importance as mediators of this inflammatory response is limited. Furthermore, they probably do not exert their effect on vascular permeability through histamine release (as suggested by Crunkhorn & Willis) as other histamine releasers (e.g. dextran) respond uniformly when injected intradermally into rats. It is unwise to test compounds for anti-prostaglandin activity by the intradermal route in rats until it has been shown that the particular colony of animals responds in a consistent manner.

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Department of Applied Biology,
North East London Polytechnic,
Longbridge Road, Dagenham, Essex, U.K.

PATRICIA C. FREEMAN
G. B. WEST

February 10, 1972

REFERENCE

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Blockade by pimozide of (+)-amphetamine-induced hyperkinesia in mice

Mediation of (+)-amphetamine's action has been attributed to catecholamine systems (Weissman, Koe & Tenen, 1966). Although there is indirect evidence implicating dopaminergic as well as noradrenergic neurons (Svensson, 1970), a direct test of the importance of dopamine has not as yet been made. Pimozide, a putative dopamine receptor blocker (Janssen, Niemegeers & others, 1968; Andén, Butcher & others, 1970), would appear to provide an opportunity for such a test. There is evidence that pimozide blocks (+)-amphetamine-induced stereotyped behaviours such as "agitation" and "chewing" (Janssen, Niemegeers & others, 1967) and (+)-amphetamine-induced hyperthermia in rats (Matsumoto & Griffin, 1971). We now present quantitative evidence that pimozide also blocks the increased locomotor activity observed in mice after (+)-amphetamine.

Male albino Swiss-Webster mice (Simonsen Laboratories, Gilroy, California, U.S.A.) 24–35 g were given pimozide (0·5 mg/kg) and (+)-amphetamine sulphate (5 mg/kg) intraperitoneally, the doses being expressed in terms of the salt. At 0·5 mg/kg, pimozide apparently blocks only dopamine receptors (Andén & others, 1970). Pimozide was dissolved in a glucose-acetic acid vehicle (cf., Andén & others, 1970), and (+)-amphetamine was dissolved in 0·9% saline. The vehicles were used for control injections. The volume of administered fluid was approximately 0·015 ml per injection.

The 48 mice used were randomly assigned to groups of 12 animals. Two of the groups were given pimozide; the remaining two groups received the glucose-acetic acid vehicle. Four h later, one vehicle and one pimozide group were injected with (+)-amphetamine whilst the remaining two received saline, the (+)-amphetamine vehicle. The mice were then placed individually in stabilimeters (Davis & Ellison, 1964). Five min later activity measurements were begun and continued for 2 h.

As shown in Fig. 1, pimozide completely blocked the (+)-amphetamine-induced hyperkinesia at all intervals measured whereas administration of pimozide alone had no significant effect, compared to control, on spontaneous motor activity. No other differences among the various treatment conditions were statistically significant at any of the time intervals studied (Fig. 1). In view of these results and also those of Svensson (1970) showing only moderate diminution of the locomotor stimulatory

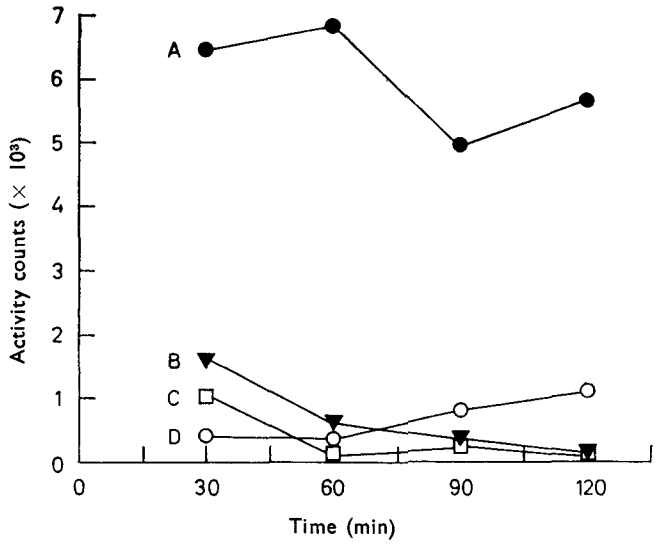

FIG. 1. Effects of pimozide on (+)-amphetamine-induced hyperkinesia. Each point represents the mean of 12 values. A: Glucose-acetic acid vehicle + 5 mg/kg (+)-amphetamine ●——●. B: Glucose-acetic acid vehicle + 0·9% saline ▲——▲. C: 0·5 mg/kg pimozide + 0·9% saline □——□. D: 0·5 mg/kg pimozide + 5 mg/kg (+)-amphetamine ○——○. The second drug in each treatment series was administered 4 h after the first with activity measurements commencing 5 min after injection of the second. Analysis of variance and subsequent analyses using the Newman–Keuls' procedure (Winer, 1962) revealed that at each time interval comparisons A–B, A–C and A–D were significant at $P < 0.01$. All possible remaining comparisons were not significant ($P > 0.05$).

effects of (+)-amphetamine after dopamine-β-hydroxylase inhibition, it may be concluded that intact dopamine functioning is of major importance for the mediation of (+)-amphetamine-induced increases in spontaneous motor activity.

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Department of Psychology,
University of California at Los Angeles,
Los Angeles, California 90024,
U.S.A.

JAY M. SCHLECHTER
LARRY L. BUTCHER

February 9, 1972

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