THE BEHAVIORAL TOXICOLOGY OF SOLVENTS

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Volatile organic solvents debilitate normal behavioral functioning and serve as drugs of abuse. Their unique route of administration has hindered behavioral studies. Initially, concentration-related disruption in normal behavioral functioning by different solvents was described. Subsequent analyses focussed on developing methods, based on individual differences in effect, to assess risks following low levels of exposure. Recent pharmacological studies have aided in the assessment of specific behavioral effects of solvents, and challenged traditional views of mechanism of action Most recently, attempts to relate behavioral and neuroendocrine effects of solvents have provided even more interesting challenges to understanding the behavioral effects of solvents

SORTING OUT THE VARIOUS TYPES OF DRUG-INDUCED CONDITIONED RESPONSES

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Evidence that psychoactive drugs can produce conditioned responses in human subjects is based on laboratory evidence as well as clinical observations Most of the work has been done using opioids as the unconditioned stimulus and using a classical conditioning paradigm Conditioning stimuli repeatedly presented in association with the drug effects have later been shown to be capable of eliciting a response in the absence of the drug The conditioning responses have varied depending on the circumstances, i e , time of presentation and whether or not the subject was drug-free, drug-dependent or in withdrawal Conditioned responses can be drug-like, drug-opposite or withdrawal-like These responses have been measured using behavioral measures, subjective measures and physiological measures The animal literature and the human literature in this area are reasonably consistent It remains to be seen whether these conditioned responses have clinical significance These phenomena have a potential role in the production of *placebo responses* in patients being studied in controlled trials of psychoactive medication Another possible role is the production of *craving* or withdrawal responses in former addicts

NEUROLEPTICS PRODUCE WITHIN-SESSION RESPONSE DECREMENTS FACTS AND THEORIES.

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Although first clearly observed in the case of operant behavior maintained by continuous reinforcement with food, neuroleptic-induced within-session response decrements have been reported for conditioned avoidance, discriminated lever release (reaction time), and fixed-ratio responding When viewed from a quantitative perspective, the magnitude of the within-session effects on response rate and latency appear to be related to the dose of the drug and to the overall motoric/postural demands of the task Theoretically, these phenomena can be understood in terms of behavioral explanations (anhedonic, dissociative, or psychomotor effects of dopamine receptor blockade) or in terms of brain neuropharmacological concepts (increased dopamine turnover occasioned by neuroleptic treatment, stimulation of dopamine release by motor activity and conditioned stimuli, and rapid depletion of presynaptic dopamine)

DRUGS AND STIMULUS CONTROL OF BEHAVIOR A CASE STUDY OF A BEHAVIORAL MECHANISM OF DRUG ACTION.

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Results of several studies indicate that pentobarbital (PB), but not *d*-amphetamine (*d*-A), can decrease the control over behavior exerted by visual stimuli in a conditional discrimination procedure Key-peck responses of pigeons on one of two keys were intermittently reinforced under a fixed-interval schedule Responses on a red key produced food if a stimulus lamp (SL) was on, responses on an amber key produced food if the SL was off. PB decreased stimulus control of responding at intermediate (3 0–10 0 mg/kg) doses that did not appreciably alter average rates of responding *d*-A, however, altered stimulus control of responding only at high doses (3 0–5 6 mg/kg) that also substantially decreased response rates Analysis of these effects indicated that (1) effects of drugs on stimulus control of behavior are situation specific, (2) drugs may affect control by certain modalities and not affect others, and (3) decreases in stimulus control produced by drugs can be "environmentally antagonized" by increasing the pre-drug degree of stimulus control The suggestion that drugs can affect stimulus control of behavior implies that drugs can affect behavioral processes as well as behavior itself As such, effects on behavioral processes can be considered behavioral mechanisms of drug action, implying that administering a drug is functionally equivalent to changing some independent variable Behavioral mechanisms of action are different in kind from several factors that have been shown to influence the effects of drugs. While a behavioral mechanism implies functional equivalence, it does not require formal equivalence nor functional exclusivity Thus, a drug may have an effect on stimulus control as well as other effects on behavior, those other effects may obscure a formal equivalence For these reasons formal equivalence should not be relied upon to assess whether a drug has a particular mechanism of action

TOLERANCE TO DRUG DISCRIMINATIVE STIMULI

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The ability to function as a discriminative stimulus appears to be a general characteristic of psychoactive drugs Development and maintenance of drug discriminative stimulus control reflect dynamic interactions of behavior, drug, and the demands imposed by the learner's environment Development of tolerance to drug stimulus control is also a dynamic process, shaped by interactions of the dose and chronicity of drug treatment, the behavioral conditions under which a drug is encountered, and the learner's stimulus control history This discussion will outline the experimental strategies employed in studies of drug stimulus control, describe interventions that modulate such control, and review the nature and determinants of tolerance development