

# THE LANCET

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## MESCALINE IN PSYCHIATRIC RESEARCH

THE field for controlled experimental research in psychiatry is still so small that it demands intensive cultivation. One of the few methods available is a pharmacological one—i.e., the use of intoxicating drugs. The psychosis thus produced can be studied with a much closer regard to experimental requirements than is possible with the mental disorders in general, dependent as they are on a variety of causes which the investigator can seldom influence in any predictable direction. Foremost, though not unique, among the intoxicants that may be used for research along such lines is mescaline. Now available as a synthetic drug, its ritual use on the American continent stretches back to the time before the Spanish Conquest. Fascinating as are the ethnological associations of the mescal plant, it is as a source of beatific visions that it has become generally and somewhat romantically known in Western Europe. The visions consist of fantastic forms and colours constantly changing but always bright. Dr. MACDONALD CRITCHLEY, who made some subjective experiments in 1930, described<sup>1</sup>—

“a meadow with buttercups and daisies; now it is changing into a stereotyped park, with a bandstand and with chairs, each one of which is whizzing rapidly round on its own axis. Butterflies are coming in from all sides; the bandstand has disappeared. The butterflies all collect into the centre and arrange themselves into a circular, brightly coloured flower-bed, rotating rapidly in a clockwise direction, in a most wonderful manner . . . now a huge field of primroses . . . a complicated pattern like Hampton Court maze, brightly coloured with objects moving quickly in a snake-like, sinuous fashion along the apparently endless pathways of the maze.”

All who have enjoyed the contemplation of just such sights and sequences in a Silly Symphony will appreciate what a state of rapture they may induce. The range of the abnormal phenomena to which mescaline gives rise is, however, wider and more important from the investigator's point of view than the visual disturbances alone. The independent phenomena in other sensory territories, the synæsthesiæ, the alteration in bodily feeling, the disorder experienced in space and time-judgments, the effects on mood and thought, the depersonalisation and the power of detached observation of oneself are among varied manifestations which have been closely studied by psychiatrists. WEIR MITCHELL and HAVELOCK ELLIS drew attention to them in the last century; since the war some workers at Heidelberg, ROUHIER in France and others have examined the matter thoroughly.

At the meeting of the Royal Medico-Psychological Association on Feb. 26th Dr. ERICH GUTTMANN described investigations to which he had contributed before he came to England, and gave an account of the further mescaline research which he and others are carrying out at the Maudsley Hospital. By means of the Rohrschach test, administered to the same persons before and after intoxication, he had observed the changes in those responses which are regarded as indicative of the psychological type and personality of the subject. By this means the contribution of the individual to the psychosis—a question of the first importance for psychopathology—can be studied, as well as the effect of specific noxae on psychic structure; the rôle of perception in the total personality also enters into the field of experiment. On the same subjects (normal volunteers) Dr. W. H. HUBERT and Dr. AUBREY LEWIS studied by a special optical technique the changes in Gestalt-formation produced by the drug; striking variations were found, again bearing on the importance of the perceptual side of personality. Comparative investigations, using the same technique, but without mescaline, on schizophrenic patients and others with depersonalisation were made, and provide an instance of the valuable approach which mescaline affords to the study of mental illness, especially where, as in schizophrenia, the investigator cannot otherwise than by mescaline himself gain any subjective experience of the incommunicable phenomena. Dr. GUTTMANN has, moreover, in conjunction with Dr. W. S. MACLAY, attempted to make therapeutic use of the drug. The known effects on sensory function led them to expect that the symptom of depersonalisation with feeling of unreality might be so modified or abolished temporarily by small doses of mescaline that the patient would be more accessible, after this relief, to psychotherapy. The results, so far as feelings of external reality were concerned, conformed to expectation (though not in all cases) and the change extended beyond the period of intoxication. Incidentally Dr. GUTTMANN and Dr. MACLAY hold that to give mescaline continuously to any patient would not be justifiable while we know so little about the dangers of chronic mescaline intoxication.

The information available about the oxidative and enzymic activities of the brain during mescaline intoxication has so far indicated only a common mode of action of narcotics and throws no light on the specific effects of the drug. Dr. P. K. McCOWAN stressed the importance of further research into these activities. Dr. GUTTMANN referred to the physical changes which appear during intoxication and to their metabolic significance. It is noteworthy that in 1932 an observer reported that in hashish intoxication the output of salt and water is increased, without any concomitant hydræmia; it is not known whether any corresponding change is associated with mescaline. It is an attractive speculation that there may be links between mescaline and some of the end-products of protein metabolism—e.g., tyrosine—

<sup>1</sup> See THE LANCET, 1930, *ii.*, 863.

to which it is chemically allied; an attempt to discover whether some perversions of normal metabolism result in the production of a toxic substance closely akin to mescaline pharmacologically as well as chemically might be fruitful. Admittedly no substance closely related chemically to mescaline has as yet been found capable of giving rise to its remarkable effects; whether further research be metabolic or psychological, the value of a pharmacological approach to the problems of psychiatry can hardly be doubted.

### HEAT REGULATION AND FEVER

IN his Arris and Gale lectures just delivered before the Royal College of Surgeons of England Dr. JOHN BEATTIE reviewed various aspects of the heat-regulating mechanism of the body, and expressed his belief that this mechanism is much more complicated than has hitherto been realised. The notion that heat regulation is dominated completely by a single centre is in his opinion misleading, and he was able to show that sections at different levels of the central nervous system produce widely different effects. The argument in favour of a single centre has been founded largely on experimental demonstration that section of the cervical cord completely abolishes the heat-regulating mechanism so that the animals become poikilothermic. To support this conception there is also the older evidence from heat piqûre, and the more recent observations that local heating of the hypothalamus is followed by lowering of the body temperature, and local cooling by a rise in the body temperature. To the contrary, however, we have abundant clinical evidence, beginning with a case recorded by BRODIE in 1837, that in man complete destruction of the cervical cord is not always followed by a loss of heat regulation and that even fever has been observed in such patients. A few isolated observations on animals are also on record such as those of GOLTZ and EWALD in 1896, and the more recent ones of POPOFF,<sup>1</sup> where heat regulation was maintained after removal of the spinal cord from the cervical region downward with subsequent cutting of the vagus and sympathetic in the neck. In order to determine the reason for this contradiction, THAUER,<sup>2</sup> working in BETHE'S laboratory, has lately carried out an extensive experimental reinvestigation of the effects of section of the cervical cord on a large number of rabbits, guinea-pigs, and rats. Suspecting that the discrepancies might be due to immediate shock effects masking the true results of the operation, he endeavoured to improve the operative technique and post-operative treatment. By keeping the animals immediately after the operation in a thermostat at 28°-30° C. and by careful attention to their feeding, he succeeded in keeping a number of animals alive for several weeks, and three rabbits for two months after the operation. In all these animals the heat-regulating mechanism was almost completely restored, although during the first few

days after the operation it was severely impaired. When once the heat regulation had been restored subsequent cutting of the cervical sympathetic and of the vagi, and even subsequent partial removal of the thoracic spinal cord, failed to impair it. THAUER'S results agree, therefore, with those of POPOFF in showing that in warm-blooded animals after complete exclusion of the central nervous system the heat regulation of the body can be efficiently maintained by a peripheral mechanism. The nature of this peripheral mechanism has been indicated by the work of CRAMER, who showed in his well-known monograph<sup>3</sup> that in addition to the nervous mechanism for heat regulation there is a humoral mechanism with which the thyroid and adrenal glands are particularly concerned. Since most of the factors concerned in heat regulation are controlled by the sympathetic nervous system, they can be brought into play either by nervous or by humoral stimulation. Thus fever can be produced experimentally by functional hyperactivity of the thyroid or adrenal glands, and THAUER has shown that his animals deprived of their central nervous control still respond to infections or to the injection of pyrogenic substances by fever.

The experiments of POPOFF and of THAUER must, of course, not be interpreted as denying the existence of a nervous mechanism for heat regulation or of a central coördination of such a mechanism. Such a conclusion would be as crude and as misleading as the reverse one that the thyroid or adrenal glands have no part in the processes of heat regulation because these processes can still be efficiently maintained after removal of one or other of these organs. We are being led to a belief that there are two mechanisms for heat regulation, one central and the other peripheral, a conception in keeping with modern physiological trends in other bodily functions. In the control of water metabolism, the control of equilibrium, and in sensory discrimination there are parallels for the overlaying of a crude peripheral type of regulation by a more delicate centralised one. On our present knowledge of heat regulation it must be supposed that the intracranial apparatus is not essential to an adequate working, but rather by allowing an interplay between the different peripheral factors serves to increase their efficiency, especially under pathological conditions.

The conception of a single centre dominating heat regulation has tended to sterilise progress, and a study of LAKIN'S Lettsomian lectures<sup>4</sup> reveals how scarce investigations on the phenomenon of fever—one of the most frequent and important clinical symptoms—are in the recent physiological, pathological, and clinical literature. It is easy to understand why this should be so. On the unitary conception fever is explained as being due to some action on the heat-regulating centre in the brain which is likened to a thermostat, and in fever is

<sup>1</sup> Popoff, N. F.: Arch. f. d. ges. Physiol., 1934, ccxxxiv., 137.

<sup>2</sup> Thauer, R.: Ibid., 1935, ccxxxvi., 102.

<sup>3</sup> Cramer, W.: Fever, Heat Regulation, Climate, and the Thyroid-Adrenal Apparatus, London, 1928.

<sup>4</sup> Lakin, C. E.: Disturbances of the Body Temperature, THE LANCET, 1934, ii., 467.