

mic variables (e.g., psychopathology) that may influence severity of drug dependence, much less has been directed toward examining environmental variables (e.g., types of drug, schedule of reinforcement) as indicators of severity. This paper reviews drug self-administration model which has been developed and refined over the last 15–20 years. In this model, animals are given access to a manipulandum, and responding on the manipulandum results in drug delivery to the subject. The model has been established across species (e.g., rats, cats, humans), types of responses (e.g., lever press, panel press), and routes of drug self-administration (e.g., intravenous, oral, intragastric, inhalation). In general, drugs which are self-administered by animals are the same drugs abused by humans. The purpose of this paper is to examine the evidence for environmental factors as indicators of severity using the animal model of drug self-administration, and to discuss how this relates to human studies of severity of drug dependence.

SYMPOSIUM

Nicotine Replacement in Tobacco Dependence
Pharmacology, Therapeutics, and Policy

Monday August 31, 1987 • 9:00 a.m. – 10:50 a.m.

Marriott Marquis Hotel • Empire/Hudson/Chelsea Room

Chair: Jack Henningfield, Biology of Dependence and Abuse Potential Assessment Laboratory, MIDA Addiction Research Center, Baltimore, MD, and Gregory Connolly, Division of Dental Health, Massachusetts Department of Public Health, Boston, MA

PHARMACOLOGIC AND NEUROENDOCRINE BASIS OF NICOTINE REPLACEMENT, Jack E. Henningfield, Ph.D. and Ovide F. Pomerleau, Ph.D. Johns Hopkins University and University of Michigan

This presentation will provide an overview of recent data supporting the biologic basis for using nicotine replacement approaches to treat tobacco dependence. A simple, but not entirely satisfactory, view of the dependence process entailed by the compulsive use of tobacco products is as follows: when tobacco products are used as advertised by manufacturers, nicotine is delivered to the central nervous system, repeated use leads to tolerance, physiologic and behavioral dependence, treatment may be attempted in which the nicotine usually obtained by tobacco self-administration is replaced with another source to facilitate behavioral change, then the nicotine replacement is gradually removed. In fact, however, the process of tobacco dependence is no less complex than dependence to opium, sedative, alcohol, or stimulant derived products. Dependence to any of these substances is a confluence of pharmacologic and nonpharmacologic factors. The nonpharmacologic factors include social and other non-drug environmental factors. Among the pharmacologic factors, the control over behavior is also complexly mediated. For instance, nicotine may serve as a positive reinforcer in its own right, its reinforcing efficacy may be sharply increased or decreased depending on situational factors such as stress and performance demands, intake of other drugs, food deprivation, and prior level of nicotine intake, nicotine may even serve as a punisher at higher dose levels and thereby restrain levels of tobacco self-

administration which otherwise might occur. A further complexity among pharmacologic factors is that nicotine, like other drugs of abuse, produces a cascade of neurohormonal responses which mediate many of the effects commonly ascribed simply to the taking of the primary substance. Since the nicotine dose which is obtained when tobacco serves as the vehicle for delivery is easily and rather precisely regulated by the experienced tobacco user, a high degree of "fine-tuning" of neuroregulatory systems is possible. Recent data suggest that the powerful control exerted by nicotine over the behavior of the tobacco user, is not simply due to the reinforcing properties of nicotine in its own right, or to the avoidance of short term withdrawal effects, but is also a function of the multitude of individually- and situationally-specific benefits in the regulation of mood, in performance enhancement, and for weight control. It is plausible that the potential utility of nicotine for certain individuals is due to vulnerability factors which are either (1) common to those which may predispose individuals to other forms of drug abuse, (2) specific to nicotine, (3) are due to long term chronic exposure to nicotine beginning in adolescence or earlier (nearly 90% of cigarette smokers), or (4) represent a protracted withdrawal syndrome. Recent data from a residential withdrawal study, studies of neuroendocrine effects of nicotine, and the potential utility of nicotine for therapeutic application other than as a short term tobacco detoxification agent relevant to the above described issues and will be reviewed.

RECENT FINDINGS ON BEHAVIORAL AND PHYSICAL DEPENDENCE TO NICOTINE GUM Dorothy K. Hatsukami, Ph.D. and John R. Hughes, M.D. University of Minnesota and University of Vermont College of Medicine

Previous studies have shown that nicotine gum replacement improves smoking cessation rates, particularly when combined with behavioral treatment. However, the results from double-blind placebo-controlled studies indicate that improvement of smoking cessation with nicotine gum fades over time. Even the most successful nicotine gum treatment studies show smoking cessation rates no greater than 50%. These results have led to the impetus to market a higher dose of nicotine gum. The use of a higher dose of nicotine gum may have associated problems such as a potential physical or behavioral dependence on the gum. We have conducted two studies in which these issues were examined. The first study was an evaluation of the incidence of use of the gum beyond the prescribed period. In addition, the incidence of withdrawal symptoms from the gum and the relationship between duration of gum use and severity of withdrawal symptoms was determined. In the study, 315 smokers (seen in a family practice clinic) who wanted to stop smoking were randomly assigned to receive either placebo or 2 mg nicotine gum in a double-blind manner. The smokers were instructed to chew the gum for up to three months according to Food and Drug Administration approved instructions. The main findings were the following: (1) The incidence of persistent gum use, that is use of gum beyond the recommended period, among all those who were prescribed gum, was 8% among placebo gum users, and was 12% for nicotine gum users. (2) The incidence of persistent gum use among those who had quit smoking was 35%, whether nicotine-delivering or placebo gum had been prescribed. Thus, persistent use of gum may not be solely dependent on the pharmacological properties of