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Psychological and Biochemical Effects of Lysergic Acid Diethylamide

Stoll[1] and Condrau[2] have shown that the psychological effects of lysergic acid diethylamide (*LSD*—25), an amide of one of the constituents of ergot, are similar to those obtained in mescaline intoxication, but are produced by the oral administration of quantities as small as 0·02–0·06 mgm. While, in our experiments, the symptoms varied greatly from one person to another, the basic pattern of reaction seemed the same in twenty subjects who were members of the hospital staff. After initial slight autonomic symptoms, such as enlarged pupils, feeling of cold, 'goose flesh' and mild nausea, the most marked changes were emotional, a pleasurable feeling tone amounting to euphoria and bursts of laughter; this sometimes alternated with, or later was followed by, depression. There was also a general complaint of a feeling of lassitude and muscular weakness. In spite of some difficulty in concentrating, consciousness

remained clear and introspection almost undisturbed. Visual illusions and hallucinations, especially illusions of movement, colour and distortions of the body image were frequently present.

The minute dosage required to produce the psychological effect of lysergic acid diethylamide suggested that its mode of action was due to an anti-enzyme action. Since, normally, the only substrate metabolised by the brain cell is glucose, an investigation of the effect of the drug on carbohydrate metabolism *in vivo* was undertaken.

Blood samples were taken from the fasting subjects and at intervals of one and two hours after the administration of the drug, the following analyses being made by the methods indicated: glucose[3], hexosemonophosphate[4], lactic acid[5], alkali reserve[6], pyruvic acid[7], inorganic phosphate, total acid-soluble phosphate, lipoid phosphate and adenosine triphosphate[8]. On a subsequent day, identical control analyses were made on most of the subjects, but with the substitution of a placebo for the drug.

No significant variations in the result of the two sets of analyses were found, except in the cases of glucose and hexosemonophosphate. For the latter the mean level of the experimental analyses rose by 1·66 mgm./100 ml. one hour after taking the drug and fell by 0·6 mgm./100 ml. during the subsequent hour. The corresponding figures for the control analyses were falls of 2·3 and 2·4 mgm./100 ml. respectively. In the case of blood glucose the experi-

mental results showed a mean rise of 15 mgm./100 ml. after one hour and 11 mgm./100 ml. after two hours. The control analyses showed a mean fall of 1 mgm./100 ml. after one hour and a mean rise of 1 mgm./100 ml. after two hours.

The subjects were fasting and at rest throughout both the experimental and control periods. In these circumstances the only available source of carbohydrate would be glycogen, the first step in the metabolism of which is the formation of hexosemonophosphate. Under conditions of complete rest the rate of glycogen metabolism might be expected to fall, and this was reflected by a fall in the blood concentration of hexosemonophosphate in the control analyses. The increases in hexosemonophosphate and glucose in the experimental observations suggest that there is an increased metabolism of glycogen coupled with a probable block in the breakdown of hexosemonophosphate. If the increase of hexosemonophosphate should be due to increased demand for carbohydrate by the central nervous system, one would expect increases also in lactate, pyruvate, etc., together with a decrease in glucose. The fact that, on the contrary, no such changes occurred and the glucose is raised, suggests that the raised level of hexosemonophosphate is caused by a break of the cycle at this point.

A certain hypobulia and absorption in the passive state of feeling made the relation in time of biochemical to psychological change somewhat imprecise. However, symptoms of the vegetative system and of emotional nature appeared during the first hour and before the more specific symptoms such as illusions, hallucinations and other disorders of the perceptive field, which were of longer duration.

It is suggested that the changes in carbohydrate metabolism observed after the intake of lysergic acid diethylamide are responsible for at least part of the psychological symptoms. The alternative view that the alterations in carbohydrate metabolism are a parallel effect of the drug unconnected with its psychological effect seems improbable. Further studies which are now in progress should elucidate this point.

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[1] Stoll, W. A., *Schweiz. Arch. f. Neurol. u. Psychiat.*, **60**, 279 (1947).
[2] Condrau, G., *Acta Psychiat. et Neurol.*, **24**, 9 (1949).
[3] Ling, E. G., Hadlewood, G. A. D., and Delory, G. E., *Lancet*, **1**, 386 (1947).
[4] Cori, G. T., and Cori, C. F., *J. Biol. Chem.*, **94**, 561 (1931).
[5] Barker, A., and Summerson, W. H., *J. Biol. Chem.*, **138**, 535 (1941).
[6] Hawk, B. P., Oser, B. L., and Summerson, W. H., "Practical Physiological Chemistry" (J. and A. Churchill, Ltd., London).
[7] Friedemann, T. E., and Haugen, G. E., *J. Biol. Chem.*, **147**, 415 (1943).
[8] Gottfried, S. P., and Wilmer, H. H., *Schweiz. Arch. f. Neurol. u. Psychiat.*, **62**, 290 (1949).