In contrast amylobarbitone and methaqualone only reduced the hyper-reactivity at hypnotic or near-hypnotic dose-levels (20–40 mg/kg). The hyper-reactivity was unaffected by pethidine (10 mg/kg). This result largely eliminated the possibility that the behavioural effects of the lesions were due to chronic pain.

The results of this investigation indicate that animals with anterior hypothalamic lesions could be of value in evaluating the "tranquillizing" as distinct from the hypnotic properties of drugs.

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Interactions of oestrogenic and progestational steroids with dexamphetamine and fencamfamin in mice

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Increased progestational activity in both man and experimental animals is associated with increased tissue monoamine oxidase (MAO) activity (Cohen, Bitensky, Chayen, Cunningham & Russell, 1964; Southgate, Grant, Pollard, Pryse-Davies & Sandler, 1967; Kuwabara, Russfield, Weisz & Lloyd, 1967). The occurrence of depression in susceptible women receiving these agents may be due to this enhanced MAO activity (Grant & Pryse-Davies, 1968). Enhanced MAO activity might also change the properties of other drugs administered concomitantly with these steroids. The responses of mice to dexamphetamine and fencamfamin were observed after pretreatment with progestational or oestrogenic steroids.

Female TO mice were injected daily for 6 days, subcutaneously, with a progestin (lynestrenol, 10 mg/kg) or an oestrogen (mestranol, 1 mg/kg). On the seventh day, the effects of dexamphetamine and fencamfamin given intraperitoneally were assessed on body temperature, locomotor activity; their acute toxicity was also determined.

Mestranol increased while lynestrenol reduced the hyperthermia induced by dexamphetamine (10 mg/kg) in mice. Fencamfamin (20 mg/kg) failed to induce hyperthermia in control and lynestrenol-pretreated mice, but did induce hyperthermia after mestranol pretreatment. The potentiating effects of mestranol could be mimicked by pretreatment with the MAO inhibitor, nialamide, but not by the inhibitor of microsomal enzyme activity, SKF 525A.

The increased locomotor activity induced by dexamphetamine (5 mg/kg) and fencamfamin (10 mg/kg) was enhanced by mestranol, and reduced by lynestrenol.

In uncrowded conditions, the acute toxicities of neither dexamphetamine nor fencamfamin were altered by steroid pretreatment. Under crowded conditions, the usual increase in dexamphetamine toxicity was still further increased by mestranol but unchanged after lynestrenol. Crowding normally increases the toxicity of fencamfamin only marginally; steroid pretreatment was without effect on its toxicity in crowded conditions.

Finally, the effects of lynestrenol (10 mg/kg) and mestranol (1 mg/kg) on brain amine levels were studied. Using the spectrophotofluorometric assay method of Spencer & Turner (1969) whole-brain levels of dopamine, noradrenaline and 5-hydroxytryptamine were determined after pretreatment with steroid for 6 days. The levels of each amine were slightly reduced with lynestrenol ($P=0{\cdot}1$ to $0{\cdot}05$), while 5-hydroxytryptamine was increased with mestranol ($P=0{\cdot}1$ to $0{\cdot}05$).

If the actions of dexamphetamine (and fencamfamin) are due predominantly to the release of endogenous amines, then an increase (with lynestrenol) or a decrease (with mestranol) of tissue MAO activity should change the potency of these two stimulant drugs. Since Hotovy, Enenkel, Gillisen, Hoffmann, Jahn, Kraft, Muller-Calgan, Sommer & Struller (1961) showed that the peripheral effects of fencamfamin were weaker than those of dexamphetamine, it might be expected that the peripheral effects of dexamphetamine would be the most affected by steroid pretreatment. Our results support this. Mestranol potentiated dexamphetamine-induced hyperthermia and aggregation toxicity (enhanced by hyperthermia) to a greater degree than those induced by fencamfamin. However, the effects of both drugs on locomotor activity (assumed to be a central effect) were affected similarly by steroid pretreatment.

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Ambient temperature and thermal responses to hexamethonium in the mouse

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There is ample evidence that ambient temperature (T_A) can markedly affect the thermal responses to drugs (for example, Shemano & Nickerson, 1958). We have investigated the effect of a single intraperitoneal (I.P.) injection of hexamethonium bromide (10 or 40 mg/kg) on the rectal temperature of mice, at three ambient temperatures. Two hours before the experiment, mice (5–10 per group) were removed