**25b Monoaminoxydase Inhibitors and the Potentiation of Experimental Sleep.** P. LECHAT and M. LEMEIGNAN (France).

The effect of preliminary administration of inhibitors of mono-amine-oxydase of varying degrees of effectiveness on experimental sleep was studied on the mouse and on the rat. The three hypnotics used were of different chemical structure: chloral, hexobarbital and methyl-4-β-chlorethyl-5-thiazole (Hemineurine). The three inhibitors were: isoniazide (100 mg/kg), iproniazide (100 mg/kg) and JL 1314 (10 mg/kg). In these doses only the latter two had a marked inhibitory effect on MAO which was approximately equal. They were administered intraperitoneally 30 min before the hypnotics which were injected intravenously.

Considering a duration of at least twice that of control sleep to be a significant sign of potentiation, we found the following results: (1) hexobarbital is potentiated to practically the same extent by all three substances in the mouse and rat; (2) chloral was potentiated by only JL 1314 in the mouse; (3) methyl-4-β-chlorethyl-5-thiazole was only potentiated by iproniazid in the mouse.

It can be concluded that the inhibition of MAO and the augmentation of the effect of hypnotics do not systematically go hand in hand as, depending on their chemical composition, the hypnotics are either potentiated or not by substances which show very different potency as MAO inhibitors.

**26 Further Studies on Monoamine Oxidase Inhibitors.** S. S. PARMAR and M. NICKERSON (Canada).

We previously reported that several hydrazine derivatives, including iproniazid (Marsilid) and pheneprazine (Catron), react relatively irreversibly with the active sites on the enzyme monoamine oxidase (MAO) to produce a "non-equilibrium antagonism". In the present study the antagonism between hydrazine MAO inhibitors and amphetamine and two of its derivatives (P-1726, *p*-trifluoromethyl, and P-1882, *p*-S-methyl) was investigated using rat liver mitochondria as a source of MAO. Enzyme activity was determined on the basis of both oxygen uptake and substrate (tyramine) utilization, which were found to give equivalent results. Preincubation for 15 min with subinhibitory concentrations of amphetamine or of P-1882 protected MAO against inactivation by pheneprazine. Greater protection by higher, inhibitory, concentrations of these agents was demonstrated by determinations of enzyme activity after dialysis. With respect to both inhibition of MAO and protection against pheneprazine inhibition, D-amphetamine was more active than the L-isomer. P-1726 was found to be a more potent and considerably more persistent inhibitor of MAO than either amphetamine or P-1882. It was not possible to demonstrate antagonism between pheneprazine and P-1726. However, the action of the latter was antagonized by amphetamine. The above results indicate that amphetamine, P-1726, P-1882, and pheneprazine all combine with the same active sites on the MAO molecule.

**27 A New Test for MAOI Detecting Effects.** A. LEHMANN and R. G. BUSNEL (France).

Specific effects of substances related to the metabolism of biogenic amines led us to study the effect of monoamine oxidase inhibitors (MAOI).

The clinical anti-depressing effect of these substances can hardly be studied on animals or only indirectly by using their antagonism against reserpine.

As reserpine potentializes lethal audiogenic convulsions in most animals an antagonism between reserpine and MAOI can be demonstrated. The test is quite clear: (a) total protection (suppression of seizure); (b) partial protection (clonic seizure only or tonic non-lethal seizures); and (c) death after convulsions.

The experimental drugs are: Tranylcypramine, nialamide, iproniazide, harmaline and feeble MAOI's like benactysine and D-amphetamine. Injections intraperitoneally to mice of the sub-line Rb.

Only tranylcypramine (30 mg/kg), nialamide (500 mg/kg), benactysine (80 mg/kg), and D-amphetamine (40 mg/kg) give a 100 per cent protection against audiogenic seizures.

On the other hand, all these drugs injected at threshold, non-protective doses (tranylcypramine (25 mg/kg), nialamide (20 mg/kg), iproniazide (100 mg/kg), harmaline (30 mg/kg), benactysine (60 mg/kg), D-amphetamine (10 mg/kg) and associated to reserpine (1 mg/kg) prevent the mortality during seizure generally provoked by reserpine alone and give complete or partial protection.

This antagonism is quite different from that obtained when associating tranquilizing drug like carbamate of methyl pentynol, and reserpine; in this case one only obtains a protection with a dose of tranquilizer high enough to have a protecting action by itself (50 mg/kg). It seems worthwhile to draw attention to this test for detecting MAOI effects. One objection can be raised: imipramine (25 mg/kg) and azetazolamid (50 mg/kg) have a similar action as the classical MAOI's but at present we have no biochemical proof that they act like MAOI's. This must still be investigated.

**28 Depletion of Catecholamines by Shigella Shigae Toxin in the Mouse Brain.** K. MAŠEK, R. SMETANA and H. RAŠKOVÁ (Czechoslovakia).

The influence of *Shigella shigae* toxin on the content of serotonin, adrenaline and noradrenaline in mouse brain was investigated.

In preliminary experiments the content of these compounds in the brain was measured every 12 hr. It was found that maximal changes develop 48 hr