

Introduction: Behavioral Factors in Human Drug Abuse

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THE work described in the following chapters provides an excellent example of the power of a behavioral analysis in the elucidation of factors which can influence drug seeking and drug taking behavior in man. For historical and technical reasons, much previous research effort has centered upon the problem of developing animal paradigms where drugs can be reliably self-administered on a chronic basis. Data derived from such research is essential to develop precise knowledge of the conditions which can support the maintenance of drug-seeking and drug-taking behaviors. Similarly, the contribution of antecedent and consequent events to processes underlying drug dependence can be systematically analyzed. Results from this research can serve as an empirical basis for developing effective drug treatment strategies in man. The work presented in the following chapters demonstrates that the methodology and technology for obtaining these necessary data are now available and that there is a continuing accumulation of pertinent findings derived from laboratory and ward settings which can have a direct bearing upon the design and implementation of treatment.

The writings of Vaillant (11) and Wikler (13) serve to underscore the necessity for investigating the role of learning factors as they apply to the natural history of the etiology, maintenance, treatment and relapse associated with drug-seeking, drug usage, and dependence in man. Vaillant (11) has described the results of his follow-up of 100 male narcotic addicts who

had been treated at the United States Public Health Service Hospital, Lexington, Kentucky. His analysis of antecedent, maintenance, and relapse factors associated with human opiate addiction was carried out within the framework of an operant analysis of drug dependence. As such, he is one of the first investigators working in the natural environment to emphasize the importance of schedules of reinforcement in the addict's career. Wikler (13) has also implicated conditioning factors in drug use by man. Specifically, he has emphasized the role of Pavlovian conditioning factors in relapse. His theory of conditioned abstinence suggests a testable rationale for the observation that detoxified addicts, once dependent upon narcotics, who return to the setting where they were addicted, experience withdrawal symptoms. Such reports have important implications for our understanding of the addiction process and tactics for treating dependence and relapse. The work of both Vaillant and Wikler is directly related to the experiments described by O'Brien (9) and Schuster (10) in the papers which follow.

The analysis by Vaillant is also important because it focuses upon the necessary tests that any effective treatment modality must pass. He has correctly emphasized that successful treatment strategies must develop alternative, socially acceptable, reinforcers that can compete with abused substances in the natural environment and can be used to shape and maintain new behaviors. What the dependent individual

does when confronted with a choice between drugs and acceptable reinforcers is an essential criterion of behavioral change. The work of Johanson (7) and Griffiths *et al.* (5) in this volume address the issue of choice in the animal laboratory. The work of Schuster (10) and Bigelow *et al.* (2) described in this volume address the same issue in the clinical and experimental ward settings.

If treatment is viewed in this way, then a logical research focus becomes an analysis of drug-taking behavior as it may occur in the natural environment. Such research is an essential compliment to information collected under controlled laboratory conditions and has a direct bearing upon the design of treatment modalities and evaluation of efficacy. Just as ethological methods have augmented our knowledge and understanding of basic behavioral mechanisms, a similar analytical approach could extend our appreciation of the scheduling conditions and reinforcers which maintain drug-seeking and drug-taking behaviors in man. At the very least, a description of such factors in terms of their frequency of occurrence and temporal patterning could establish basal conditions necessary for conducting treatment evaluation studies.

Implications of the Present Conditions for Human Experimentation

Many difficulties face scientists conducting clinical research studies with human subjects. These difficulties are particularly apparent when the research involves the use of drugs which are classed in schedules I and II. In addition to the commissions investigating the ethics of research practice, we are witnessing a more and more careful deliniation of the conditions which govern the protection of human subjects, the local institutional review of experimental protocols and the informed consent of patients.

Procedures once accepted as ethical and necessary to carry out an experimental

design are now being closely questioned. For example, in the field of human behavior modification, Ayllon and Azrin (1) used procedures in their original token economy studies conducted at the Anna State Hospital which are now controversial and the subject of legal debate. Recent court decisions imply that lack of privileges should not be made contingent on specified behavior for the purposes of treatment studies. The original studies of Ayllon and Azrin made it evident that severely psychotic patients could be motivated to engage in constructive behaviors and alter their own environments. The recent decisions alluded to above (3, 12) have resulted in a new level of concern for such patients who are now accorded rights and privileges that may, unfortunately, limit further inquiry designed for their benefit.

Excesses also occur in clinical research where trivial experiments may be conducted which expose subjects to unnecessary risks. New regulations which govern human experimentation can serve a useful role by subjecting proposed studies to peer review at local institutional levels, which will help to insure that relevant and necessary safeguards are included in experimental protocols and that proposed research is well designed to explore important problems.

Role of Drug Self-Administration Paradigms in Determining Abuse Liability

One of the issues of continuing concern for public policy as it applies to drug abuse is how to predict the possible abuse liability of new compounds prior to their release for therapeutic use. Animal models of drug-seeking and drug-taking behavior already play an important role in the preclinical evaluation of drugs for abuse liability (14). Schuster (10) alludes to this problem and indicates that few studies have directly assessed drug taking in man. This state of affairs makes it difficult to compare the results of animal studies on drug-

reinforcing efficacy with what is known in the field of human clinical psychopharmacology.

The experiments discussed by Schuster (10) as well as the methodological issues and experimental results detailed by Bigelow *et al.* (2) address the problem of comparability. The main thrust of arguments by these investigators is that drug taking behavior should be measured directly in man by adapting the models developed in the animal laboratory to the research ward setting. This methodological approach would allow direct comparison of animal and human experiments and would provide an opportunity to validate the animal models currently in use. The need for this validation approach is essential in light of the increased role that animal models may assume in the years ahead if the present trend in regulations governing the use of human subjects continues. The work of Bigelow is also important because it points to alternative albeit complementary approaches to the traditional measurement techniques used in human psychopharmacology laboratories to assess drug abuse liability.

There are two possible limitations in interpretation of data obtained from animal studies of drug-seeking and drug-taking behavior. First, there may be difficulty in generalizing findings from animals to drug use by man. Although many drugs which are used by man are self-administered by animals in the laboratory, the conditions necessary for certain drugs, such as marijuana, to maintain behavior of experimental animals have not yet been determined (6). Secondly, it is not axiomatic that a drug which functions well as a reinforcer to maintain behavior in experimental animals will have high abuse potential in man. This volume attests to the host of nonpharmacological factors that can exert powerful control over drug-maintained behavior. Drug-seeking and drug-taking behavior can be maintained in part by: (a) the schedule of reinforcement relating behavior to consequent drug injections;

(b) the history of the individual subject; and (c) the regular and predictable occurrence of environmental stimuli in association with drug seeking behavior and consequent injections of drug (4, 8, 10). Thus, one must not draw too heavily upon animal models of drug-seeking and drug-taking behavior for the purpose of classifying psychotropic drugs into one of the five schedules in current use by the Food and Drug Administration.

The methods described in this volume represent one approach to determining potential drug abuse liability and scheduling of psychoactive compounds. Further studies of the pharmacological, environmental, and historical factors that determine the way that drugs come to control and maintain behavior may allow the future development of animal self-administration models to be more predictive of human drug abuse liability. Clearly, controlled studies of human drug-seeking and drug-taking behavior will continue to have an important role in the drug abuse liability and scheduling process. The following chapters provide a window to view new approaches and future trends in this area of research.

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