BACKGROUND PAPER

Research Priorities for Drugs Other Than Alcohol

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INTRODUCTION

The drug research that is needed for traffic safety purposes can be viewed as having at least two distinct components. The first priority has to be research to establish whether and how potentially impairing drugs affect driving performance. The research needs encompass drugs that have been available for some time, new drugs, and drugs for which the labeling has been changed. Data for those purposes can be obtained from laboratory experiments and field studies.

The second component is research to identify the behavioral signs and symptoms of drug impairment. There is a very large difference between the detection of impairment with sensitive measures in the research laboratory and the detection of impairment with observations of a suspect at roadside. The laboratory and field data are essential for sound policies and legislation, but many of the policies and much of the legislation must be followed by enforcement if there is to be a positive impact on drug-related problems. Traffic enforcement can proceed effectively only if an officer can recognize the signs and symptoms of drug impairment.

The world of drugs, both licit and illicit, changes continually with the result that research inevitably lags behind the usage curve. Also, because research is driven largely by society's perceptions of the illicit drugs which are most problematic, as well as by the pharmaceutical industry's requirement for data for Federal Drug Administration applications, it often proceeds somewhat haphazardly and incompletely. This paper focuses on just some of the mismatch between what is known and what needs to be known.

ANXIOLYTICS AND ANTIDEPRESSANTS

Effects on Driving Performance

Studies of the effects of tranquilizers and antidepressants on driving skills report impairment ranging from minor to serious. Scant research attention has been directed, however, to some of the newer drugs in these categories or to certain conditions of use. An examination of new drugs, including those that claim to be nonimpairing, is important, but further study of some of the older drugs may actually be more important for traffic safety, because they are extensively prescribed and, in some cases, misused.

Examinations of the effects of medicines on driving skills typically begin with acute dose studies with samples of young adults. Those studies are appropriate beginnings, but when they are the entire body of published research, key questions remain unanswered. The current research issues are effects of chronic dosing, effects for patients (as opposed to healthy subjects), and effects for older users. Although difficult and under-researched, these are important topics.

Chronic dosing issues arise for example in connection with performance effects for patients who now have taken fluoxetine (Prozac) for extended time periods. Although acute dose studies reported no significant impairment of driving skills, both the effects on performance and patients' perceptions of the drug's effects may change with continued use. To illustrate the latter, if subjective awareness of the drug's effects fades over time, does a patient's attention to labeling and package insert warnings also fade? Do patients eventually disregard the admonition to avoid alcohol use in combination with the drug?

Traffic safety issues dictate laboratory study of acute and long-term effects of drugs that calm, sedate, or relieve anxiety and depression. These medicines provide enormous benefits for patients, but they differ in impairment potential. At minimum, research can generate data that will allow prescribing physicians and patients to weigh the relative driving-impairment risks of equally efficacious drugs.

Signs and Symptoms

Traffic officers regularly contact drivers who are impaired by prescription drugs. They can perform their duties proficiently in connection with those drivers only if they know the signs and symptoms of abuse levels and of therapeutic doses for drugs that have been shown to impair driving.

The patients who are stopped by officers often do not understand either that a drug poses significant driving risks, or that operating a motor vehicle while impaired by licit (in some jurisdictions) and illicit drugs is prohibited by law. Officers also encounter drivers who have ingested psychoactive drugs, sometimes in very large amounts, for non-medicinal purposes. For example, diazepam and alprazolam are drugs of choice for "highs" and also to augment or offset the effects of illicit drugs.

A current problem for law enforcement is flunitrazepam (Rohypnol), the date rape drug, which is not legal in the United States but is nonetheless available and cheap. "Roofies," as the drug is known on the street, has no odor or taste and cannot be detected in a drink. Within about 10 min of unknowingly ingesting the drug, a victim experiences severe dizziness, disorientation, difficulty speaking or moving, and passes out. Upon awakening, there will be no memory of sexual assault that may have occurred, and by the time the assault finally is recognized, the drug may no longer be detectable in body fluids. Thus, the extent of the problems associated with Rohypnol is unknown. It is a dangerous drug, and police officers urgently need information about it.

MARIJUANA

Effects on Driving Performance

The drug-impaired drivers most frequently detected and examined at roadside by traffic officers are those who are under the influence of marijuana. Although a substantial marijuana literature dates back several decades, the drug and its users have changed during the 1990s, but the potential consequences of those changes for traffic safety are as yet poorly understood. For example, users are beginning at a younger age. The percentage of 8th graders who *ever* used marijuana more than doubled between 1991and 1997. One worrisome aspect

of that particular change is that because youngsters are smaller in body size, they will get larger active doses than adults when they use the same amount. A larger dose, of course, means greater impairment. Whether age of initiation and duration of marijuana use have an effect on the acquisition and development of complex skills such as driving merits examination.

The increase in the potency of marijuana creates yet another 1990s research issue. Although the tetrahydrocannabinol (THC) content of marijuana now sometimes is higher than 20 percent, and 8 to 10 percent is common, the material used in extant driving research was 3 percent THC (or less). Since high potencies can produce panic attacks, nausea, and fainting, it is not surprising that marijuana-related emergency room visits have increased by 48 percent. Examination of the effects of marijuana, as it currently is used, on driving skills is a research priority.

Signs and Symptoms

Officers are hampered by a lack of data directly relevant to their problems in arresting marijuana-impaired drivers. Prosecutors face a difficult task in meeting the court's requirement for evidence showing beyond a reasonable doubt that a suspect's driving ability was impaired by the drug.

Marijuana users typically exhibit a somewhat unique pattern of signs and symptoms. When a suspect has an odor of marijuana, reddened conjunctiva, rebound dilation, and a high pulse rate, an officer can reasonably conclude the person has used marijuana. Arrest and prosecution problems arise, however, because that may be the extent of reasonable and possible conclusions. The THC content of a blood or urine specimen will bear little relationship to impairment. Users will exhibit rebound dilation, and officers rely on that eye sign, but there are no scientific data to support its validity. On the Standardized Field Sobriety Tests (SFSTs), the user will not exhibit nystagmus, but walking and balance may show impairment. The SFSTs, however, were developed for alcohol, and the criteria for their performance with marijuana are ambiguous at best. At minimum, traffic officers need SFST validation data for marijuana.

METHAMPHETAMINE

Effects on Driving Performance

The current popularity of stimulants creates a need for data about their effects on driving performance. It also creates research problems of method and dosage. Users snort, smoke, or inject large amounts of methamphetamine over extended periods. Laboratory experiments with human subjects, however, are limited by regulation and ethics to acute or short-term, low-to-moderate doses. Such research provides only limited relevant data.

Although speeded responses can be measured with small amounts of a potent stimulant, it is difficult within laboratory restrictions to elicit and measure the aggressive, impulsive, disorganized responses that occur with over-stimulation. The research problem is compounded by the fact that some dose levels and some usage patterns produce severe

impairment during the rebound phase; i.e., when the drug has been eliminated and the user is functioning in a depressed state.

Research as usual will not suffice for methamphetamine. Innovative methods are needed to examine the drug's effects on novice versus long-term users, the effects of acute doses versus runs of several days, the effects of speed versus ice, and the effects during the high versus the down side.

Signs and Symptoms

Detection of a driver's impairment by methamphetamine, or other stimulants, can be very difficult for a traffic officer. Although dilated pupils, rapid pulse, and agitation are excellent clues, they are nonspecific and may be nonexistent at moderate doses in tolerant users. Law enforcement needs laboratory research and systematic documentation of the observations of arrested drivers to establish signs and symptoms of methamphetamine, including SFST performance.

DESIGNER DRUGS

Effects on Driving Performance

A short list of the names of underground chemists' products includes Ecstasy, GHB, Blue Nitro, Firewater, Gamma G, Vitality, and Revivarant. There are other names for the same substances, and there are other designer drugs. Most are created by altering the molecular structure of an existing drug. Although laws now have closed the loophole, the initial intent was to create street drugs not specifically listed as a controlled substance. They are potent, and they are dangerous.

GHB, an odorless and tasteless substance that goes unnoticed in a drink is made from butyrolactone and sodium hydroxide (lye). An Internet site is a sales area for several different companies selling these products with different names in different colors and forms. Typically, they are marketed as a muscle builder or growth hormone (http://www.cyberstrengthnutr.com/ghstimulators.htm). The substances produce euphoria, but they can result in coma and respiratory failure with large doses or combined with alcohol.

MDMA or Ecstasy was originally synthesized as a diet pill but was never marketed for that use. It is chemically related to methamphetamine and mescaline, and it acts simultaneously as a stimulant and a hallucinogen. It is reputed to produce sociability and excitement, but these are at the cost of nausea, increased blood pressure, and uncontrollable rapid eye movement. Disorientation, sleeplessness, and paranoia can occur and may persist for weeks after a single dose. In animal studies, the drug has been shown to reduce serotonin by 90 percent for as long as 2 weeks, and to damage neurons.

These drugs, and others like them, are popular with young people, particularly at underground parties. After all-night partying and drug use, drivers clearly would be at risk of being impaired both by fatigue and the effects or aftereffects of the drugs. Research will be extraordinarily difficult, but this recipe for disaster among adolescents and young adults begs for attention.

Signs and Symptoms

Although some information has accumulated within the ranks of law enforcement, there is no systematic body of knowledge about the signs and symptoms of designer drugs. Forensic labs do not routinely test specimens for most of them. Traffic officers may incorrectly attribute their observations of suspects who have used them to a closely related substance. When that incorrectly identified substance is not detected in a specimen, charges against the suspect probably will be dismissed. The number of these products is growing rapidly, and officers presently are hard pressed to know what to look for or how to recognize what they find.

HERBAL PREPARATIONS

Effects on Driving Performance

Combinations of legal and inexpensive herbals are being marketed as sources of a natural high. Ephedra (ma huang) is a primary ingredient in such products as Cloud 9 and Ultimate Xphoria, which promise *cosmic experiences* and *sexual sensations*. Users usually report somewhat less exotic effects, typically saying only that they feel relaxed and sociable.

The Food and Drug Administration has received reports of serious adverse reactions, but at this point in time there are few directly relevant data about effects on driving. Note, however, that ephedrine, which is the principal active ingredient of the herb ephedra, has CNS stimulant properties, and psychoactive properties such as stimulation, by definition, yield both abuse and impairment potential. Since herbal products are increasingly available over-the-counter and appear to be gaining in popularity, there is a need to examine their effects on performance.

Signs and Symptoms

The state of knowledge and the needs of law enforcement, as described for designer drugs, applies also to herbal preparations.

SUMMARY (POTPOURRI)

The high priority topics for drug research, as identified by this paper, include anxiolytics and antidepressants, marijuana, methamphetamine, designer drugs, and herbal preparations. The scientific literature lacks data about the effects of these substances on driving performance or lacks data about specific users, doses, and conditions of use.

Although traffic officers' duties include the enforcement of statutes that prohibit driving under the influence of drugs, the research implications of those duties are seldom addressed. An officer's task at roadside can be simple if the driver is obviously intoxicated, but it also can be extremely difficult if the driver is tolerant to the impairing substance, is impaired by multiple substances, or is impaired by a newly developed drug. The

problem is compounded by the fact that body fluids most often do not provide definitive proof of drug impairment.

Ineffective enforcement is counterproductive for traffic safety. Each failure by an officer to detect drug impairment, and each failed prosecution of a drug-impaired driver diminishes the effectiveness of impaired-driving statutes. Research can provide many of the tools that law enforcement officers need.

The human life span is increasing. Although most of us believe that longevity is desirable, we also understand that serious diseases and disorders often are associated with aging. Given the expected age distribution for the next century, we can predict that a significant number of drivers will be experiencing performance losses associated with aging together with the effects of medications. For example, a high blood pressure patient will be prescribed a medicine, which may carry the potential for diminished alertness, and he may take it for the rest of his life. Will there be either acute or cumulative adverse consequences for driving skills? Whether licensing criteria for aging drivers should include drug usage is a question to be answered by research.

The SFSTs have become a valuable tool for traffic officers. Recent field validation studies confirm high rates of correct arrest decisions for alcohol-impaired drivers. Research to validate the test battery for other drug categories, at minimum for stimulants and marijuana, would increase their value at roadside and in the courtroom.