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Different Effects of Apomorphine on Locomotor Activity in C57BL/6 and DBA/2 Mice

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SANSONE, M., M. AMMASSARI-TEULE, P. RENZI AND A. OLIVERIO. *Different effects of apomorphine on locomotor activity in C57BL/6 and DBA/2 mice.* PHARMAC. BIOCHEM. BEHAV. **14**(5) 741–743, 1981.—The effects of apomorphine on spontaneous locomotor activity have been studied in two inbred strains of mice, the C57BL/6 and the DBA/2. In C57 mice low doses of apomorphine reduced motor activity, while higher doses produced hypermotility. In DBA mice the drug always depressed locomotor activity. The results have also been discussed in relation to the different sensitivities to morphine exhibited by the same two strains of mice.

Apomorphine Locomotor activity Mice

DIFFERENT strains of mice show opposite responses to morphine when their locomotor activity or sensitivity to pain is considered. Morphine, in fact, exerts a strong stimulatory effect (running fit) on the locomotor activity of C57BL/6 (C57) mice [1, 9, 11], while the same doses of the opiate do not affect or even depress the locomotor activity of DBA/2 (DBA) mice [1, 9, 11]. On the contrary a clear analgesic effect is evident following administration of morphine in DBA but not in C57 mice [1,9].

Recent findings have demonstrated that morphine-induced hyperactivity in C57 mice is related to an activation of dopaminergic neurons in the striatum [10]. Therefore it seemed interesting to test the reactivity of C57 and DBA mice to a direct stimulation of dopamine receptors: in this study the locomotor activity of C57 and DBA mice has been assessed following the administration of apomorphine, a dopamine receptor agonist.

METHOD

The subjects were naive male mice (23–28 g) of the inbred C57BL/6 and DBA/2 strains (Charles River, Calco-Como, Italy).

The apparatus consisted of eight toggle-floor boxes, each divided into two 20×10 cm compartments connected by a 3×3 cm opening. For each mouse the number of crossings from one compartment to the other was automatically recorded by means of a microswitch connected to the tilting floor of the box. The apparatus was located in a sound-insulated cubicle and a dim light was the source of illumination.

Mice were subjected to a 60-min activity test, 15 min after treatment with saline solution (0.9% NaCl) or apomorphine hydrochloride, at the doses indicated in Fig. 1. All injections were made intraperitoneally at a dosage volume of 10 ml/kg. Treatment groups consisted of 8 mice. The activity session was divided into two 30-min periods and the data were statistically analyzed by a two-factor analysis of variance. The first factor was the mouse strain (2 levels: C57 and DBA). The second factor consisted of 7 levels of apomorphine treatment (including saline as dose 0). Individual between-groups comparisons were carried out by employing the error term of the overall analysis of variance. Some additional experiments were carried out in order to observe the behavioral repertoire of the mice in the toggle-floor boxes following apomorphine administration.

RESULTS

The mean activity scores exhibited by all the experimental groups during the first 30 min have been reported in Fig. 1. A two-factor analysis of variance showed significant strain, $F(1,98)=36.43$, $p<0.001$, and treatment $F(6,98)=10.44$, $p<0.001$, effects and a significant strain ×treatment interaction, $F(6,98)=11.40$, $p<0.001$. This interaction arose because a biphasic effect of apomorphine was present in C57, but not in DBA mice. In fact, apomorphine depressed the locomotor activity of C57 mice at low doses (0.5 and 1 mg/kg), while activity increments were produced by the higher doses (4 and 8 mg/kg). In DBA mice all doses of apomorphine (from 0.1 to 8 mg/kg) depressed locomotor activity.

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In C57 mice the stimulatory effect produced by higher doses (4 and 8 mg/kg) of apomorphine during the first 30 min was followed by a strong activity depression in the second part of the session. Since no other significant findings were evident the data of the second 30-min period were not reported.

No stereotyped behaviors were evident in mice treated with low doses of apomorphine. Following the administration of the higher doses of the drug C57 mice exhibited high levels of locomotor activity but also sniffing and vertical postures along the walls of the cage. DBA mice, on the contrary, remained almost motionless; only sniffing was apparent. Increased excitability to external stimuli was present in mice of both strains.

DISCUSSION

The present findings show that apomorphine exerts a biphasic effect on locomotor activity of C57 mice: low doses of the drug reduce motor activity, while higher doses produce hypermotility. In DBA mice, instead, apomorphine depresses locomotor activity over a wide range of doses.

In previous researches [1, 9, 11] the same two inbred strains of mice showed opposite responses to morphine: locomotor activity was strongly stimulated in C57 mice, while in DBA mice the opiate had no effect or depressed activity at high dosage levels only. Thus the effects of the two drugs appear somewhat different, since morphine, contrary to apomorphine, never depressed locomotor activity of C57 mice. Moreover the activity increments produced by the higher doses of apomorphine in C57 mice do not reach the high levels of hypermotility (running fit) induced by morphine. Therefore the results now obtained with apomorphine, a dopamine receptor agonist, seem to indicate that differences in dopaminergic mechanisms [10,13] do not completely explain strain differences in the effects of morphine on locomotor activity.

As concerns the effects of apomorphine on locomotor activity, a biphasic action of the drug, similar to that now observed in C57 mice, has often been described [2, 4, 5, 12], but locomotor depression at high dosages, as evident in DBA mice, has also been reported for other strains of mice [7,8].

In order to explain the biphasic effect of apomorphine, it has been suggested that low doses of the drug depress locomotor activity by stimulating presynaptic dopamine receptors (autoreceptors) with a consequent reduction in dopamine synthesis. On the contrary, an activation of postsynaptic dopamine receptors would be the cause of the hypermotility produced by the higher doses of apomorphine [2,4]. This interpretation may be suitable for the effects exerted by apomorphine in C57 mice, but cannot explain the depressant effects always produced by the drug in DBA mice. Strain differences in the behavioral response to apomorphine can perhaps be interpreted on the basis of the two receptor model [3,6] which was also used to explain the behavioral depression or stimulation induced by different dopamine agonists [5]. The existence of two different dopamine receptors and their different distribution in the brain may also account for the opposite behavioral response to apomorphine exhibited by C57 and DBA mice.

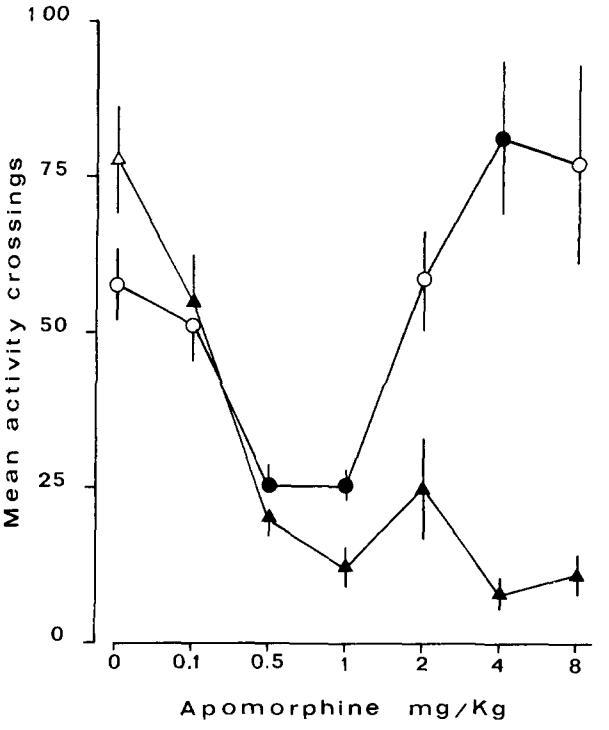

FIG. 1. Effects of apomorphine on spontaneous locomotor activity (crossings) of C57BL/6 (circles) and DBA/2 (triangles) mice, during 30 min. Vertical bars indicate standard errors of the means. Full symbols denote a significant difference ($p<0.05$) vs saline (dose 0 of apomorphine).

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