RELATES OF BEHAVIORAL INHIBITION SYSTEM DEFICITS. Peter R. Finn. Indiana University, Bloomington, IN.

Disinhibitory behavioral characteristics such as impulsivity, risk-taking, thrill or novelty seeking, and conduct disorder have often been associated with alcoholism. In fact, such characteristics have been found to be predictors of current drinking patterns (Earleywine and Finn, 1990), later onset alcoholism (Jones, 1968) and comprise the essential description of a personality-risk factor for alcoholism. Recent models of the familial transmission of alcoholism describe a highly heritable familial subtype of alcoholism (Type 2) that is characterized by increased impulsivity, risk-taking and novelty seeking (Cloninger, 1987). The precise mechanisms that underlie these characteristics in this population have yet to be elucidated, however, Gray's (1987) construct of the Behavioral Inhibition System (BIS) provides a useful heuristic framework for such investigations. The BIS is the neurophysiological pathway responsible for the experience of anxiety. The BIS is activated in the presence of cues for punishment or nonreward. In this conceptual framework, disinhibited behavior is viewed as underresponding to cues for punishment and would be associated with a weak BIS. Thus the cues fail to inhibit behavior. The paper will present data from a variety of studies that provide support for the notion that the nonalcoholic sons of alcoholic fathers (high-risk men), who also have a multigenerational family history of alcoholism, have a weak Behavioral Inhibition System as evidenced by psychophysiological and personality characteristics. Such support is drawn from studies that demonstrate a pattern of cardiovascular over-activation and electrodermal underactivation in this population in situations involving unavoidable threat, and data indicating that these men fail to develop a conditioned electrodermal and vasoconstrictive response to tones that signal the occurrence of punishment. The psychophysiological response patterns seem to reflect a regulatory deficit that is significantly related to self-report measures of disinhibitory personality traits.

ALCOHOLISM RISK AND VISUOSPATIAL INFORMATION PROCESSING. Steven L. Schandler. Chapman College, Orange, CA.

An understanding of commonalities between alcoholic populations and persons at risk for developing alcoholism is dependent on an accurate understanding of the specific effects of chronic alcohol abuse on human biology and behavior. This paper will present the results from a series of studies which show detoxified alcoholics, intoxicated nonalcoholics, and children of alcoholics to display deficits in the processing of visuospatial information. The deficits in visuospatial information processing reflect neither a general decrement in intellectual activity nor disruptions of motor activity associated with a response. Rather, the deficits appear in very selected operations within the information processing cycle. The accumulating literature suggests that the effects of alcohol on visuospatial information processing reflects a reduced attention/incorrect cue encoding effect. Visuospatial information processing deficits appear as a risk factor related to the onset of alcoholism. Young and adult children of alcoholic parents appear at risk for alcoholism. These persons display visuospatial learning that is significantly poorer and patterns of autonomic activation significantly less differentiated than displayed by the persons with no family alcoholism history. Further, the patterns of learning and activation displayed by persons with a family alcoholism history are similar to those displayed by previously studied detoxified alcoholics using a similar learning task. These data suggest that deficits in visuospatial information processing may reflect an antecedent to rather than a consequence of chronic alcohol abuse.

SUBGROUPS OF MEN AT RISK FOR ALCOHOLISM. Vicki E. Pollock. University of Southern California, Los Angeles, CA.

Two distinctive theoretical perspectives specify differences in biological and psychological factors that are involved in the development of alcoholism. One theoretical perspective, put forth by Tarter and colleagues (1984), is that prealcoholics are characterized by excessive physiological lability while sober. Such individuals might be especially vulnerable to alcohol effects because alcohol regulates aspects of their physiological function. Due to excessive physiological lability that they manifest while sober, however, prealcoholics may have difficulty in accurately identifying and reporting their internal experiential states. A different theory, put forth by Goodwin (1981), is that in order to develop alcoholism, an individual must possess high initial tolerance for alcohol effects. The term "initial tolerance" refers to variations in individual sensitivity to alcohol, and does not denote acquired tolerance associated with the development of dependence. According to this perspective, prealcoholics, possessing high initial tolerance for alcohol effects, would be characterized by reduced sensitivity to alcohol as compared to normal subjects. These two theories are similar in that they both hypothesize that subjective measures should reveal evidence of reduced sensitivity to alcohol in subjects predisposed to alcoholism. These theories differ, however, in their hypotheses concerning physiological functions. From Tarter's perspective, prealcoholics would be characterized by greater physiological changes following alcohol administration than would normal controls. Under Goodwin's perspective, however, prealcoholics should be characterized by reduced physiological changes following alcohol as compared to controls. In this presentation, empirical evidence bearing on each of the hypotheses derived from these two theoretical perspectives will be considered by using data acquired in an ongoing, longitudinal study of alcoholism in Denmark.

SYMPOSIUM

From Opioid Receptors to Behavior and Vice Versa

Chair: *James H. Woods,* University of Michigan Medical School, Ann Arbor, MI.

Discussant: *Linda Dykstra,* University of North Carolina, Chapel Hill, NC.

INTRODUCTION TO RECEPTOR THEORY. James H. Woods. University of Michigan, Ann Arbor, MI.

Receptor theory has a great deal to offer the behavioral pharmacologist in the explanation of the behavioral actions of drugs. To attempt to establish the plausibility of this claim, this symposium will show some examples of the manner that it can be utilized with the study of the actions of opioids. To introduce the major concepts that are utilized within the theory, an overview of the notions of null methods, affinity, efficacy, and receptor reserve will be given. These concepts will be illustrated with data from both in vitro and, where possible, in vivo systems. Emphasis will be placed on the validity of the concepts and their general applicability.

AFFINITY OF OPIOID ANTAGONISTS. Sandra D. Comer.

University of Michigan, Ann Arbor, MI.

An important concept in pharmacology is affinity, the attraction that a drug molecule has for a receptor. When measurements are made of the effects produced by an agonist in both the presence and absence of a competitive, reversible antagonist, it is possible to obtain a quantitative estimate of the affinity of the antagonist for a given receptor using pA_2 analysis. A pA_2 value is the negative logarithm of the dose of antagonist which when given in combination with an agonist results in a two-fold increase in the dose of agonist required to produce a given response. The pA_2 method is particularly useful in that it can be used to determine whether or not 1) two different agonists are producing their effects through the same receptor type and 2) a number of different effects produced by a particular agonist are mediated through the same or different receptors. In opioid receptor systems, for example, both mu- and kappa-receptor-selective agonists produce analgesia under certain conditions. In order to determine whether or not these agonists are producing their effects through the same receptor, apparent pA_2 values can be determined for an antagonist with both agonists. If the pA_2 is the same, then it can be assumed that the two agonists are producing the effect through the same receptor, while different pA_2 values indicate that more than one receptor is involved. In addition to producing analgesia, many mu-receptor-selective agonists are self-administered and produce discriminative stimulus effects. In order to determine whether these effects are mediated through the same receptor, pA_2 analysis can also be used. Again, similar pA_2 values indicate that the same receptor mediates the different effects while different pA_2 values suggest multiple receptor involvement. These examples thus illustrate that the pA_2 method can be a very useful tool for evaluating various pharmacological effects.

RELATIVE EFFICACY OF OPIOID AGONISTS: A BEHAVIORAL ANALYSIS. Charles P. France. University of Michigan, Ann Arbor, MI.

Two pharmacological constants, affinity and efficacy, describe interactions among drugs, receptors and receptor-coupled effectors and are unifying principles of receptor theory by which drug actions can be characterized across different biological conditions. Differences in affinity (potency) among agonists are well established at many levels of analysis; however, efficacy has not been widely examined in vivo, despite the well-demonstrated utility of this theoretical construct in vitro both for the classification of drugs and for the classification of receptors. In order to establish efficacy differences among agonists several empirical requirements must be satisfied. First, all of the relevant drugs must produce the measured responses by acting at the same receptor which can be established by showing similar affinity estimates for a competitive, reversible antagonist across all drugs and conditions. Second, compounds of low efficacy must attenuate the actions of compounds with higher efficacy under conditions in which the lower efficacy compounds fail to produce the maximum obtainable response. Presumed differences in efficacy among agonists can be further substantiated under conditions in which receptor reserve is altered, either by administration of irreversible antagonists or by the induction of tolerance. At sufficiently large doses, irreversible antagonists will decrease the maximal response; because low efficacy compounds have smaller receptor reserve, the maximum will be diminished for lower efficacy agonists at doses of antagonists that do not change the maximum produced by more efficacious compounds. The later approach (irreversible antagonism) is critical for differentiating among agonists that have different efficacies but produce maximal responses under all test conditions. To the extent receptor theory has been evaluated *in vivo,* it appears to provide useful and appropriate principles for assessing behavioral effects of drugs. Examples from behavioral studies will be used to demonstrate empirically verifiable hypotheses regarding efficacy differences among opioids. (Supported by USPHS Grants DA05018 and DA00254.)

TOLERANCE AND RECEPTORS. Alice M. Young. Wayne State University, Detroit, MI.

Tolerance to the behavioral effects of repeatedly administered opioids is modulated jointly by pharmacological and behavioral processes. This presentation will examine how pharmacological and behavioral principles can be used to examine the processes underlying the development, characteristics, and persistence of opioid tolerance. Tolerance to opioids is modulated by the opioid employed for repeated treatment, its dose and frequency, the duration of treatment, and the behavioral conditions under which tolerance is developed and assessed. Tolerance to the behavioral effects of the prototypic opioid morphine, for example, can vary directly with the maintenance dose and duration of chronic treatment. Patterns of cross-tolerance suggest that tolerance produced by chronic morphine treatment is limited to μ opioids, and differences in patterns of cross-tolerance among μ opioids suggest that tolerance may result from changes in the receptor populations that underlie opioid effects. Other lines of evidence suggest that development and persistence of tolerance to the behavioral effects of opioids are also modulated by respondent and operant conditioning processes. Tolerance to the analgesic effects of morphine, for example, can be brought under conditional control of the testing environment. Such conditional tolerance is responsive to many of the processes known to modulate respondent conditioning, including blocking, sensory preconditioning, and extinction. Development of tolerance to the disrup-tive effects of opioids on well-developed operant behaviors is also modulated by stimulus control and reinforcement processes. Similar behavioral contingencies modulate tolerance to the discriminative stimulus effects of opioids, with tolerance developing most readily under training conditions that limit transfer of control to lower drug doses. A fuller characterization of opioid tolerance will require both pharmacological and behavioral studies. Both receptor and conditioning theory can provide useful guideposts to studies of tolerance to the behavioral effects of opioids.

SYMPOSIUM

Psychologists in Substance Abuse: Current Activities and Growing Opportunities

Chair: *Joan Ellen Zweben,* The East Bay Community Recovery Project, Oakland, CA.

Discussant: *George DeLeon,* Community Studies Institute, New York, NY.

OPPORTUNITIES FOR PSYCHOLOGISTS THROUGH NIDA. Charles R. Schuster. National Institute on Drug Abuse, Rockville, MD.

The National Institute on Drug Abuse involves psychologists in a wide range of specialties in the research and related activities it conducts or sponsors. Psychologists currently lead or participate in a wide range of research activities, focusing on topics ranging from the behavioral pharmacology and abuse liability of