Table 1 Effect of (+)-amphetamine (AMPH, 10 mg/kg) on the inhibition of ^{14}C-serotonin deamination by phenelzine (PHEN, 2 mg/kg) in striatum and rest of the brain

*Drug Treatment**	*MAO activity* *n mol deaminated (mg tissue)$^{-1}$h^{-1} ± s.e. mean (n)* *Striatum*	*Rest of the brain*
None	14.23 ± 1.76 (4)	13.84 ± 1.07 (4)
Phenelzine	3.92 ± 0.50 (5)†	4.54 ± 0.29 (5)†
Amphetamine	14.30 ± 1.02 (4)	14.30 ± 0.75 (4)
Amphetamine + Phenelzine	7.17 ± 0.61 (6)‡	7.13 ± 0.40 (6)‡

*(+)-Amphetamine was given s.c. at zero time, phenelzine s.c. at 1 h and the rats were killed at 25 h. Significance of differences: † from None $P < 0.001$; ‡ from Phenelzine, $P < 0.01$ (Student's t-test).

protection against type A MAO inhibition by phenelzine. These data confirm those reported by Green & El Hait (1978) for whole mouse brain. In other experiments, (−)-amphetamine (10 mg/kg) and cocaine (15 mg/kg) failed to protect. Additionally, with phenylethylamine (a type B substrate), (+)-amphetamine failed to protect against phenelzine. Phenelzine itself, inhibited serotonin deamination to a greater extent than phenylethylamine, suggesting preferential MAO type A inhibition.

The same 'protection experiment' was made but the reserpine-like agent Ro4-1284 (2 mg/kg, i.p.) was given 30 min prior to sacrifice and striatal dopamine measured. Phenelzine alone greatly retarded dopamine depletion. (+)-Amphetamine, prior to phenelzine, restored significantly the effect of Ro4-1284.

We conclude that (+)-amphetamine inhibits MAO type A within striatal dopaminergic neurons. Differences in the ability of (+)- and (−)-amphetamine to lower striatal DOPAC may be related, at least in part, to their relative potencies as MAO inhibitors.

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Inhibition of early embryogenic development in mice by α-difluoromethyl ornithine, an enzyme-activated irreversible inhibitor of L-ornithine decarboxylase

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Decarboxylation of L-ornithine by L-ornithine decarboxylase (ODC; E.C. 4.1.1.17) is the initial and, at least in mammals, rate-limiting step in the biosynthesis of the polyamines, putrescine, spermidine and spermine (Williams-Ashman *et al.*, 1972). Although basal activity of ODC is generally low in most tissues, marked increases are characteristically associated with rapid tissue growth (Jänne, Pösö & Raina, 1978), and particularly with mammalian and non-mammalian embryogenesis (Russell & McVicker, 1972; Manen, Hadfield & Russell, 1977). The development in our laboratories of the irreversible inhibitor of ODC, α-difluoromethylornithine (α-DFMO, RMI 71782, Metcalf, Bey, Danzin, Jung, Casara & Vevert, 1978) provided the opportunity to investigate the functional significance of ODC for early embryogenesis in the mouse.

Proven fertile, CDA, HAM-ICR albino mice of 30–45 g initial body weight were mated, and the day following detection of the vaginal plug was designated day 1 of gestation. α-DFMO was included in the drinking water at a concentration of 2% and the 24 h intake by this means was constant at approximately

120 mg/mouse. Uterine ODC activity and polyamine concentrations were measured by methods previously described (Prakash, Schechter, Grove & Koch-Weser, 1978). Tissues were examined histologically after fixation in Bouin's solution and staining of serial sections with Haematoxylin-Eosin.

Uterine ODC activity was low (0.5–3.1 nmol g^{-1} h^{-1} total CO_2) in non-pregnant mice and during the first 5 days of gestation. It increased sharply between days 6 and 7 to reach a peak of 26.8 ± 4.6 (mean $\pm$ s.e. mean; $n = 8$) nmol g^{-1} h^{-1} total CO_2 on day 8, and declined significantly by days 9 and 10. Qualitatively similar changes were observed in the uterine putrescine and spermidine concentrations, but spermine levels remained unchanged. On day 8 of gestation, the levels of ODC activity and putrescine concentrations in individual uteri correlated significantly with the number of implantation sites. Treatment with α-DFMO from day 5 to day 9 of gestation abolished the increases in uterine ODC activity and putrescine and spermidine concentrations. Spermine concentrations were significantly elevated compared to untreated mice. Uteri from treated animals showed no signs of pregnancy when examined on day 18 of gestation. Histological examination of uteri from treated mice from the sixth gestational day onwards revealed decidualization and implantation to be normal but subsequent embryogenic development to be greatly retarded. As early as day 9, signs of resorption were evident. Decidual swellings in uteri from 16 day pregnant mice contained no embryos. Deciduomata became smaller and increasingly detached from the uterine endometrium, culminating in their total resorption/explusion between days 16 and 18.

These results provide direct proof of a fundamental role for ODC in a normal mammalian physiological process, namely, the early stage of murine embryogenesis.

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Decreased nephrotoxic effect of mercuric chloride on the regenerating kidneys

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Pretreatment with Hg^{2+} (Yoshikawa, 1970) or Cd^{2+} (Magos, Webb & Butler, 1974) decreased the sensitivity of the kidneys of rats to a following dose of sublimate. As both Hg^{2+} and Cd^{2+} are known to induce metallothionein, the protective effect could be explained by the induction of thionein and the competition of thionein for Hg^{2+} with vital binding sites. However, it was shown that Cd pretreatment increased both the amount of thionein and non-thionein bound mercury in the kidneys (Webb & Magos, 1976) and therefore, thionein synthesis alone cannot explain the protection.

Renotoxic agents which do not induce thionein offered a way to separate the effects of regeneration and thionein synthesis on this protective effect. Thus, the effects of pretreatment with sodium chromate (20 mg/kg, s.c.), uranyl acetate (4 mg/kg, s.c.), p-aminophenol (100 mg/kg, s.c.) and sodium maleate (500 mg/kg, s.c.) were studied on $HgCl_2$ nephrotoxicity.