We have examined the effect of adrenalectomy on the thermogenic response of antidepressants and morphine in reserpinized mice. Groups of six T.O. mice (male, 20–22 g) were adrenalectomized 40–44 h before the administration of reserpine (2 mg base/kg, s.c.) or saline. Three hours later the test compound or saline was given. Oesophageal temperatures were recorded every hour (room temp., 20±1° C) using an orally-inserted probe.

Adrenalectomized mice showed an enhanced sensitivity to the temperature-lowering effect of reserpine.

It was not possible to demonstrate reversal of reserpine-induced hypothermia in adrenalectomized mice with the following compounds which effect a reversal in normal mice: (+)-amphetamine (1 and 10 mg base/kg, p.o.), desmethylimipramine (1 and 10 mg base/kg, p.o., see Fig. 1), morphine (75 mg base/kg, s.c.), diprenorphine (30 mg base/kg, s.c.) and the dihydrocodeinone R & S 336-M (10 mg base/kg, s.c.).

Since the thermogenic effect of these compounds was only demonstrated in reserpinized mice with functional adrenal glands, this response would appear to be a peripheral phenomenon mediated by the release of catecholamines from the adrenal medulla.

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Alterations in the sleep/wakefulness cycle in rats after administration of (−)-LSD or BOL-148: a comparison with (+)-LSD

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In a previous communication (Depoortere & Loew, 1971a) we reported that treatment of rats with (+)-LSD produces quantitative and qualitative changes in the sleep/wakefulness cycle. In particular, (+)-LSD administration causes qualitative changes in paradoxical sleep as evidenced by changes in the electrical activity of the visual system. In the following experiments the effects of (+)-LSD were compared with those of its laevorotatory isomer and its non-hallucinogenic bromine derivative BOL-148.

Male Wistar rats, bearing chronically implanted electrodes for electroencephalographic and electromyographic recordings were used. Continuous recordings were made during 6 h after injection of drug or saline. Control experiments, using the same animals, were performed on the day preceeding treatment. In addition to the quantitative analysis of the durations of various phases of the cycle, the qualitative changes in paradoxical sleep were evaluated using a method recently described (Depoortere & Loew, 1971b).

(−)-LSD tartrate, 1 or 3 mg/kg, or BOL-148 bitartrate, 3 mg/kg were injected intraperitoneally in a volume of 5 ml/kg 15 min before the recordings. All the results

presented are the means of six experiments, with the exception of the higher dose of (−)-LSD which was tested in three animals.

Treatment with (−)-LSD at 1 or 3 mg/kg did not change the content of the sleep/wakefulness cycle nor did it affect the quality of the phases. In particular, the drug did not cause any inhibition of the duration of paradoxical sleep. (+)-LSD causes a significant inhibition of paradoxical sleep, and also significantly delays the onset of the first phase of paradoxical sleep (Depoortere & Loew, 1971a). Treatment with BOL-148 led to a 27% decrease ($P<0.05$) in paradoxical sleep and a 14% increase ($P<0.05$) in slow wave sleep. The delay in onset of the first phase of paradoxical sleep was increased by the drug, but this effect was not significant. Thus, the effects of BOL-148 on paradoxical sleep were found to be qualitatively similar to those of (+)-LSD.

Evaluation of the qualitative changes in paradoxical sleep revealed that (+)-LSD reduced the number of phases of body movement occurring during paradoxical sleep, but increased the intensity of such movements. Both these qualitative changes were seen after BOL-148 treatment, although this drug was not as potent as (+)-LSD in this respect.

Thus, in these experiments, (−)-LSD was found to be devoid of central activity whereas BOL-148 exerted definite central actions. Although less potent, BOL-148 has an activity which is similar to that of its hallucinogenic congener (+)-LSD. The two compounds differ in that (+)-LSD induces initial stimulation which is not seen following BOL-148 administration.

The results are consistent with the view that the effects of (+)-LSD on the rat sleep electroencephalogram are not related to its hallucinogenic effects.

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Influence of endocrine glands on central and peripheral monoamine oxidase activity

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The influence of steroid producing glands on the activity of enzyme monoamine oxidase (monoamine: O_2 oxidoreductase (deaminating) EC 1.4.3.4.) was studied in male and female rats which were kept under constant lighting conditions. It was measured in four brain regions (septum, hypothalamus, caudate nucleus and part of the amygdala-hippocampus complex), heart, liver, adrenal glands, uterus and ovaries during periods of low locomotor activity (white light) and high locomotor activity (red light).

In male rats, the monoamine oxidase activity was increased in all four brain regions (25–120%) when the animals were physically active and that of the heart was nearly doubled. The enzyme activity in the liver was, however, only slightly raised.

In the female rats, monoamine oxidase activity showed significant variations