Vertical Motor Activity Is Inhibited in Mice by Lower Doses of Psychotropic Drugs Than Horizontal Activity

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This study of 19 psychotropic drugs for their effect on motor activity of mice showed that all types of drugs (tranquilizers, sedatives, neuroleptics, antidepressants, and anticonvulsants) inhibit vertical activity to a greater extent than horizontal activity.

Key Words: *vertical activity; horizontal activity; mice; inhibitory action of drugs*

Experiments on mice and rats using different classes of psychotropic drugs [4-6] have repeatedly demonstrated that the vertical component of orienting motor activity (rearings) is more susceptible to the inhibitory action of these drugs than the horizontal component (locomotion). To date, however, no special quantitative comparisons of these components have been reported. We therefore decided to summarize and process the data of our own experiments where rearings and locomotion were measured concurrently and a dose-effect curve was plotted. We were especially interested in finding out whether drugs of different classes have differential inhibitory effects on rearings and locomotion.

MATERIALS AND METHODS

Male SHR mice (body weight 18-22 g) from the *Rappolovo* nursery were used in the experiment. Locomotions and rearings in response to ethanol [3], antidepressants and cholinolytics [4], and apomorphine [5] were also compared in male BALB/c, C57Bl/6, CC57BR, and C3H/A mice.

The locomotion and rearings of individual mice were measured in a 30×30×15 cm chamber (electronic integrator) [2] or a 20×10×10 cm chamber [3] during the first 2 or 5 minutes after the mice had been placed there. Each mouse was placed in the chamber only once. Before the measurements the mice were kept in 20×10×10 cm metal cases, 8 to 10 animals in each. In some test series, in order that the size of the group from which a mouse was taken to the actometer be kept constant, an intact mice was placed in the box to replace the one removed. This procedure, which did not significantly influence the effects of the drugs under study, was necessary because it had been noticed that the locomotion and rearings of a control mouse (one injected with physiological saline instead of a drug) taken to the actometer from a larger group (5-10 animals) were at significantly lower levels than those of a mouse taken from a smaller group (1-5 animals). The tests were run in the daytime (between 10 am and 4 pm) at room temperature under constant artificial illumination (100-140 luxes).

Drugs were injected intraperitoneally in a volume equal to 1% of body weight 30 min before the test. Ethanol was administered via a stomach tube 15 min before the test. ED_{50} values for inhibition of locomotion (LED_{50}) and rearings (RED_{50}) were calculated by the Wilcoxon and Litchfield method [1]. The significance of differences between LED_{50} and RED_{50} was determined for each drug (but not between drugs) using Mebistat-F software.

RESULTS

The RED_{50} values of all drugs were significantly lower than their LED_{50}, with the exception of halo-

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TABLE 1. ED_{50} Ratios for Psychotropic Drugs as Calculated for Inhibition of Locomotion and Rearings in Mice

Drug	LED_{50}, mg/kg	RED_{50}, mg/kg	LED_{50}/RED_{50}, %
Tranquilizers			
Diazepam (Seduxen)	1.9	0.7	271
Chlordiazepoxide (Elenium)	5.7	4.2	136
Meprobamate (Meprotan)*	133	90.1	148
Phenibut*	73	51	143
Baclofen	6.8	3.5	194
Sedatives			
Sodium oxybutyrate*	57	44	129
Phenobarbital*	60	45	133
Ethanol*	5200	3000	173
Neuroleptics			
Chlorpromazine (Aminazine)*	2.6	2.0	130
Promazine (Propazine)*	18	11	164
Haloperidol	0.1	0.1	100
Trifluoperazine (Stelazine)	1.4	0.5	280
Anticonvulsants			
Trimethadione (Trimetin)*	1000	420	238
Carbamazepine (Finlepsin)	27.1	12.0	226
Phenytoin (Diphenin)*	180.2	75.1	240
Antidepressants			
Imipramine (Tofranil)	25.7	9.5	270
Desmethylimipramine (Pertorfran)	24.8	14.0	177
Amitriptyline (Saroten)	15.0	6.2	241
Lithium carbonate*	72.2	45.0	160

Note. Proprietary names are given in parentheses; *Russian—manufactured drugs. The differences between LED_{50} and RED_{50} are significant for all drugs with the exception of haloperidol.

peridol (Table 1). Individual classes of drugs did not differ in LED_{50}/RED_{50} ratios, but these ratios were not equal within each of the groups examined. Thus, they ranged from 136% (chlordiazepoxide) to 271% (diazepam) among the tranquilizers, from 100% (haloperidol) to 280% (trifluoperazine) among the neuroleptics, and from 160% (lithium carbonate) to 270% (imipramine) among the antidepressants.

All three anticonvulsants tested (trimethadione, carbamazepine, and phenytoin) differed on the whole from the other groups by having high ratios (238, 226, and 240%). None of the drugs tested had an LED_{50} lower than the RED_{50}, i.e., locomotion was not inhibited by lower doses than rearings. We are aware of only one exception: neuroactive endogenous kynurenines (metabolites of the essential amino acid tryptophan), namely kynurenine, quinolinic, 3-hydroxyanthranilic, and nicotinic acids, when injected intraperitoneally, inhibited the locomotion of mice and rats more strongly than their rearings, whereas picolinic and anthranilic acids inhibited them almost equally. The reasons for this characteristic of kynurenines have not been explored [6].

As we tested only 19 drugs, it would be incorrect to conclude that the inhibitory action of all psychotropics is stronger on rearing than on locomotion. In our view, our results emphasize the need for measuring rearings when studying new drugs. In certain instances, for example in evaluating the effect of ethanol on motor activity, the dose-effect curve for locomotion is dome-shaped, and analysis of the frequency of rearings can elucidate whether the test drug that reduces ethanol-induced excitation enhances or weakens the effect of ethanol [3]. This question cannot be answered unless rearing parameters are measured. If the rearing frequency has also decreased (the curve has shifted to the right), this means that the effect of ethanol has intensified. If the rearing frequency has increased (the curve has shifted to the left), then the effect of ethanol has weakened. Rearing frequencies help evaluate the effects of phenamine in a similar way [4].

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