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BRIEF COMMUNICATION

Spontaneous and Apomorphine-Induced Locomotor Changes Parallel Dopamine Receptor Differences in Two Rat Strains

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HELMESTE, D. M. *Spontaneous and apomorphine-induced locomotor changes parallel dopamine receptor differences in two rat strains.* PHARMACOL BIOCHEM BEHAV 19(1) 153–155, 1983.—Two inbred strains of rats (F344 and Buffalo) were tested for differences in spontaneous and apomorphine-induced inhibition of locomotor activity. F344 rats showed greater percentage decreases in locomotion after apomorphine (0.25, 1.0 and 2.5 mg/kg) compared to the Buffalo strain. F344 rats also showed higher levels and slower habituation of spontaneous locomotor activity. F344 rats had previously been shown to have significantly higher densities of D_2-dopamine receptors in the striatum and olfactory tubercle and also more apomorphine-induced stereotypy when compared to Buffalo rats. These results confirm and extend previous studies suggesting that genetic differences in brain D_2-dopamine receptors can predict behavioral differences in locomotor activity.

Inbred rat strains Locomotor activity Dopamine receptor Apomorphine

RECENT work on various strains of rats and mice suggests that genetic differences in the brain dopamine receptor system may predict differences in locomotor and stereotypic behaviours [6, 7, 8, 13, 15]. Experiments on two of these rat strains (F344 and Buffalo) have shown that F344 rats have significantly higher densities of D_2-dopamine receptors in both the striatum and olfactory tubercle [8]. The D_2-dopamine receptor is the receptor subtype that seems to mediate dopaminergic behaviours [14]. F344 rats show more apomorphine-induced stereotypy when compared to Buffalo rats [8], suggesting a relationship between receptor density and behavioural sensitivity. Since locomotor activity is also thought to be under strong dopaminergic control [10], it was of interest to test these strains to see if the behavioural sensitivity differences extended to these other types of motor activities as well. Specifically, the hypothesis tested was that genetic differences in brain D_2-dopamine receptors may predict sensitivity differences in both apomorphine-induced inhibition of locomotion and apomorphine-induced stereotypy. Apomorphine, a direct-acting and specific dopamine receptor agonist [4,5], was used to test for differences in dopamine receptor mediated inhibition of locomotor activity. Since previous studies have also suggested a relationship between the brain dopamine system, the level of spontaneous locomotor activity and habituation of this activity [1, 6, 7, 11], F344 and Buffalo rats were also examined for possible differences in this area.

The findings reported here confirm and extend previous studies suggesting that genetic differences in brain D_2-dopamine receptors can predict behavioural differences in locomotor activity.

METHOD

Male rats of the F344 and Buffalo (BUFF) strains were obtained from Charles River (Boston, MA) and Microbiological Asst's (Maryland), respectively. The rats were housed in groups of five with 12 hr light-dark cycles and fed ad lib for two weeks prior to use, at which time they weighed 180–200 g. For the apomorphine study, rats of each strain were randomly assigned to one of four groups (10 rats per group): one group received vehicle subcutaneously (1 mg/kg ascorbic acid in 0.9% sodium chloride solution; 1 ml solution/kg rat) under the nape of the neck. Three other groups received either 0.25, 1.0 or 2.5 mg/kg apomorphine solution subcutaneously. Fifteen minutes after injection of apomorphine or vehicle, each rat was placed in an open field test apparatus. This apparatus consisted of a 67 cm square box with 60 cm high Plexiglas walls. The floor was composed of stainless steel wire-grid (0.5 inch mesh, 12 cm above base of field). Photo-cells were positioned along each wall at intervals of 15 cm. This apparatus was located in a small room, where the sole source of illumination was a 15 W light-bulb, 60 cm above the base of the floor. Rats were not previously habituated to the test environment. Apomorphine-induced locomotor changes were recorded in the time period 15 to 30 minutes after apomorphine or vehicle administration. Counts were summated at five minute intervals and the results for

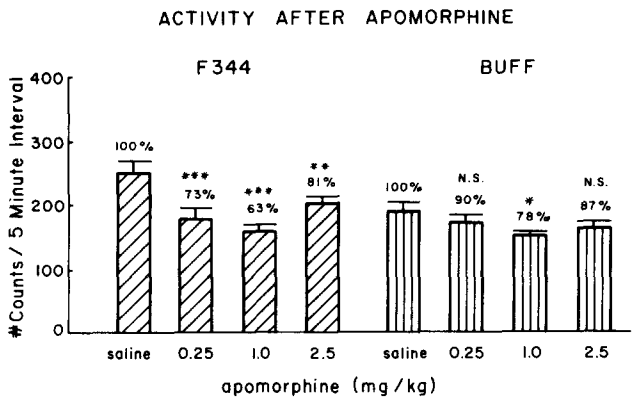

FIG. 1. Locomotor activity after apomorphine in F344 and Buffalo (BUFF) rat strains. Ordinate: mean counts (±SE), summated at five minute intervals, per 15 min test period. Abscissa: dose of apomorphine administered. N.S.=not significantly different from vehicle-injected animals; *$p<0.05$; **$p<0.01$; ***$p<0.001$ compared to vehicle-injected grp (two-tailed t-test).

each rat are expressed as the mean No. counts per 5 minute interval in the 15 min test period. This time interval was chosen because maximum brain apomorphine concentrations are known to occur in this time interval and because preliminary experiments had shown that maximum behavioural changes occurred in this time interval [2].

A fifth group of rats (n=11–12) were not injected with vehicle and had spontaneous locomotor activity recorded by this method for a total period of one hour. Photo-cell counts were summated at 5 min intervals and plotted over the full one hour period.

RESULTS

Figure 1 shows that F344 rats had greater percentage decreases in locomotion after the three doses of apomorphine (0.25, 1.0 and 2.5 mg/kg) compared to the Buffalo strain, $F(1,72)=5.54$, $p<0.02$. Locomotion also decreased as a function of dose for both strains, $F(3,72)=5.01$, $p<0.003$. With regard to spontaneous locomotion (Fig. 2), F344 rats showed significantly higher levels of activity ($p<0.001$) at all time intervals, compared to Buffalo rats. The rate of decrease (percentage change over time) in locomotion was slower in F344 rats as well (one-third the rate of Buffalo rats), suggesting habituation differences between these two strains.

DISCUSSION

The results of this study show that F344 rats have higher levels and slower habituation of spontaneous locomotion compared to Buffalo rats. After apomorphine, larger percentage decreases in locomotion are also seen. Previous experiments have shown that F344 rats have higher densities of D_2-dopamine receptors in the striatum and olfactory tubercle, and show greater levels of stereotyped behaviour after apomorphine, compared to Buffalo rats [8]. A correlation between genetic differences in locomotion and stereotypy and densities of brain D_2-dopamine receptors is in agreement with recent investigations in other strains of animals as well. Recent work on spontaneously hypertensive rats (SHR) has

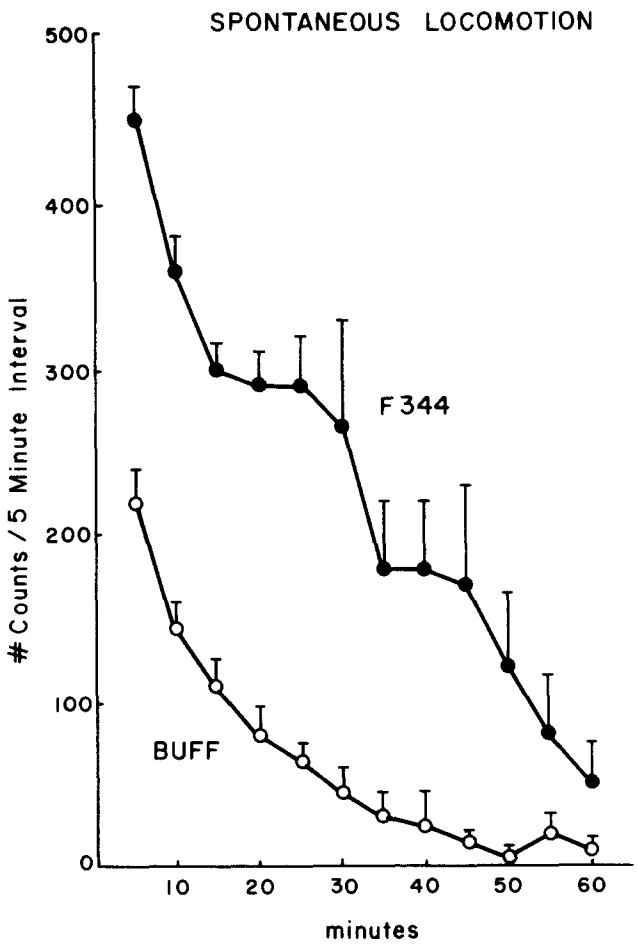

FIG. 2. Spontaneous locomotor activity in F344 and Buffalo rat strains. Ordinate: mean counts (±SE) per 5 minute time interval. Abscissa: time (min) after introduction of rat to test cage.

shown that these animals have higher brain D_2-dopamine receptor densities compared to their normotensive controls [11]. Behaviourally, they show higher spontaneous locomotion and slower habituation [1]. Studies on BALB/cJ and CBA/J mouse strains have shown that BALB/cJ have higher densities of brain D_2-dopamine receptors [7, 13, 15]. They also have higher levels of spontaneous locomotor activity and slower habituation compared to CBA/J mice [6,7]. Withdrawal from chronic haloperidol treatment has also been reported to be associated with higher spontaneous activity and/or slower habituation and increased D_2-dopamine receptor densities in mice and rats [9,16]. With regard to the literature on drug-induced motor changes, the results are more difficult to interpret. A recent study on three inbred strains of mice suggested a general covariance between dopamine receptor densities and apomorphine-induced stereotypes [15], but emphasized that qualitative differences in stereotypy across strains and after chronic drug treatment made comparisons difficult [12,15]. Other studies in strains of rats and mice suggest a correlation between brain D_2-dopamine receptors and locomotor activation after d-amphetamine or (−) N-n-propylnorapomorphine [3, 6, 7, 13].

Taken as a whole, these studies suggest that genetic differences in brain D_2-dopamine receptors may have predictive value in terms of drug-induced and spontaneous motor activities. One interesting trend was the tendency for slower habituation of spontaneous locomotor activity in animals with higher brain D_2-dopamine receptor densities. This has interesting theoretical implications for the function of the brain dopamine system. Future studies should examine these differences more closely, to determine the relative contributions of the mesolimbic and nigrostriatal dopamine systems and the function of changes in dopamine turnover.

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