The effect of β-phenethylamine on noradrenaline concentrations in guinea-pig brain

β-Phenethylamine (PE) is an indirectly acting sympathomimetic amine which crosses the blood brain barrier to cause central nervous system (c.n.s.) stimulation (Mantegazza & Riva, 1963). PE occurs *in vivo* in human urine (Asatoor & Dalgliesh, 1959), rabbit brain and other tissues; (Najakima, Kakimoto & Sano, 1964; Jackson & Temple, 1970). On animals it exerts a c.n.s. stimulant effect resembling that of amphetamine (Mantegazza & Riva, 1963; Saavedra & Fischer, 1970), and like amphetamine causes marked depletion of noradrenaline in heart and brain (Jonsson, Grobecker & Holtz, 1966) and some depletion of dopamine (Fuxe, Grobecker & Jonsson, 1967). PE may serve as a neurohumor *in vivo* (Nakajima & others, 1964; Mantegazza & Riva, 1963), and evidence has been presented (Saavedra & Fischer, 1970) that PE and tryptamine may play opposing roles in the c.n.s. in much the same way as has been proposed for noradrenaline and 5-hydroxytryptamine.

With these considerations in mind, I now report the effect of PE on noradrenaline and dopamine concentrations in guinea-pig brain.

Guinea-pigs of either sex (400–550 g) were killed by decapitation and the brain immediately removed and extracted with 0·4M perchloric acid. Noradrenaline and dopamine were extracted (Anton & Sayre, 1962) and the former estimated according to Haggendal (1963) and the latter according to Anton & Sayre (1964). Recovery of both amines was between 70 and 80%. PE was administered intraperitoneally as the hydrochloride, dissolved in normal saline to give a dose volume of 1 ml/100 g. Saline was used for control injections. After injection and until death, animals were kept isolated in quiet surroundings. Each brain was assayed individually and the values are uncorrected for % yield.

Animals received one dose of either 100 or 200 mg/kg of PE and were killed at various intervals after injection. An effect was observed on brain noradrenaline concentration within 15 min. Peak depletion was one h after injection and recovery to control values was within 24 h (with the high dose) (Fig. 1). The depletion of

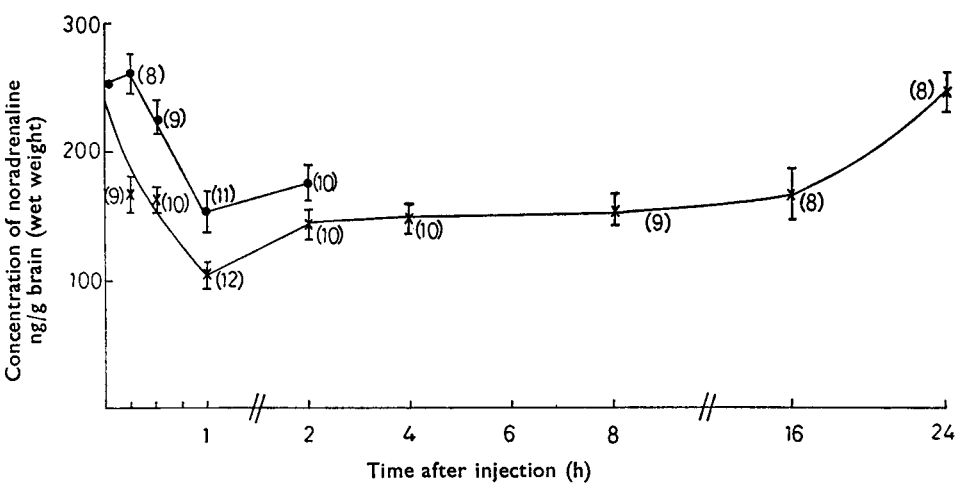

FIG. 1. The effect of a single dose of β-phenethylamine on the concentration of noradrenaline in guinea-pig brain. Animals were given a single dose of either 100 or 200 mg/kg, i.p. and a number killed at various time intervals after this injection. The vertical bars represent the standard errors of the means. The values in brackets are the number of animals in each group. ●, 100 mg/kg. ×, 200 mg/kg.

noradrenaline was dose-dependent, and at the highest dose, marked behavioural changes, including licking, and clonic convulsions in some animals, were observed. These changes were maximal 1 h after injection of PE. There was no detectable change in brain dopamine levels.

Repeated doses of PE (100 mg/kg) at 1 h intervals to another group of guinea-pigs showed that maximum noradrenaline depletion (representing 74% of total noradrenaline stores) occurred after the third injection (total dose of 300 mg/kg PE at 100 mg/kg h^{-1}), and that the concentration after three injections was not significantly different from that after six injections ($P > 0{\cdot}1$).

The findings are in agreement with those of Jonsson, Grobecker & Holtz (1966), that PE in rats causes a marked depletion of brain noradrenaline concentrations, without significantly affecting those of dopamine, although Fuxe, Grobecker & Jonsson (1967) found small but significant changes in brain dopamine concentrations in rats. The doses of PE I used were high but it is rapidly broken down by monoamine oxidase (Blaschko, 1952; Mantegazza & Riva, 1963). The depletion of brain noradrenaline was accompanied by behavioural changes which appeared maximal when maximum noradrenaline depletion had occurred (at 1 h). The depletion produced resembled that caused by amphetamine (Moore & Lariviere, 1963), except that maximal depletion took 1 h compared to 4 h with amphetamine, and the effect lasted 24 h compared to 7 days with amphetamine. Maximum noradrenaline depletion of 74% agreed well with the depletion of approximately 70% in rats found by Jonsson & others (1966).

Measures of spontaneous motor activity in mice suggests that peak activity after intraperitoneal injection of PE is reached in 5–7 min (Nakajima & others 1964; Jackson & Temple, unpublished observations), and a return to normal levels of motor activity occurs within 15 min. In spite of the species difference, these reports suggest that there may not be a clear correlation between spontaneous coordinated motor activity and noradrenaline depletion by PE, and that other factors, one of which may be a direct component of action, may be operating, in the same way as has been suggested for the cns effects of amphetamine (Smith, 1963, 1964). The work of Saavedra & Fischer (1970) and my preliminary experiments seem to support such a hypothesis.

Department of Pharmacology,
The University of Sydney,
Sydney, Australia.

D. M. JACKSON

March 9, 1971

REFERENCES

ANTON, A. H. & SAYRE, D. F. (1962). *J. Pharmac. exp. Ther.*, **138**, 360–375.
ANTON, A. H. & SAYRE, D. F. (1964). *Ibid.*, **145**, 325–336.
ASATOOR, A. M. & DALGLIESH, C. E. (1959). *Biochem. J.*, **73**, 26P.
BLASCHKO, H. (1952). *Pharmac. Rev.*, **4**, 415–458.
FUXE, K., GROBECKER, H. & JONSSON, J. (1967). *Europ. J. Pharmac.*, **2**, 292–207.
HAGGENDAL, J. (1963). *Acta. physiol. scand.*, **59**, 242–254.
JACKSON, D. M. & TEMPLE, D. M. (1970). *Comp: gen. Pharmac.*, **1**, 155–159.
JONSSON, J., GROBECKER, H. & HOLTZ, P. (1966), *Life Sci.*, **5**, 2235–2246.
MANTEGAZZA, P. & RIVA, M. (1963). *J. Pharm. Pharmac.*, **15**, 472–478.
MOORE, K. E. & LARIVIERE, E. W. (1963). *Biochem. Pharmac.*, **12**, 1283–1288.
NAKAJIMA, T., KAKIMOTO, Y. & SANO, I. (1964). *J. Pharmac. exp. Ther.*, **143**, 319–325.
SAAVEDRA, J. M. & FISCHER, E. (1970). *Arzneimittel-Forsch.*, **20**, 952–956.
SMITH, C. B. (1963). *J. Pharmac. exp. Ther.*, **142**, 343–350.
SMITH, C. B. (1964). *Ibid.*, **146**, 167–174.