Effect of Dopalanine on Behaviour in Mice Depleted of Norepinephrine or Serotonin

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Received June 14, 1968
Final Version: October 30, 1968

Summary. These studies were performed to investigate the behavioral and biochemical effects of DOPA in mice which had undergone selective depletion of NE or 5-HT. PCPA caused an increase of locomotor activity and DOPA potentiated this effect. α-MT inhibited locomotor activity and DOPA had no consistent effect on locomotor activity which had been inhibited in this way. DOPA caused a transient increase of locomotor activity. These behavioral changes are discussed in relation to biochemical changes observed in the brain.

Key-Words: Dopalanine -- p-Chlorophenylalanine -- α-Methyltyrosine -- Mice -- Behaviour.

The stimulant action of dopalanine (DOPA) in various species has been described by several authors (Carlsson et al., 1967; Bertler and Rosengren, 1959; Blaschko and Chrusińciel, 1960; Chrusińciel, 1960; Everett and Wiegand, 1962; Halpern et al., 1963; Boissier and Simon, 1966). The mechanism of this action of DOPA is still unknown. In the present study we have determined the influence of DOPA on the behaviour of mice after depletion of their stores of norepinephrine (NE) with α-methyltyrosine (α-MT) or serotonin (5-HT) with p-chlorophenylalanine (PCPA).

Method

The compounds used were p-chlorophenylalanine (PCPA, Aldrich); d,l- or l-3,4-dihydroxyphenylalanine (DOPA, Calbiochem); α-methyltyrosine (α-MT, Merck, Sharp and Dohme); reserpine (NBC); nialamide (Pfizer). Doses of these compounds were calculated in terms of the free base. Reserpine was dissolved in two drops of glacial acetic acid and diluted with distilled water; other substances were dissolved in distilled water.

The experiments were performed on male, white mice, weighing approximately 20 g each. Each treated group consisted of at least 10 animals. A parallel control groups of animals injected with adequate
volumes of distilled water was used in each experiment. All substances were injected intraperitoneally. The animals were placed in the cages of Knoll's motimeter (Knoll, 1961), or in jiggling cages constructed according to Schlagintweit's principle (Schlagintweit, 1928) at different periods of time after the injection of the tested substances. The motility of 20 mice in Knoll's apparatus or 10 mice in Schlagintweit's apparatus was measured simultaneously. Locomotor activity was measured for 2—3 hours; counts were recorded every ten minutes the results were expressed as counts per 10 min.

For catecholamine assay the brains of three mice killed by cervical dislocation were pooled for one estimation. Frozen brain tissue was weighed and homogenized in a glass homogenizer with 4 volumes of cold 0.4 N perchloric acid. Norepinephrine and dopamine (DA) were estimated by the spectrophotofluorimetric method of Chang (1964) using Farrand spectrofluorometer. Each group of mice used for catecholamines assay consisted of nine animals.

Results

In mice injected with PCPA, 50 mg/kg or d,l-DOPA, 50 mg/kg a transient increase of locomotor activity was observed. In animals injected with PCPA and d,l-DOPA concomitantly the intensity of locomotor activity was doubled as compared with the activity of animals treated with PCPA or d,l-DOPA separately (Fig. 1).

Animals depleted of 5-HT by PCPA, which was given in a daily dose of 320 mg/kg for 3 consecutive days preceding the experiment, showed an increase of locomotor activity as compared with control, untreated animals. d,l-DOPA in a dose of 50 mg/kg in animals depleted of 5-HT caused a remarkable increase of locomotor activity (Fig. 2).

α-MT, in a dose of 200 mg/kg, which depleted NE stores in the brain, induced an almost complete loss of spontaneous activity of mice.

When locomotor activity was measured in Knoll’s apparatus, PCPA 50 mg/kg and d,l-DOPA 50 mg/kg given concomitantly did not restore the locomotor activity which was abolished by α-MT. On the contrary, the locomotor activity of mice treated with α-MT was increased after the administration of d,l-DOPA and very markedly increased after the concomitant application of d,l-DOPA and PCPA, when locomotor activity was measured in Schlagintweit’s apparatus (Fig. 3).

In fully reserpinised mice no spontaneous locomotor activity was observed. d,l-DOPA and especially d,l-DOPA injected concomitantly with PCPA increased markedly the locomotor activity of these animals (Fig. 4).