EDITORIAL

PSYCHOSOMIMETIC AGENTS

It has been known for centuries that man's behaviour can be altered by drugs. Both acute and chronic psychotic states can be produced by a number of central nervous depressants, stimulants, analgesics, autonomic drugs like atropine and hyoscine, cocaine, and numerous others including quinine and mepacrine, arsenic and mercury, thyroid, and so on. Especially in recent years, by the administration of a variety of drugs and by other procedures experimental psychiatrists have sought to produce 'model' psychoses in animals and man that might shed some light on conditions such as schizophrenia.[1] Many of the methods used in animals have not been suitable for human experimentation, and much study has therefore been made on alterations in behaviour encountered in the course of treatment or during research on other problems.

The administration of LSD 25 (lysergic acid diethylamide) or of mescaline has been much used to produce 'model' psychoses, particularly for exploring the aetiology of schizophrenia. No simple relationship appears to exist between 'clinical' and 'model' psychoses but some features common to both are likely to be elucidated.

The discovery of the mental effects of LSD 25 and an account of the symptomatology have received wide publicity in medical journals since the first descriptions by Stohl in 1943 in Swiss literature; later in the English language by such workers as De Shon *et al.*,[2] Osmond and Smythies,[3] Hoch *et al.*,[4] Isbell *et al.*,[5] and Hurst *et al.*[6] As originally recounted by Stohl the ingestion of LSD 25 (usually 30 micrograms) produced symptoms in about $\frac{1}{2}$ hour which reached a peak in $1\frac{1}{2}$ hours and completely disappeared by the end of 8 hours. At first such features were noted as atoxia, dysarthria, tremor, nausea, headache, palpitations, conjunctival injection, sweating, and deepening of respiration; i.e. of a motor and autonomic nature. Later there were marked disturbances of perception; visual hallucinations were prominent with a variety of scintillations and geometric patterns varying in design and colour and often grotesque in nature. Insight was retained throughout regarding these unreal phenomena. Illusions were common, also disturbances of taste, and of tactile and deep sensibility. Consciousness was never seriously disturbed. There is a general resemblance in the LSD-25 syndrome to that produced by mescaline, cannabis, and cocaine. In the different descriptions given by various investigators it is necessary to take into account such factors as dosage, environmental conditions, type of subject, and the object of the observers in making the investigation. However, by studies of this nature some relationship may become established between the clinical effects produced by these drugs and their mechanisms of action.

Much remains to be learned about the biochemical mechanisms of action of drugs used in psychiatry. Cerebral glycolysis and oxidation may be affected and other metabolic processes which are still obscure. Very little is known about 'physical' action apart from metabolic action on neural activity,[7] and in addition to such mechanisms others of neurophysiological and psychological type may contribute to the total pattern of drug modification of behaviour. There are already numerous reports on the neurophysiological actions of psychosomimetic drugs on the electrical activity of the cerebral cortex, the long sensory pathways and the projection systems. They can profoundly affect the patterns of afferent impulses passing to the cortex, thus altering mental and motor output. Neurophysiological findings have, however, not yet been sufficient to detect the many variables influencing human behaviour.

As emphasized by Wikler,[8] it matters little whether 'model' psychoses resemble schizophrenia. The use of drugs as tools to detect and manipulate the biochemical, physiological and psychological variables of cerebral function will make it more possible to develop concepts about the dynamic processes underlying normal or abnormal behaviour. Psychiatrists and pharmacologists will need to embark on a joint effort in searching for 'pattern-specificity' of drug action, which may reveal common denominators upon which they act, and so provide a means for studying theories of behaviour. In this way progress may be made in the clinic and the laboratory.

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