Short Communications

Effects of Acute and Chronic Administration of Phencyclidine on Tyrosine Hydroxylase Activity in Rat Striatum

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With 1 Figure

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Summary

Following a single dose of phencyclidine (PCP) striatal tyrosine hydroxylase (TH) activity was decreased 42% 15 min after PCP administration, but returned toward baseline levels by 45 min post-drug. Twenty-four hours after the 30th dose of PCP, TH activity remained depressed when compared to the chronic saline controls. TH activity was not further depressed 15 or 45 min after the 31st dose of PCP.

Introduction

Phencyclidine (PCP) is an anesthetic drug which has psychotomimetic properties in man (Domino et al., 1973; Luby et al., 1959). PCP produces stereotypic and ataxic behavior in rats and monkeys (Smith et al., 1978; Schlemmer et al., 1978; Murray and Horita, 1979), behavioral effects which may be partially mediated by the drug's interaction with striatal dopaminergic neurons. Behavioral and biochemical studies indicate that PCP may have some properties of an indirectly acting dopamine agonist. In rats with unilateral nigrostriatal lesions, PCP produces turning towards the side of the lesion
(Kanner et al., 1975). In vitro PCP is also a potent inhibitor of dopamine uptake in the striatum (Smith et al., 1977). These behavioral and biochemical effects are similar to those of amphetamine, an indirectly acting dopamine agonist, which produces stereotyped behavior in the rat and has psychotomimetic properties in man (Ellingwood and Sudikusky, 1973; Fog, 1972). Chronic administration of PCP produces tolerance to some of its effects on operant behavior in monkeys (Balster and Chait, 1978; Chait and Balster, 1978), but augmented effects on stereotypic and ataxic behavior in rats (Smith et al., 1978; Smith et al., 1979). To further characterize the effects of PCP on striatal dopaminergic neurons, we investigated the effects of acute and chronic PCP on striatal tyrosine hydroxylase (TH) activity in rat striatum.

**Methods**

Sprague-Dawley rats (225—325 gm) were used in the experiment. Rats were housed in group cages under standard laboratory conditions maintained at 76 ± 2 °F with a 12-hour light-dark cycle, and ad libitum access to Purina rat chow.

Rats were divided into six treatment groups defined as follows: (1) SAL-SAL—rats received saline for 30 days and saline on the 31st day; (2 and 3) acute-PCP (AP-15 or 45)—rats received saline for 30 days and PCP 10 mg/kg on the 31st day, and were sacrificed 15 or 45 min after the last drug administration; (4) chronic PCP-SAL (CP-SAL)—rats received PCP 10 mg/kg for 30 days and saline on the 31st day, and were sacrificed approximately 24—25 hours after the last (30th) dose of PCP; (5 and 6) chronic PCP-PCP (CP-15 or 45)—rats received PCP 10 mg/kg for 30 days, PCP 10 mg/kg on the 31st day, and were sacrificed either 15 or 45 min after the 31st PCP dose. PCP hydrochloride powder (obtained from the Office of Research Technology, NIDA) was dissolved in saline and injected i.p. On weekends, rats received PCP in the drinking water (2 mg per 100 ml). Rats were killed by decapitation, striata dissected out over ice, frozen in liquid nitrogen, and stored at −20 °C until used for analysis.

Tissues were homogenized in 10 volumes of 0.05 M Tris-acetate buffer, pH 6.1, containing 0.2 % Triton X-100. Tyrosine hydroxylase activity was determined in the striatum by the method of Waymire et al. (1971) using 1-14C-tyrosine as substrate. The reaction mixture was carried out in a total volume of 120 µl, and the 14CO2 was trapped in filters impregnated with hyamine hydrochloride. To 50 µl of homogenate was added: 20 µl of 0.2 N Tris-acetate buffer, pH 6.1; 10 µl ferrous ammonium sulfate, 10 mM; 10 µl DMPH4, 2 mM in mercaptoethanol 400 mM; 10 µl pyridoxal phosphate, 0.5 mM; 20 µl hog kidney decarboxylase prepared by a modified procedure of Inaki and Tanaka (1978). 1-14C-tyrosine (100 nmoles/0.5 µCi) was added and the tubes were covered with rubber vial caps (Kontes Glass Co.) in which were suspended plastic wells containing a folded filter