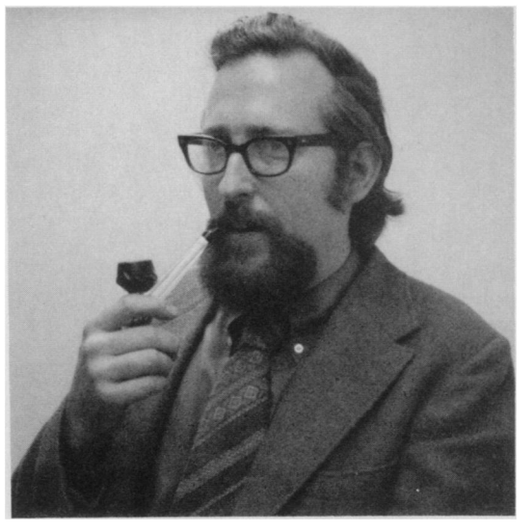
Learning to be drunk

Research on learning and conditioning while under the influence of drugs may provide some new answers to questions about drug abuse and addiction



Photos: Overton

Overton: Cannot overlook human implications.

by Robert J. Trotter

"Oh . . . Wow . . . I feel horrible. What happened last night? I don't remember a thing." Thus goes the frequent refrain of the bleary-eyed partygoer the morning after the night before.

"What do you mean? You know exactly what happened last night. You made a fool of yourself as usual. I just don't understand it. You are a completely different person when you drink." Thus answers the long-suffering spouse in an oft-repeated and easily identified scene.

Because the situation is so recognizable, it has become a classic comic cliché. But it is more than that. It represents a traumatic circumstance for those involved and it asks some fundamental questions about the nature of alcoholism and drug abuse. Why, for instance, can't the drinker remember what happened? Why is the drinker a completely different person when under the influence of alcohol? Why does the drinker become addicted to alcohol if the end result (physical and mental anguish) is always the same? What can be done to change the pattern?

Much research has gone into answering these questions, and the answers have not been completely satisfactory. But one field of research that has received relatively little attention may produce some better answers and may eventually help to solve some of the problems of drug abuse.

The research began in 1937 when Edward Girden and E. A. Culler at Brooklyn College discovered the phenomenon of dissociated or state-dependent learning. While studying conditioned leg flexion in dogs they found that if a dog was conditioned while undrugged it would subsequently fail to respond when drugged with curare extract. Girden and Culler then found that a dog conditioned while drugged with curare would subsequently respond when the drug condition was reinstated, but would not respond while undrugged. They concluded that the response performed by a nondrugged dog was somehow separated or dissociated from that performed by the same dog while drugged. In other words, learning was not transferred from the drug to the nondrug state.

These findings were not immediately followed up by other scientists—probably because the curareform drug they used, erythroidine, is uncommon. But the recent discovery that many commonly used drugs that act on the central nervous system, including alcohol, can dissociate learning has revived research on the phenomenon.

Donald A. Overton of Temple Medical Center and the Eastern Pennsylvania Psychiatric Institute in Philadelphia has been studying dissociated learning for more than 10 years. As yet, no direct relationship between state-dependent learning and alcoholism has been demonstrated. But Overton says there is virtually a one-to-one correspondence between the drugs that produce dissociation and those that are subject to abuse. This correlation, he says, suggests that state-dependent learning may play a causal role in the addictive process.

Overton explained his experimental design and discussed the implications of his findings in an invited address at a meeting of the American Psychological Association in Hawaii and in subsequent discussions with SCIENCE NEWS.

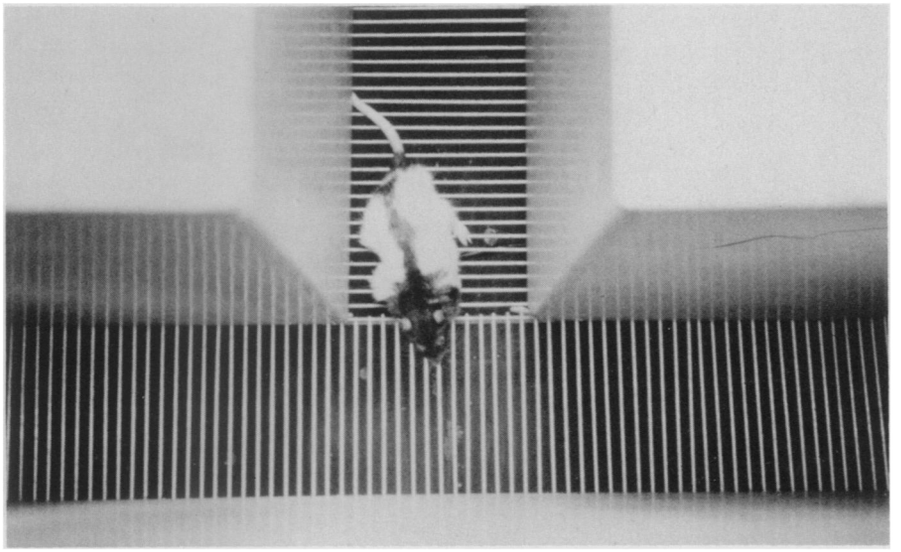
He uses two basic types of experiments to study the dissociative effects of drugs. In one, animal subjects are trained while they are drugged. On the following day half of them are tested for retention in the nondrug condition, while the other half are tested with the drug condition reestablished. If dissociation is complete, explains Overton, only the second group will show evidence of the previous training. The first group will behave as if they had never been trained.

In a second type of experiment, animals are taught to perform one response when drugged and a different response when undrugged. Overton has demonstrated this with rats. One response (turn right in a T maze) was reinforced when the animal was drugged. A different response (turn left) was rewarded when no drug was injected. The rats were trained within 10 to 20 sessions to reliably differentiate the presence or absence of a drug dosage as low as one-fifth that required to produce complete dissociation. Such discriminations, says Overton, are apparently based on the same drug effects that produce total dissociation when high doses are used.

Using this discrimination technique, Overton has found that rats can differentiate between different doses of a single drug just as they can between the drug and no-drug state. He and other researchers have further demonstrated that rats will give a drug response when tested with appropriate doses of similar drugs, but not when tested with dissimilar drugs. With this information Overton has compiled a list of drugs known to be discriminable, and found that the drugs most subject to abuse are among those most readily discriminable.

One of the most often abused drugs, alcohol, has frequently been used to demonstrate state-dependent learning in humans. Statistically significant dissociation has been observed using simple verbal and visual learning tasks. It is clear that total dissociation is not produced by moderate drinking, says Overton, but "experiments with human subjects indicate that moderate doses of alcohol produce partial dissociation with some types of learning."

Because dissociation is a quality of many abused drugs, and because al-



A drugged rat's response in a T maze can demonstrate dissociated learning.

cohol has a dissociative effect on humans, Overton feels that studies of state-dependent learning may supply some of the answers to questions about alcoholism and drug abuse.

Why can't the drinker remember what happened? Studies by Donald W. Goodwin of Washington University School of Medicine in St. Louis show that high doses of alcohol produce a dose-dependent defect in memory registration in such a way that permanent engrams (memory impressions) tend not to be formed. Immediate memory remains intact so that the drinker can answer questions and do mental arithmetic, but memory tests show that many ongoing events are forgotten within 2 to 30 minutes. If the short-term memory defect is severe, a permanent blackout results covering the time during which the memory defect was present. Recall for both significant and emotionally trivial experiences is equally affected.

This is not the only type of memory loss that occurs with drinking. Some alcoholics report that drinking improves their memory for events that happened during previous drinking episodes. Overton says this temporary amnesia, in which recall can be recovered under proper conditions, is apparently caused by deficits in memory retrieval rather than memory registration. The difficulty with retrieval may result from drug dissociation, although this has not as yet been demonstrated experimentally.

Why is the drinker a completely different person when under the influence of alcohol? Why does the drinker become addicted? Most answers to these questions are based on pharmacological properties of alcohol such as its anxiety-reducing or disinhibiting effects. Overton suggests that the dissociative effects of alcohol may also be involved. His animal data show that rats repeatedly experiencing drug states can develop behavior patterns conditional on a drug state much more easily than was previously believed possible. Similarly, he says, a habitual drinker might develop a whole set of behaviors and emotional responses peculiar to the drug condition. This would make the drinker a different person when intoxicated. If these drug-state behaviors are more reinforcing than sober behaviors, the drug state will acquire a more positive value than it initially possessed. This could be involved in the addiction process. There is nothing about this argument, Overton adds, that uniquely applies to alcoholism. It appears equally relevant to other drugs with strong stimulus properties such as nicotine and tetrahydrocannabinol.

What can be done to change the drug abuse pattern? Psychotherapy and behavior modification techniques are often used to treat alcoholics. But these maneuvers tend to lose effectiveness rapidly once the alcoholic starts to drink. This is usually attributed to the disinhibiting and thought-dissolving properties of alcohol. Overton feels that dissociation might be another mechanism active in making the treated alcoholic look untreated once drinking resumes. The obvious answer, if this is the case, is to carry out therapy while the alcoholic is intoxicated. Conditioning would be more difficult to obtain with intoxicated subjects but it might be worth a try, says Overton, because dissociation data indicate that such treatment techniques might be more effective than those presently in use.

Overton's experimental work has been done with animals, but he feels the implications for humans should not be overlooked. "An obvious need exists for further investigations on many aspects of this topic, particularly on the occurrence of drug discriminations in man and on the relationship of dissociation to the addictive process." □

CENTRALLY ACTING DRUGS TESTED FOR DISCRIMINATIVE CONTROL

STRONG CONTROL	MODERATE CONTROL	WEAK CONTROL
ANESTHETICS	ANTIMUSCARINICS	MUSCARINICS
Pentobarbital	Atropine	Physostigmine
Phenobarbital	Scopolamine	Arecoline
Secobarbital	Benactyzine	Carbacol
Na. Barbital	Ditran	
Amobarbital		PHENOTHIAZINES
E. Alcohol	TETRAHYDROCANNABINOLS	Chlorpromazine
Paraldehyde	Delta-9 THC	Acepromazine
Ethyl Carbamate	Delta-3 THC	Perphenazine
Hydroxydione	Marijuana Extract	Prothipendyl
Progesterone		
Ether	NARCOTICS	DIBENZAZEPINES
Nitrous Oxide	Morphine	Imipramine
DISSOCIATIVE ANESTHETICS	HALLUCINOGENS	VIRTUALLY INACTIVE DRUGS
Ketamine	Mescaline	Pryilamine
Sernylan	LSD	Phenoxybenzamine
	STIMULANTS	Dilantin
MINOR TRANQUILIZERS	Amphetamine	Caffeine
Librium	Methylphenidate	Aspirin
Meprobamate		Lithium
	CONVULSANTS	
NICOTINICS	Metrazol	
Nicotine	Bemegride	
Lobeline		
	ANTINICOTINICS	
	Mecamylamine	

Data by Barry, Hendriksson, Hill, Overton, Winter & others.