striatal or mesolimbic dopamine receptors, identified using [^{3}H]-spiperone. So if the difference between 'climbers' and

'non-climbers' relates to pharmacodynamic factors this must involve other features of the drug-receptor interaction or other neuronal systems.

In conclusion, following initial selection apomorphine consistently induces climbing behaviour in rats previously acclimatised to the test environment. Approximately half the rats examined showed climbing in response to apomorphine and this appears to be related to the ability of the drug to induce rearing in these animals but not in 'non-climbing' rats. The reasons for this difference are not known but they do not seem to be due to differences in apomorphine penetration into the dopamine regions of the brain, or variations in the number or affinity of the receptors that mediate the climbing response. Under controlled conditions drug-induced climbing behaviour in the rat can be routinely used to examine facets of brain dopamine function in this species.

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