

### CONDITIONED TOLERANCE AND STRESS-INDUCED ANALGESIA IMPLICATIONS FOR DRUG RELAPSE

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Animals that have a series of morphine injections reliably paired with a distinctive context will subsequently exhibit tolerance to the analgesic effects of the drug only if they are assessed for analgesia in the drug-paired environment. The compensatory-response model (Siegel, 1975) hypothesizes that this context-specific tolerance is produced because the distinctive context acquires the properties of a CS that elicits a behavioral response that is counterdirectional to the direct drug effects, i.e., hyperalgesia. Although there is considerable evidence that conditioning processes can make a substantial contribution to tolerance development, a tabulation of available data indicates that a behaviorally manifest, compensatory response of hyperalgesia is not a necessary component of associative tolerance to morphine's effects. Recent research from our laboratory will be summarized indicating that, although associative tolerance to the analgesic effects of morphine in rats was not subserved by conditioned, hyperalgesic responses, evidence for the operation of associative tolerance processes did emerge when animals were stressed in a drug-predictive context. That is, animals exposed to a brief footshock in an environment that had previously been paired with morphine administration developed less stress-induced analgesia (SIA) than appropriate control animals. These data suggest that associative-morphine tolerance and this form of SIA exhibit cross-tolerance. The relevance of these findings for the compensatory response model of drug tolerance will be addressed. The implications of these data for a role of stress in one aspect of addictive behavior, i.e., drug relapse, will also be discussed. For instance, if the stress responses of animals are moderated by the concomitant presentation of drug paired stimuli, similar effects may be obtained in opiate addicts. That is, the stress responses of addicts may differ as a function of the extent to which they are stressed in the presence of environmental stimuli previously associated with drug administration.

### SYMPOSIUM

Drugs of Abuse in Social Context: Animal-Human Parallels?

Sunday August 30, 1987 • 9:00 a.m. - 10:50 a.m.  
Marriott Marquis Hotel • Jolson/Cantor Room  
Chair: Klaus Miczek, Tufts University

MARIJUANA SMOKING IN A SOCIAL CONTEXT: Marian W. Fischman and Richard W. Foltin, Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21205

Marijuana is generally smoked within a social context, and the effects of that drug can both modify and be modified by interaction within the group. A series of studies investigating this complex interaction were carried out. Subjects resided continuously, in groups of three, in a relatively naturalistic laboratory, for periods up to 18 days. All contact with the experimenters was through a networked computer system, and subjects' behaviors, including social interaction, were continuously recorded. Subjects either were allowed to

self-administer up to five placebo or active marijuana cigarettes (1.84%  $\Delta^9$  THC) each day, or the cigarettes were administered by the experimenters at programmed times during the day. When marijuana was available on request, subjects self-administered it in a regular pattern over days, despite changing contingencies on other aspects of their behavior. Whether the pattern of drug administration was subject- or experimenter-controlled, social interaction was generally facilitated by marijuana smoking. Drug effects varied as a function of baseline interaction time, with increases apparent in those subjects having high baseline interaction times. These increases in social behavior were manifested differentially in different groups of subjects. For example, in one group, increases in dyadic interaction times were accompanied by a marked decrease in triadic interaction time, while in a second group triadic interaction time increased markedly with little or no change in dyadic interaction time. The results of these studies show the utility of studying drug effects in a residential laboratory in which subjects are free to socialize while behavior is continuously observed and recorded.

DRUG EFFECTS ON HUMAN SOCIAL AND VERBAL BEHAVIOR: Maxine L. Stitzer, Ph.D., Behavioral Pharmacology Research Unit, Psychiatry Department D-5-West, Francis Scott Key Medical Center, Baltimore, MD 21224

Drugs effects on behavior are important to understand since they may represent a component of drug reinforcement. That is, people may take drugs in part to experience or achieve their behavioral effects. Drug effects on social behavior seem especially important since socializing is such a ubiquitous part of the human behavioral repertoire and since drugs are frequently ingested in a social context. In order to systematically assess effects of drugs on human social behavior, several drugs have been tested in a standardized dyadic social interaction situation with the following results. Three drugs, d-amphetamine, ethanol, and secobarbital, have increased or facilitated social conversation in hired research volunteers while hydromorphone also increased talking in opiate post-addict subjects. Two drugs, chlorpromazine and smoked marijuana have decreased social conversation in hired research volunteers. Data documenting these effects will be presented. These observed behavior changes may represent specific drug effects on social behavior and/or drug-produced changes in the reinforcing value of social interaction. Alternatively, they may represent general nonspecific effects upon on-going behavior. Two approaches have been pursued in recent years to better understand the specificity of effects observed during dyadic social interaction. First, d-amphetamine, ethanol and secobarbital have been tested under conditions where subjects produced verbal monologues in the absence of a social partner. All three drugs produced increases in monologue speech, suggesting a nonspecific effect on talkativeness. This effect on speech in the absence of a partner is difficult to interpret, however, since monologue speech content under these conditions is very similar to the content of social conversation. A second approach has been to test drug effects on preference for social interaction during a behavioral choice procedure. Preliminary data for d-amphetamine effects will be presented. A reliable preference shift toward the social option would suggest a specific drug-produced increase in social behavior or in the reinforcing value of social interaction.