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Controlled Sensory Input: A Note on the Technic of Drug Evaluation with a Preliminary Report on a Comparative Study of Sernyl, Psilocybin, and LSD-25

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A TECHNIC of altering the sensory environment,[1] which produced many of the phenomena described by Arctic explorers, shipwrecked sailors, and others who had spent long periods of time in relative isolation,[2,3,4] was developed at McGill University five years ago. Since the first publication of the work at McGill, considerable work has been done which demonstrates the reproducibility of many of these effects in a variety of conditions, using both normal subjects and psychiatric patients. It is recognized that the degree of sensory deprivation is not absolute, and it is certainly conceivable that some of the effects are a reaction to the stress of the unusualness of the situation rather than depend upon the degree of deprivation. It is, for example, very likely that factors other than sensory deprivation are involved when the subject has to be immersed totally or partially nude in a tank of warm water,[5] or is left alone for an extended period of time in a sunken room (which is not without implication; e.g., the room being described as similar to a dungeon[6]). Many hypotheses regarding the nature of the sensory deprivation phenomena, now widely known, have been put forward, ranging from neurophysiological explanations[7] to psychoanalytical interpretations.[8] Some skepticism has also been expressed whether the effects do not follow previous conditioning and do not result from a heightened state of suggestibility.[9] Nevertheless, an increasing number of laboratories continue to investigate the nature of sensory deprivation phenomena. These intensive studies, however, are focusing on the unusual effects of sensory isolation, and little or no effort has been made to explore other possible uses, except that sensory deprivation type set-ups have been tried as a form of treatment.

One of the most difficult problems in drug research arises out of the interaction of the many factors which underlie even simple modes of behavior with the great technical difficulties of successfully isolating simple systems for experimentation. This is most certainly true regarding the study of drugs which influence the social behavior of human beings, and of this we have become more and more aware in recent years in our studies of the tranquilizers and psychotomimetics. We have become increasingly aware of the so-called placebo effect,[10,11] and it is actually somewhat surprising that our only answer to this problem has been the development of the double-blind method of drug evaluation. It seems clear that we need to create a laboratory setting for drug experimentation in which more control of input and measurable variations of it are possible.

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The basic set-up of the sensory deprivation experiment lends itself readily to adaptation for drug experimentation and will afford maximum control of such factors as environmental influence, body movements, and sensory input in general. By using experimental set-ups in which the external environment had been modified and its stimuli had been altered or diminished, we attempted to compare the mode of action of three psychotomimetic drugs, Sernyl, Psilocybin, and LSD-25.

The physical arrangement of our controlled sensory input situation was as follows: the subject is loosely strapped to a foam rubber pad, his hands are placed in cotton mitts, and "white noise" is amplified through comfortably fitting sound barrier type earphones. A homogeneous, milky visual field is provided by the use of a 36-inch diameter Ganzfeld semisphere of sandblasted lucite placed over the subject's head 12 inches above his eyes. The subjects enter the experiment unaware of what is required of them except that they know that they will be expected to take a drug, but as soon as they are in the experimental situation prerecorded instructions are played on the tape recorder which the subject hears via the earphones. In this manner he is informed that the liquid he drank immediately before entering the room where the experiment takes place, may or may not have contained a drug. While he is not required to talk continually, he is told to report any feelings that he considers unusual and that anything he says will be tape recorded. He is informed that he is not in direct communication with anyone, and that the voice heard over the earphones is a tape recording, and that after three hours he will be released from the situation.

Five minutes after the onset of the experiment a 20-minute battery of previously taped orally administerable tests of immediate memory, perception, cognition, and imagination is given. This battery is repeated in matched form three times, in an attempt to evaluate objectively the onset of the drug effect during the first hour following ingestion. This is followed by 45 minutes of complete control of external inputs, that is, the omninodal silence of random white noise and sensory deprivation. Following a 10-minute period of answers of the subject to self-appraisal questions about behavior and symptoms comes a 30-minute period during which ambiguous, provocative stimuli are presented to the subject.

This standardized procedure, with structural tape recorded instructions and tests and sensory control, was used to eliminate some of the uncontrolled variables to the greatest possible extent. The attempt to completely control the external sensations which impinge upon the subject was deemed of value in distinguishing central from peripheral drug effects in studies which attempt to clarify the role and the importance of external sensory inputs as triggering or mediating variables of drug effects, and which focus attention on the central cognitive and emotional effects, the external sensory input now no longer being intricately intermingled with sensation and perception of the drugs.

Summary and Review of the First Experiment

In this sensory attenuation situation, eight normal subjects, four men and four women, all college students over 21 years old, were examined in a self-con-

trolled experiment concerned with the effects of the following drugs: (1) Psilocybin, 20 mg., (2) Lysergic Acid-25, 150 μg., (3) matching placebo, (4) Sernyl, 10 mg. The order of drug application was the same for all subjects. The drugs were administered orally, dissolved in cherry syrup of identical taste, the subjects but not the experimenter being "blind." As a result the following general trends were observed. (Detailed data will be presented in a subsequent paper.)

Psilocybin and Lysergic Acid caused the subject to experience a wide variety of hallucinatory and delusional experiences, but the effect of Psilocybin was experienced as unusually pleasant in contradistinction to Lysergic Acid which was experienced as unpleasant, anxiety provoking, and disruptive. All eight subjects agreed on this rating of these two drugs, with the effect of Sernyl in between and the placebo having no effect. This finding conflicts with other studies in which Psilocybin effects were found to be virtually indistinguishable from those of Lysergic Acid.[12]

We suggest the possibility that the differences in the structuring of the experiments (the non-threatening experiences without personal contacts with a probing authority figure vs. diagnostic interviews in a hospital setting) and in the personalities of the subjects (thoroughly screened mentally healthy students vs. mental patients or drug addicts) account for these discrepancies; and that the emotional tone in our experiment is more completely a function of drug induced alterations, with fewer aberrations produced by interpersonal and situational factors. Psilocybin and Lysergic Acid induce marked perceptual and cognitive changes and distortions, both during the experiment and for the remainder of the subject's day. While the effects of Psilocybin in the experimental situation seem to be the more marked ones, the psychotomimetic effects of LSD persisted with greater severity for the rest of the day. Subjects were almost completely unaware of the effects of Sernyl except for minimal body image disturbances until they were taken out of the experimental situation. With their first visual and proprioceptive stimulation they were then immediately aware of distortions in perception, especially of the proprioceptive sense and of perceptual constancies.

The results suggest that Psilocybin and Lysergic Acid act by increasing neural firing in the sensory pathways independently of sensed inputs, while Sernyl decreases sensory activity with effects similar to the effects of sensory control, or, alternatively, has no effects or sensation. We conclude that psychotomimetic effects of these drugs are markedly influenced by the controlled sensory input situation used and by the structuring of the experiment and its meaning to the subjects. It is suggested that the experimental control of sensory and emotional aspects in studies of psychoactive drugs may help to disentangle the many factors which play a part in determining drug effects. The controlled sensory input situation described should be considered the basic experimental setting which can be altered to investigate specific questions concerning the drugs under study. For instance the question whether body motion is necessary for Sernyl to become effective could readily be studied by modifying the apparatus in such a way that the subject is obliged to move his extremities regularly.

Summary

Sensory attenuation, a modified form of sensory deprivation where sensory inputs are controlled, is described as a method useful for the study of drug responses. The above is a preliminary report about a comparative study, using this technic, of the following three psychotomimetic drugs:

1. Sernyl 1—(1-phenylcyclohexyl) piperidine monohydrochloride (May and Baker CI395)
2. Psilocybin, a tryptamine derivative: isolated active principle of Psilocybe Mexicana Heim, a Mexican mushroom. (Sandoz)
3. LSD-25, D. lysergic acid diethylamide. (Sandoz)

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