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Differential Antagonism of Reserpine Eyelid Closure by Imipramine and Amphetamine. (27354)

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Stimulants such as amphetamine and antidepressants such as imipramine antagonize reserpine-induced eyelid closure in laboratory animals(1-5). Although amphetamine and imipramine seem to have similar effects in this respect, they belong to different classes of compounds with different pharmacological and clinical activities. The present paper will describe a differentiation of imipramine from amphetamine in the antireserpine eyelid closure test in mice.

Methods and materials. The tests were performed using Carworth Farms mice CF No. 1 weighing 16 to 24 g. Male and female animals were equally distributed throughout all groups. The animals were starved 4 hours prior to drug administration. Imipramine hydrochloride or d,l-amphetamine sulfate was administered orally at graded dose levels to 4 groups of 10 mice per dose. Control groups received the vehicle (water) only. In acute experiments, the animals were challenged with reserpine one hour after a single treatment with amphetamine or imipramine. In subacute experiments, mice were treated once daily with amphetamine or imipramine for 2 (in one experiment for 3) consecutive days, and challenged with reserpine 24 hours after the last drug treatment.

Reserpine U.S.P. (S.B. Penick), solubilized with a few drops of glacial acetic acid and diluted with water, was injected intraperitoneally at a dose of 2.5 mg/kg. At one-half, one and two hours after reserpine treatment, eyelid closure scores were taken according to the method of Rubin(6). The scores of the imipramine and amphetamine groups were averaged per group and expressed as percentages of the water control; the values of the 3 readings were averaged. The treatment with amphetamine or imipramine was performed while the mice were aggregated, 10 per cage. After the reserpine injection, each animal was placed under a 1000-ml glass beaker. The animals were not handled during the observation period of 2 hours.

Results. In acute studies, both imipramine (100 mg base/kg) and amphetamine (0.5 to 4.0 mg base/kg) showed marked antagonism to reserpine ptosis (imipramine, 45%; amphetamine, 18 to 63%). In contrast, after repeated administration, imipramine (50 to 200 mg base/kg/day) showed appreciable antagonism (7 to 72%), but amphetamine (4.0 to 64.0 mg base/kg/day) produced only slight antagonism (4 to 14%). The results of the 2-day experiments are shown in Fig. 1. It should be pointed out that an increase in the dose of amphetamine above 64 mg/kg resulted in death. Administration of imipramine for 3 days gave similar effects to the 2-day treatment. When amphetamine was administered for 3 days the reserpine eyelid closure was increased.

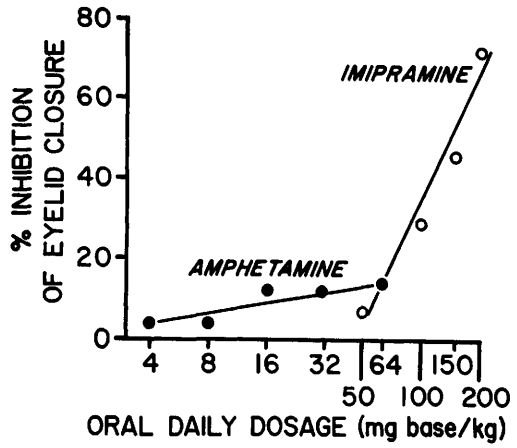

FIG. 1. Inhibition of reserpine eyelid closure in mice by pretreatment for 2 days with amphetamine or imipramine. Challenge with reserpine (2.5 mg/kg i.p.) on third day.

Discussion. Pretreatment with imipramine, an "antidepressant", or with amphetamine, a "stimulant", for at least 2 consecutive days, followed by challenge with reserpine 24 hours after the last drug treatment, produced a differential antagonism to reserpine eyelid closure; only imipramine produced appreciable antagonism. On the other hand, with single administration of the drugs followed by reserpine challenge one hour later, both amphetamine and imipramine were equally active, but higher doses of imipramine were required. These results indicate that the antagonism to reserpine eyelid closure resulting from imipramine lasts longer than that from amphetamine. This difference is similar to differences seen with these compounds in man; amphetamine is a shorter acting drug than imipramine.*

Summary. A differentiation of imipramine, an antidepressant drug, from amphetamine, a stimulant, in the antireserpine eyelid closure test has been described; after administration for 2 days, and reserpine challenge on the third day, imipramine was considerably more active than amphetamine in antagonizing eyelid closure in mice.

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* Possibly the difference of effects observed by us is indicative of a different mechanism of action.

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Streptokinase Induced Lysinemethylesterase Activity of Human Euglobulin.* (27355)

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When streptokinase (SK) reacts with human plasma, or fractions which contain plasminogen, several types of enzymatic activity are produced. The present concept of SK action attributes each of these activities to the interaction between SK and the single proenzyme, plasminogen. This concept stems from a number of studies(1-5). These indicate that, following SK activation of human plasminogen preparations, activity toward

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