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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