51 Pharmacological Action of a New Antidepressant Drug, Propazepine, in Comparison with Imipramine. J. METYŠOVÁ and Z. VOTAVA (Czechoslovakia).

In the search for new drugs with antihistaminic effect carried out in the year 1956, a series of homopromazine derivatives was synthetized. One of these drugs, N-(3-di-methylaminopropyl)-homoacridane hydrochloride, is a structural analogue of imipramine. The pharmacological action of this drug, under the name propazepine, was tested in comparison with imipramine.

Both drugs show similar acute toxicity and action in the test of the rotating rod. Contrary to chloropromazine they do not lower body temperature and their effect on the vegetative nervous system is low.

Both drugs do not affect substantially the toxicity of the central nervous stimulants, amphetamine, pentazol and strychnine. On the other hand, an interesting difference in the interaction with the toxicity of caffein was found. Propazepine decreased the toxicity of caffeine, whereas imipramine and especially chloropromazine increased the toxicity.

52a Mode de l'Action de la Centrophénoxine et ces Dérivatives chez le Poisson. H. NAKAJIMA, J. R. L'HUILLIER, L. BAJINSKI et J. THUILLIER (France).

La Centrophénoxine (ester diméthylaminoéthylique de l'acide *p*-chlorophénoxyacétique) provoque chez le poisson une excitation pouvant entrainer des convulsions et une dilation des chromatophores. Cette action est étudiée en comparaison avec d'autres drogues neuro et psychotropes. L'influence du pH et les conditions physico-chimiques de la réaction sont examinées. L'antagonisme entre Mélatonine et Centrophénoxine est spécialement analysé.

52b Mode of Action of Centrophen-oxin and Derivatives in Fish (Behaviour and Chromatophores). H. NAKAJIMA, J. R. L'HUILLIER, L. BAJINSKI and J. THUILLIER (France).

Centrophenoxin (dimethylaminoethyl ester of *p*-chlorophenoxyacetic acid) induces excitation in fishes capable of producing convulsions and dilation of the chromatophores. This action has been compared with other neuro- and psycho-tropic drugs. The effects of the pH and physico-chemical conditions of the reaction have been studied. A special analysis has been made of the antagonism between Melatonin and Centrophenoxin.

53a Analyse Pharmacologique de la Narcose et de la Stimulation Respiratoire Provoquées Simultanément par une Même Drogue. J. THUILLIER (France).

Le diethylamide de l'acide 2-méthoxy-4-allyl phénoxyacétique (G. 29.505) est le premier composé chimique connu possédant à la fois des actions narcotiques et analeptiques respiratoires puissantes.[1] L'anesthésie générale obtenue avec cette substance est profonde et de courte durée. En même temps que la narcose, l'injection intraveineuse de G.29.505 provoque une stimulation respiratoire plus forte que celle obtenue avec la plupart des analeptiques connu; cette action eupnéique peut s'opposer à la dépression respiratoire provoquée par la morphine ou des composés analogues.

Des hypothèses sont discutées pour tenter d'expliquer la coexistence dans une même molécule de deux actions thériquement opposées: narcotique et analeptique.

53b Pharmacological Analysis of Concomitant Narcosis and Respiratory Stimulation Induced by a Single Drug. J. THUILLIER (France).

The diethylamide of 2-methoxy-4-allylphenoxyacetic acid (G. 29.505) is the first chemical compound known to possess at the same time narcotic and powerful analeptic respiratory actions.[1] The general anaesthesia obtained with this substance is deep and of short duration. Together with narcosis, intravenous injection of G. 29.505 causes stronger respiratory stimulation than obtained with most known analeptics: this eupneic action can resist the respiratory depression induced by morphine or similar compounds.

There is a discussion of hypotheses attempting to explain the co-existence in the same molecule of two theoretically opposed actions: narcotic and analeptic.

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1. THUILLIER, J. and DOMENJOZ, R. (1957), *Anaesthetist (Berlin)*, **6**, 163–7.

54 The Pneumokinetic Activity of Dimefline (3-Methyl-7-Methoxy-8-dimethylamino-methylflavone, Rec 7-0267) compared with that of Other Central Nervous System Stimulants. I. SETNIKAR (Italy).

Dimefline has been compared with the following drugs for pneumokinetic activity: (a) other brain stem stimulants (bemegride, picrotoxin, pentetrazol and 2:3-dimethyl-7-methoxy-8-morpholino-methylchromone or Rec 7-0105); (b) some other general central nervous system stimulants (prethcamide, nikethamide, diethylamide of 3-ethoxy-4-hydroxybenzoic acid or DEHB); (c) strychnine; and (d) lobeline.

The experiments were performed on non-anaesthetized rabbits. By means of a body plethysmograph the tidal volume (V_T), the pulmonary ventilation (V_{Pul}) and the frequency (F) were recorded.

Pentetrazol, nikethamide, strychnine and lobe-

line caused practically no increase in V_{Pul}. Bemegride, picrotoxin, Rec 7-0105 and DEHB showed a moderate action. Prethcamide and dimefline exerted the greatest and most lasting stimulant action on the respiration, the former acting more on the F and the latter more upon the V_T.

Experiments on rabbits with morphine-depressed respiration yielded similar results. In fact, only dimefline, prethcamide, bemegride, DEHB and picrotoxin brought the V_{Pul} back to normal or supranormal levels.

Taking account of toxicity, the widest therapeutic margin was shown by dimefline, followed by bemegride, prethcamide and Rec 7-0105.

The pneumokinetic activity of dimefline and prethcamide was confirmed in dogs and cats with barbital- or morphine-depressed respiration. Both drugs raised the HbO_2 and the blood pH in addition to the V_{Pul}.

Dimefline is, moreover, highly active in combating respiratory syncope induced by various drugs and in establishing the respiratory function in immature foetuses.

55 Immunosympathectomy as a New Approach to the Study of the Sympthetic System. R. Levi-Montalcini and P. U. Angeletti (U.S.A.).

Adult Swiss mice and albino rats were used. Injections of the antiserum were given soon after birth for 5 consecutive days at the daily doses of 0·05 ml/g of body wt. Histological examination of the superior cervical ganglia was performed in all animals used for the chemical assay of catecholamines and MAO activity.

Adrenaline and noradrenaline were measured in various organs by spectrophotofluorometric procedures. MAO was measured in the same organs by manometric technique. A marked decrease in the noradrenaline content was found in heart, spleen and other tissues of the immunosympathectomized animals. Levels of MAO activity were also found to be decreased in several organs of the same animals. The influence of the administration of various substrates on MAO activity was investigated in normal and experimental mice and rats. The results of the above experiments will be discussed with respect to mono-amine-oxidase activity and sympathetic function.

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1. Levi-Montalcini, R. and Cohen, S. (1960), *Ann. N.Y. Acad. Sci.*, **85**, 324.

56 Cholinesterase Distribution in the Sympathetic Nervous System of the Cat. F. Sjöqvist and B. Fredricsson (Sweden).

Sympathetic ganglion cells are not homogeneous with respect to their content of acetylcholinesterase (AcChE). A small number of the neurons resemble parasympathetic ganglion cells and anterior horn cells in terms of strong histochemical staining intensity for AcChE (thiocholine method). The great majority of the sympathetic ganglion cells have very little, if any, AcChE-activity.

The characteristic AcChE-rich nerve cells are predominantly found in the stellate ganglion and at the level of L6–S1. In these particular ganglia these neurons can amount to 5–15 per cent of the cell population, but in other paravertebral ganglia they are surprisingly few. They seem to be extremely rare in the prevertebral ganglia. Denervation experiments show that most of these cells in the stellate ganglion are connected with nerve fibres to the fore leg.

The results are suggestive of two functionally different types of sympathetic ganglion cells. The AcChE-rich ganglion cells are unevenly distributed in the sympathetic nervous system with an accumulation in those ganglia giving rise to the secretory and vasomotor fibres to the fore and hind foot.[1] This is of interest since the sweat glands of the cat are exclusively found in the paws and are cholinergically innervated.[2] The possible relationship between these AcChE-rich ganglion cells and postganglionic cholinergic sympathetic fibres in general will be discussed.

1. Langley (1891).
2. Dale and Feldberg (1934).

57 On the Mechanism of Action of the Ganglion-blocking Agents. D. A. Kharkevich (U.S.S.R.).

The influence of tetraethylammonium, hexamethonium, hexonium, pendiomide and mecamylamine on the interneuronal transmission of excitation in sympathetic ganglia was studied. It was found that all the drugs tested deepen the passimal (Wedensky) inhibition of the ganglia, increase the time required for transmission of nervous excitation from the pre- to the post-ganglionic fibres (latency) and prevent after-discharges. The influence exerted by ganglion-blocking agents in respect to the above parameters seemed to be fairly uniform. A different result was obtained in experiments with postactivation potentiation. Hexamethonium, pendiomide and mecamylamine decrease or totally prevent the development of potentiation; tetraethylammonium was found to be ineffective.

In view of these data, and considering the nature of postactivation potentiation it may be suggested that hexamethonium, pendiomide and mecamylamine exert a depressing action on the activity of the presynaptic endings.

In order to analyse the action of the ganglion-blocking agents on the conduction of excitation in the post-synaptic neurones, experiments with post-activation inhibition were undertaken (the latter developing as a result of interaction of the hetero-