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Methamphetamine and Driving Impairment

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ABSTRACT: Following a review of the effects of methamphetamine on human performance, actual driving and behavior were evaluated in 28 cases in which drivers arrested or killed in traffic accidents had tested positive for methamphetamine. The circumstances surrounding the arrest or accident were examined, together with any observations by the arresting officer regarding behavioral irregularities. The investigators also made a determination of culpability. Most of the arrests resulted from accidents in which the driver was determined to be culpable. Typical driving behaviors included drifting out of the lane of travel, erratic driving, weaving, speeding, drifting off the road, and high speed collisions. Behavioral manifestations of methamphetamine use in arrestees included rapid or confused speech, rapid pulse, agitation, paranoia, dilated pupils, violent or aggressive attitude. Combined alcohol and methamphetamine use was uncommon, however use of marijuana was evident in about one third of the cases. In addition to impairing judgment and increasing risk taking, the effects of withdrawal from methamphetamine use including fatigue, hypersomnolence, and depression are likely contributors to many of these accidents. A consideration of the literature and the cases discussed here, leads to the conclusion that methamphetamine at any concentration is likely to produce symptoms that are inconsistent with safe driving.

KEYWORDS: forensic science, forensic toxicology, methamphetamine, driving impairment, driving

In areas where there is significant methamphetamine abuse, inevitably the effects of the drug on driving becomes an issue. In order to examine the links between the effects of the drug, and how these can impact skills required for safe driving, the epidemiological, clinical and toxicological literature was reviewed, together with 28 of our own impaired-driving cases involving methamphetamine.

The amphetamines are commonly abused for their central stimulant properties, the most popular abused drug in the class being d-methamphetamine (hereafter methamphetamine), also known as 'speed,' 'ice' or 'crank.' The drug can be smoked, ingested orally, or injected intravenously. The l-isomer (l-desoxyephedrine, Vicks Inhaler) is used as a decongestant, and has central nervous system potency of about 10% that of its enantiomer. The recommended dosage of l-desoxyephedrine for treatment of decongestion is two inhalations in each nostril every two hours for up to seven hours (1). Each inhalation delivers an absorbable drug dose of 21 ng (2), so a seven hour treatment should deliver no more than 300 ng, which would not result in measurable blood methamphetamine levels. The same study found that 17 doses of the drug were necessary to obtain a qualitative urine positive amphetamine screen. Abuse of inhaler contents by extraction and concentration is not unknown, but is uncommon. l-Methamphetamine is also a metabolite of the anti-Parknisonian drug selegiline (Depranyl) (3). Based on these considerations, the cases discussed in this paper are assumed to involve the d-isomer (methamphetamine), absent evidence to the contrary, since the analytical method used did not distinguish between the isomers. Furthermore, none of the subjects interviewed in the cases reviewed in this study noted use of Vicks inhaler or selegiline, and many either had illicit methamphetamine in their possession at the time of driving, or admitted to illicit methamphetamine use.

Methamphetamine is used therapeutically for the treatment of attention deficit disorder, obesity and narcolepsy (1,4). Among the effects reported at therapeutic concentrations in normal subjects are mood elevation, increased alertness, decreased appetite and a feeling of well being (5). Methamphetamine is excreted unchanged and about 10% is metabolized to amphetamine (3,5), its elimination half life ranges from 6 to 15 hours and is dependent on urinary pH (3).

Epidemiology

In two articles that deal specifically with methamphetamine and driving, first in 1976 (6), and later in 1987 (7), Hurst reviewed epidemiological data then-available and concluded that there was little evidence to specifically implicate amphetamine use in traffic accidents. He cites as a deficiency the lack of control studies, where drug-use rates in the general population are compared with a specific population (for example, arrested or fatally injured drivers), but notes that such studies are notoriously difficult to perform, and that even a low refusal rate may invalidate the control sample (6). Also limiting was the fact that many of the studies examining drugs and driving reviewed in the noted articles, did not include tests for amphetamines. The remaining epidemiological data that do suggest rates of amphetamine use in specific populations can be difficult to interpret however and tends to be of descriptive and comparative, rather than inferential value.

Subsequent to these reviews by Hurst, several studies of driver populations have included tests for amphetamines, and show a significant incidence of their use. Lund et al. in 1988 (8) studied drug use in truck drivers on a major US transcontinental highway, and found methamphetamine in 2% of those drivers voluntarily tested. Twelve percent of drivers contacted declined to participate however. In 1993, Crouch et al. (9) reported on the prevalence of drug use in fatally injured truck drivers, and found amphetamine or methamphetamine in 7% of cases. Comparing Lund's data with Crouch's suggests that methamphetamine use is over represented in fatally injured truck drivers. This would support a causal relationship between methamphetamine use and increased risk of fatal

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accident involvement, however the refusal rate in Lund's study makes this comparison less than conclusive.

Kirby et al. (10) reported drug use in traffic accident victims admitted to a level 1 trauma center in 1988, and found an incidence of amphetamine use of 2%. Robb et al. (11) in 1990 reported on drug use in drivers in New Mexico arrested under suspicion of driving under the influence of drugs (DUID), and found 1.7% positive for non-cocaine phenethylamine stimulants. Logan and Schwilke (12) in 1993 found 1.8% of fatally injured drivers in Washington state positive for methamphetamine. Unfortunately there is no corresponding control group in any of these studies to permit evaluation of the relative prevalence of amphetamine use in impaired drivers as opposed to the general driving population. In addition, since many of these studies tested only urine, blood-drug concentration data is not available. This is unfortunate since such information would be useful in establishing any link between the concentration of the drug and its role in the causation of the accident.

In summary, there is some evidence from these studies that amphetamine use is prevalent in certain driver populations, but on this basis alone, it remains difficult to infer a causal link due to the absence of control data. Studies documenting rates of methamphetamine use in driving populations do, however, allow identification of trends, and comparisons of drug use patterns between groups, and jurisdictions.

Laboratory Studies

The major limitation of clinical laboratory studies is that they deal with methamphetamine use, not abuse. Methamphetamine (Dexedrine) is administered orally at doses of up to 15 mg/day for the treatment of obesity, up to 25 mg/day in the treatment of attention deficit disorder in children, and up to 60 mg/day in the treatment of narcolepsy (1,4). Tolerance and dependency can develop to these drugs, so a course of treatment will usually only last a few weeks, however even during that period the dose may need to be increased to maintain therapeutic effect. Even so, doses used therapeutically are significantly less than those used by methamphetamine abusers, which range from 30 to 300 mg or more per dose, and can be used in sprees of several days or weeks, over which period several grams may be administered. Since they deal with low, single dose, oral administration, clinical studies are of limited value in assessing the effects of intravenously administered drug, high dose drug use, and extended runs or 'sprees' of drug use. They are useful however in helping to distinguish between therapeutic drug use and drug abuse.

Doses of methamphetamine in clinical studies generally do not exceed 60 mg, which would produce a blood methamphetamine concentration of no more than 0.2 mg/L (4,13–18). Hurst (6,7) reviewed laboratory studies using methamphetamine, and notes that many of these where small doses of methamphetamine are administered to subjects who then complete psychomotor performance testing, do show some enhancement of performance. The predominant benefit from the drug is in offsetting effects of fatigue. In non-fatigued subjects the benefits were very small. In a review of performance enhancement by the amphetamines (13), Laties and Weiss confirm that the amphetamines are most effective in restoring baseline performance in fatigued subjects. They note positive effects of amphetamines on monitoring and vigilance, motor coordination and control, and physical endurance and capacity, when the drug is administered at low therapeutic doses. Even at those doses however there is the potential for a negative effect on judgment, with many studies showing an increase in optimism and heightened self confidence. Hurst (14) examined the effects of amphetamine on risk taking, based on subjects willingness to risk real money on a game of chance, and found a willingness to take on increased risk following doses of 10–15 mg, corresponding to blood amphetamine concentrations of 0.05 mg/L. Other work by Hurst (15) examined the effects of amphetamine on judgment and decisions, and demonstrated both increased self-appraisal of performance without improving actual performance, and demonstrated greater risk-taking behavior associated with that enhanced self perception.

A recent study of methamphetamine in the treatment of narcolepsy (4) demonstrated improved performance by both narcoleptics and control subjects in some psychomotor tests including a driving task. There was no evidence to suggest however that this improvement in performance would be maintained at higher doses.

Interpreting Blood Methamphetamine Concentrations

As implied in the previous two sections, blood methamphetamine concentration is an important factor to consider, along with behavior, in determining whether a given case involves methamphetamine use or abuse, and consequently the degree and nature of any likely impairment. Blood drug levels can help distinguish those limited circumstances where methamphetamine may actually enhance performance, from those where it almost certainly causes deterioration in performance.

Baselt (3) notes a normal therapeutic concentration for methamphetamine of around 0.03 mg/L, and a volume of distribution of 3 to 7 L/Kg. Garriot (19) and Winek (20) quote a therapeutic range of around 0.01 to 0.05 mg/L. Mitler et al. (4) achieved blood methamphetamine concentrations in narcoleptics of 0.10 mg/L, and in controls of 0.02 mg/L, after doses of 60 and 10 mg, respectively. In an earlier study Änggard et al. (21) administered 160 to 200 mg of amphetamine sulphate to nonpsychotic amphetamine-dependent patients, and achieved blood amphetamine concentrations in the range 0.31 to 0.51 mg/L. Symptoms associated with low dose (10–25 mg) methamphetamine use include euphoria, wakefulness, and loss of appetite, together with less desirable side effects such as irritability, nervousness, insomnia, headache and motor restlessness (akathisia), increased libido, and increased, often compulsive, activity (4).

Higher doses (25–60 mg) can cause confusion, apprehension, volubility, hyperactive reflexes, excessive sweating, tremor, loquaciousness, fear, suspiciousness, awareness of being watched, hallucinations in the peripheral vision, paranoia and excitement (22,23). Baselt (3) indicates a toxic range beginning at 0.15 mg/L, associated with violent and irrational behavior after intravenous use, and notes fatalities at 1.5 mg/L from oral methamphetamine use and 0.8 mg/L following intravenous use. Logan et al. (24) have reported survival of a subject who swallowed a package of methamphetamine and attained a blood drug concentration of 9.5 mg/L.

In a review of 310 patients reporting to a treatment center with acute high dose methamphetamine toxicity (25), the most prominent complaints were acute anxiety (28%), amphetamine psychosis (18%), secondary illness (generally malnutrition) (12%), exhaustion syndrome (9%), and hepatitis (7%). Cellulitis, cubital abscess, nausea and vomiting, muscle pain, headache, dizziness, breathing difficulties and cardiac problems were also reported. Clearly the most prominent of these symptoms are central in nature, and would tend to have a negative effect on driving ability. Änggard et al. (21) evaluated 18 subjects with amphetamine psychosis and

found a marked incidence of lack of concentration, paranoid delusions, hallucinatory behavior, and disorganization of thoughts. The patients had amphetamine concentrations in the range 0.08 to 0.64 mg/L. Interestingly, there was no correlation between the actual blood amphetamine concentration and the extent of the symptoms described above.

Tolerance to the euphoric effects of methamphetamine are well known (26), but are difficult to quantify. The same tolerance does not appear to result in attenuation in suppression of fatigue. The use of higher doses to obtain positive effects on mood, may simultaneously trigger many of the negative effects on performance discussed above. For the same reasons, the withdrawal phase in a tolerant individual is likely to be more marked, and the symptoms more pronounced as discussed later.

Also reported in the literature is a condition know as "overamping," in which very high doses of methamphetamine are used, and there is a rapid increase in the blood methamphetamine concentration, generally after intravenous use (25,27,28). The effects are in marked contrast to the normal excitatory effects of the amphetamines. The user typically maintains consciousness, but is catatonic, unable or unwilling to speak or move. The condition occasionally manifests itself in unconsciousness lasting minutes to hours, and the user may be aphasic or paralyzed for hours or days.

Withdrawal or "Crash"

In a discussion of stimulant-induced impairment, Ellinwood and Nikaido (29) draw important distinctions between depressant and stimulant drug use. They propose a general form of a hysteresis plot of psychomotor performance with changing blood stimulant concentration. This predicts improvement in performance at low concentrations, with deteriorating performance at higher concentrations and during withdrawal. The authors do not however offer appropriate blood concentration ranges for these different phases of effect. They note the importance of considering duration of use in addition to dose, when assessing likely impairment. They also introduce the concept of withdrawal-induced impairment, with symptoms including hypersomnolence and fatigue. Abstinent symptomatology (25,28,30) resulting from abuse of stimulants includes exhaustion, depression, agitation, drug seeking behavior and, less frequently, suicidal or other self-destructive actions. These conditions are more likely to prevail after extended or spree use, after intravenous use, or after high dose use. The issue of withdrawal-induced impairment is an important consideration in assessing possible impact on driving, since these symptoms may be present even at low or negative blood methamphetamine concentrations. The net result is that although concentrations below 0.1 mg/L can be associated with performance enhancement as discussed earlier, this is almost certainly not the case during withdrawal, regardless of the blood drug concentration.

The severity of withdrawal symptoms depends on the length of the episode of use. Extended use or spree use can last for several days or even weeks, stopping only when the supply of drug is exhausted (26,27). During that period the user ingests the drug several times a day, may remain awake continuously for three to six days, becoming gradually more tense, tremulous and paranoid. The run or spree is followed by a "crash" during which the sleep debt accumulated during the run can result in bouts of profound sleep lasting for a day or two. Clearly, the symptoms of methamphetamine withdrawal are likely to have a negative impact on a subject's driving performance. The nature of withdrawal however means that these symptoms may be present when there is little or no detectable methamphetamine in the blood.

After considering the information summarized, the following project was undertaken to evaluate the circumstances surrounding a series of traffic accidents, arrests, and fatalities in which methamphetamine use by the driver was indicated.

Methods

Blood samples taken from drivers, living or deceased, were collected in 10 mL tubes containing an anticoagulant and antibacterial (Vacutainer, Becton Dickinson, NJ). The samples were extracted and tested by gas chromatography for the presence of weakly acidic/neutral drugs, and basic drugs using methods described in detail elsewhere (31,32). All drug identifications were confirmed by mass spectrometry. The limit of quantitation for this assay was 0.05 mg/L. The limit of detection was 0.01 mg/L. This method does not distinguish between d- and l-methamphetamine. Urine when available was tested for the above drugs and also for marijuana metabolites using an enzyme immunoassay (EMIT II, Syva, CA). Investigative reports from each of arrests or fatalities were reviewed, and the following information was tabulated: age, gender, blood methamphetamine level, blood amphetamine level, blood alcohol level, other drug or medication use, driving behavior which resulted in the arrest or fatality, driver culpability, and the subject's observed behavior after apprehension or when in custody. All the available information is summarized in Table 1.

Results and Discussion

The cases in Table 1 are arranged in order of increasing blood methamphetamine concentration. Of 178 cases tested for drugs, methamphetamine was detected in 29 cases, cocaine or its metabolites in 22, diazepam in 21, meprobamate in 17, morphine in 14, PCP in 1. Other drugs detected included propoxyphene, fluoxetine, and cyclobenzaprine. Blood was not tested for marijuana metabolites. No methylenedioxy-substituted amphetamines were identified, and in no case was amphetamine found in the absence of methamphetamine.

The methamphetamine concentrations ranged from the limit of detection, 0.01 mg/L, up to 9.46 mg/L. The two cases with the highest concentration are believed to have resulted from the subject's ingestion of methamphetamine in an effort to destroy potentially incriminating evidence. Of the remaining cases, the average blood methamphetamine concentration was 0.55 mg/L. In those cases where amphetamine was also detected, the concentration ranged from 5 to 38% of the methamphetamine concentration. Several cases displayed high methamphetamine concentrations with amphetamine levels below the limit of quantitation. Cook et al. (5) examined the pharmacokinetics of orally administered methamphetamine, and found peak methamphetamine concentrations occurring at 4–5 hours post ingestion, prior to which time the amphetamine concentrations were less than 5% of the corresponding methamphetamine concentration. When methamphetamine was administered either by smoking or intravenous injection (33), the ratio of amphetamine to methamphetamine in the blood was even lower, and did not approach 5% until after ten hours following administration. These findings suggest that high methamphetamine levels with low amphetamine levels most likely result either from an episode of intravenous drug use within the previous ten hours, or oral administration within the previous five hours. On the other hand, elevated amphetamine to methamphetamine ratios do not exclude recent drug use, since the ratio could be

TABLE 1—*Case information on drivers testing positive for methamphetamine use.*

Subject #	Age	Sex	Meth. (mg/L)	Amp. (mg/L)	Alcohol (g/100 mL)	Other drug use	Circumstances resulting in testing	Drivers observed behavior
1	18	f	<0.05	<0.05	neg	—*	Erratic driving starting stopping no turn signals	White powder in nose dilated pupils no nystagmus methamphetamine in vehicle violent combatative admit to drug use
2	35	f	0.05	—¶	0.03	—*	Accident multivehicle causing driver pulled out into oncoming traffic	Slight odor of alcohol
3	39	m	0.05	<0.05	0.06	marijuana	Accident multivehicle causing driver pulled out into oncoming traffic	Watery bloodshot eyes disoriented methamphetamine in possession uncooperative
4	22	m	0.1	<0.05	0.02	—*	Accident single vehicle causing driver high speed drifted off roadway	Admits to methamphetamine use watery bloodshot eyes shaking uncontrollably nervous
5	30	f	0.1	—¶	neg	—*	Accident multivehicle causing driver pulled out into oncoming traffic	No information available
6	30	f	0.17	—¶	neg	—*	Accident single vehicle causing driver drifted off road	IV paraphenalia rapid speech hysterical
7	38	m	0.22	—¶	neg	marijuana	Weaving crossed center line	Falling asleep bloodshot eyes
8	33	m	0.22	<0.05	neg	—*	Equipment stop headlight out	Dilated pupils rapid speech repetative speech white powder in nose admit to drug use cooperative finger tapping
9	24	m	0.25	<0.05	neg	cocaine	Accident single vehicle causing driver vehicle drifted off road	Dilated pupils cooperative admitted a 3 day spree hungry methamphetamine in vehicle
10	32	m	0.35	<0.05	neg	marijuana	Speeding	Dilated pupils nervous agitated slurred speech watery bloodshot eyes methamphetamine in vehicle
11	27	f	0.36	—¶	neg	marijuana pemoline	Erratic speed poor cornering weaving	Agitated bloodshot eyes nervous rapid speech methamphetamine in purse light sensitive poor coordination
12	32	f	0.38	0.14	neg	marijuana	Accident causing driver multivehicle rear ended braking vehicle	Slurred speech methamphetamine in vehicle no braking red face swearing/screaming uncooperative drug paraphenalia
13	?	m	0.4	—¶	neg	cocaine	Accident single vehicle causing driver	Driver deceased IV paraphenalia on body
14	24	f	0.47	<0.05	neg	marijuana	Failed to stop at stop sign	Disorientated confused speech agitated and restless pupils dilated

TABLE 1—*Continued*

Subject #	Age	Sex	Meth. (mg/L)	Amp. (mg/L)	Alcohol (g/100 mL)	Other drug use	Circumstances resulting in testing	Drivers observed behavior
15	26	m	0.55	<0.05	neg	—*	Accident single vehicle causing driver drifted off roadway	Needle tracks (unconscious)
16	27	f	0.57	0.14	neg	—*	Accident single vehicle eluding police rammed by police	Admits IV methamphetamine use nervous anxious very talkative rapid speech rapid pulse syringes repetative
17	24	m	0.57	0.15	neg	—*	Erratic driving missing license plate	Very talkative rapid speech rapid pulse syringes
18	28	m	0.58	—¶	neg	—*	Speeding weaving	Slurred speech methamphetamine in vehicle unsteady twitching short attention span red eyes IV paraphenalia spasm/jerking
19	26	f	0.7	<0.05	neg	—*	Accident single vehicle causing driver veered off road into tree	IV paraphenalia uncooperative trance-like state
20	18	m	0.77	<0.05	neg	—*	Accident multivehicle causing driver	Dazed admits to drug use snorting paraphernalia
21	22	m	0.8	0.3	neg	cocaine marijuana	Accident multivehicle causing driver crossed center line	Deceased methamphetamine in vehicle using for 2 days straight
22	41	m	0.81	0.05	neg	diazepam ibuprofen	Accident multiple vehicle causing driver high speed collided while attempting to pass	Dilated pupils rapid speech admission to drug use
23	30	m	0.088	<0.05	0.16	—*	passed out (physical control)	Unconscious white powder in nostrils methamphetamine in wallet confused incoherent
24	20	m	1.14	0.23	neg	—*	Accident single vehicle causing driver speeding failed to stop at stop sign	Violent argumentative incoherent paranoid
25	41	m	1.35	0.14	neg	—*	Accident single vehicle causing driver tractor trailer driver drifted off road	Deceased
26	30	m	1.88	0.14	neg	morphine	Accident multiple vehicle causing driver crossed center line	Unconscious admits to heroin use admits to methamphetamine use methamphetamine in vehicle
27	35	m	2.58	0.35	neg	—*	Accident§ single vehicle causing driver	Mood swings irrational delusional agitated violent uncooperative warm

TABLE 1—*Continued*

Subject #	Age	Sex	Meth. (mg/L)	Amp. (mg/L)	Alcohol (g/100 mL)	Other drug use	Circumstances resulting in testing	Drivers observed behavior
28	20	m	9.46	0.05	neg	—*	Tail light violation§	Panic agitated violent dilated pupils swallowed methamphetamine seizure

*No other drug use detected or admitted to.
§At least some of the drug was ingested after stop or accident.
¶No amphetamine detected.

falsely elevated from residual amphetamine from prior episodes of use.

Of the 28 cases evaluated, nine (32%) involved females and 19 (68%) involved males. The average age was 29. Twenty three cases (82%) had blood methamphetamine levels above 0.10 mg/L, the level normally considered to be the upper limit for therapeutic use, and beyond the range for which improvements in some performance measures have been demonstrated. Seventeen drivers (61%) were tested as a result of being involved in an accident, and the driver was the causing driver in all but one of these cases (in that case the driver was fleeing police and was rammed by a police car). Of those drivers involved in accidents, the accident frequently resulted from the driver allowing the vehicle to drift out of the lane of travel on to the shoulder, into fixed objects, or into oncoming traffic. This apparent lack of attention is not normally associated with stimulant use *per se,* and may be indicative of withdrawal-induced impairment as discussed later. Other accidents resulted from an apparent error of judgment by the driver, inappropriately attempting to enter traffic flow, failing to stop at stop signs, high speed collisions, generally erratic driving, weaving, and speeding (Table 2).

In a large scale detailed study of drug use by fatally injured truck drivers the National Transportation Safety Board (NTSB) (34) described 12 cases involving methamphetamine. Five of these involved drivers drifting off the road, two involved drivers using methamphetamine rear ending other vehicles, and three involved methamphetamine-related fatigue. This pattern of accident causation is very similar to that found in the cases discussed in this study.

Driving is a divided attention task, requiring fine motor skills, intelligent decision making, and rapid and appropriate responses to stimuli. The driver must simultaneously steer, brake, accelerate, operate turn signals, observe and anticipate the behavior of other road users, accurately judge time and distance, and observe and obey traffic signals and road signs. Impairment of any of these operations by drugs having an effect on the central nervous system, will have a negative effect on overall driving performance.

Behavioral manifestations of methamphetamine use observed in arrestees were typical and distinctive. They included rapid or confused speech, dilated pupils, agitation, paranoia, rapid pulse, and violent or aggressive demeanor. Sweating, and high temperature were also noted, as were watery-bloodshot eyes. Since amphetamines are not believed to irritate the eyes themselves, this may be related to fatigue. The degree of the effects present generally increased with the blood methamphetamine concentration, with violent behavior being noticably more common at higher blood methamphetamine concentrations. Methamphetamine and other drug paraphernalia were commonly found in the possession of the arrestee, and in two occassions there was drug residue reported on the subject's nose or face. Even at low concentrations, subjects had fixed and dilated pupils, which would make them more sensitive to glare in bright sunlight or from headlights of oncoming vehicles at night. Other side effects cited above, nervousness, insomnia, headache, tremor, and motor restlessness could also contribute to impairment even at therapeutic doses. The Physicians Desk Reference (1) notes that patients prescribed methamphetamine clinically, should be cautioned about its effect on driving or operating heavy machinery.

TABLE 2—*Typical driving behaviors in 28 methamphetamine: positive drivers.*

Leaving lane of travel	13
Pulled out into oncoming traffic	4
Speeding	7
Failed to stop at stop sign	2
General erratic driving	5
Rear ended another vehicle	1

Many of the cases associated with lower blood methamphetamine concentrations (<0.10 mg/L) also involved alcohol (Table 1), which most likely contributed to impairment. There is some evidence that synergistic effects can amplify the impairment from methamphetamine or alcohol when both are present together (35). Attempts to evaluate the combined effects of alcohol and amphetamines however suggest that the interaction is complex (16–18,35). Some workers have found an apparent abatement of alcohol induced narcotic effects, while in other cases, the opposite is true. Any other factors however, including fatigue and other symptoms of 'crash' or withdrawal would likely result in performance decrement, and would be manifested as 'nodding off,' or a lack of attention to driving conditions and other road users. Drivers falling asleep at the wheel are known to be significant contributors to traffic accidents (36,37). The fatigue and sleep-pattern disruption caused by methamphetamine use would thus be expected to increase the risk of an accident in drug users. As a further confounding factor, general impairment from the drug may affect the drivers ability to recognize the extent of his or her fatigue (36). Alcohol or other central nervous system depressant consumption during withdrawal would further exacerbate impairment.

Seven of the 28 cases considered here had positive results for urinary cannabinoids, suggesting marijuana use within the previous hours or days. Due to its prolonged excretion time however, the presence of marijuana metabolites in the urine does not necessarily imply that the subject is under the influence the drug. Effects from combined methamphetamine and marijuana use have not been studied. Marijuana and other antidepressants can be used during

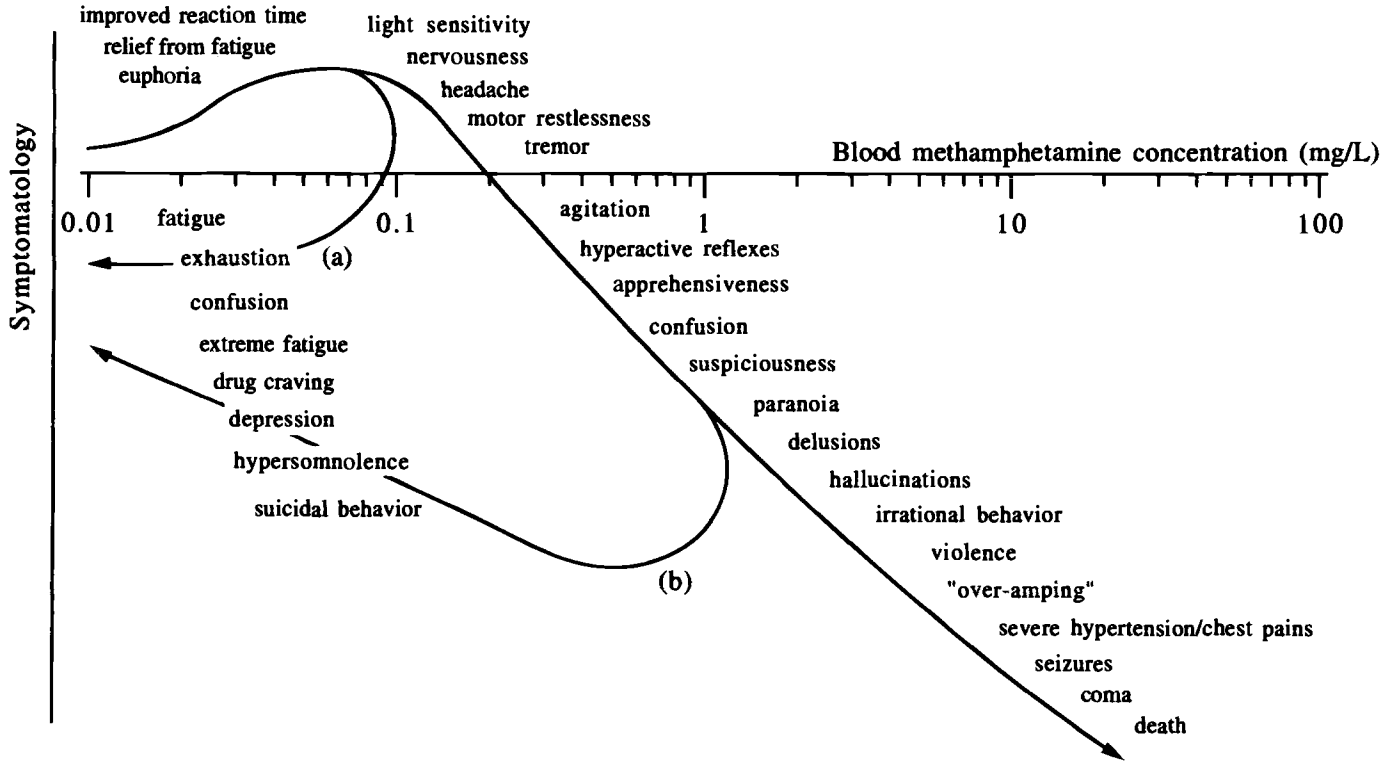

FIG. 1—*Hysteresis plot showing effects of methamphetamine that impact driving performance with respect to blood methamphetamine concentration (mg/L). The figure shows examples of withdrawal effects from* (a) *low dose and* (b) *high dose drug use.*

withdrawal to counteract the psychological effects of the crash. As with alcohol, combined stimulant and depressant use is unlikely to lead to a complete neutralization of psychomotor effects of either, and is likely to exacerbate fatigue-related impairment.

Toxic effects from methamphetamine use can begin at concentrations greater than 0.1 mg/L, and are typically well established at levels of 0.2 mg/L, although their intensity may depend on the degree of tolerance developed by the user (11,22,23). Effects include paranoia, confusion, restlessness, irritability, hyperactive reflexes and tremor, pounding in the ears, and elevated pulse and blood pressure. Severe intoxication can manifest as, delusion, delirium, panic, and mania, with high temperature, flushing and profuse sweating (18,20). Life threatening effects include violence to self or others, hallucinations, tachycardia, hypertension, severe chest pain and circulatory collapse, occasionally followed by seizure and death (17,18,20). Psychoses are possible at any level but are more commonly associated with higher blood methamphetamine concentrations, and with intravenous use. Clearly a person suffering with even minor elements from this constellation of symptoms will not be performing at a normal level, and would therefore be at increased risk for accident involvement.

Withdrawal-induced impairment is a significant issue (24,25). Withdrawal, 'crash,' or abstinence syndrome following extended methamphetamine use can manifest as severe depression, extreme fatigue, lethargy, hypersomnolence, disturbed sleep, gastrointestinal pain, an intense craving for the drug, and drug-seeking behavior. Self-destructive acts are often committed during this period. The symptoms can last for up to several days, and again are clearly not consistent with safe driving. The accumulated sleep debt from an extended use of methamphetamine, appears to be the likely cause of the accident in many of the cases summarized in Table 1, where the driver drifted out of the lane of travel onto a shoulder or into oncoming traffic. Similar patterns have been reported elsewhere (34).

Figure 1 is a hysteresis plot for impairment from methamphetamine drawn after a general form proposed by Ellinwood and Nikaido (24). The concentration ranges and effects are based on the laboratory studies, clinical reports, and case reports in the literature cited in the introduction, and on the cases discussed here. As with any drug, the concentrations required to produce these effects are not absolute, but will vary somewhat between individuals based on patterns of use, tolerance, fatigue, other drug or alcohol use and any underlying psychoses. Two examples of the withdrawal phase are included in Fig. 1 to illustrate the difference in severity of withdrawal from methamphetamine at higher and lower doses.

The net conclusion of the material reviewed in this study was that the circumstances under which any methamphetamine induced performance increment is possible are extremely narrow, and is not guaranteed because of typical side effects associated even with low dose use. Furthermore, there is ample evidence from the epidemiological, clinical, case report and toxicological data to conclude that the behavior displayed in the cases we reviewed is consistent with impairment as a result of methamphetamine use, drug withdrawal, or combined use of methamphetamine and other drugs.

References

(1) Physicians desk reference. 49th edition 1995. Medical Economics Data, Montvale NJ.

(2) Ando H, Shimizu H, Takahashi Y, Fukumoto M, Okonogi H, Kadokura M. A basic study for estimating the level of exposure to a nasal inhalant containing a stimulant. Japan J Hygiene 1993; 48(3):692–97.

(3) Baselt RC, Cravey RH. Disposition of toxic drugs and chemicals in man. Fourth edn. 1995 Chemical Toxicology Institute, Foster City, CA.
(4) Mitler M, Hajdukovic R, Erman MK. Treatment of narcolepsy with methamphetamine. Sleep 1993;16(4):306–17.
(5) Cook CE, Jeffcoat AR, Sadler BM, Hill JM, Voyksner RD, Pugh DE, White WR, Perez-Reyes M. Pharmacokinetics of oral methamphetamine and effects of repeated daily dosing in humans. Drug Met Disp 1992;20:856–62.
(6) Hurst PM. Amphetamines and driving behavior. Accid Anal Prev 1976;8:9–13.
(7) Hurst PM. Amphetamines and driving. Alcohol drugs and driving 1987;3(1):13–16.
(8) Lund AK, Preusser DF, Blomberg RD, Williams AF. Drug use by tractor trailer drivers. J Forensic Sci 1988;33(3):648–61.
(9) Crouch DJ, Birky MM, Gust SW, Rollins DE, Walsh JM, Moulden JV, Quinlan KE, Beckel RW. The prevalence of drugs and alcohol in fatally injured track drivers. J Forensic Sci 1993;38(6):1342–53.
(10) Kirby JM, Kimball IM, Fain W. Comparability of alcohol and drug use in injured drivers. Southern Med J 1992;85(8):800–02.
(11) Robb J, Wohlenberg N, Jasperson M, Lindsey T, Backer R. DUID in New Mexico: Distribution of drug types and BAC. The DRE 1992;4:11–13.
(12) Logan BK, Schwilke ES. Drug use in fatally injured drivers in Washington State. J Forensic Sci, 1996.
(13) Laties VG, Weiss B. Performance enhancement by the amphetamines: A new appraisal. Neuropsychopharmacology. Proceedings of the fifth international congress of the Collegiium Internationale Neuro-psycho-pharmacologicum. Washington DC March 1966. Editor H. Brill. International Congress Series no 129. Exerpta Medical Foundation, New York 1967.
(14) Hurst PM. The effects of d-amphetamine on risk taking. Psychopharmacologia 1962;3:283–90.
(15) Hurst PM, Weidner MF, Radlow R. The effects of amphetamines upon judgement and decisions. Psychopharmacologia 1967;11: 397–404.
(16) Wilson L, Taylor JD, Nash CW, Cameron DF. The combined effects of alcohol and amphetamine sulphate on performance of human subjects. Can Med Association J 1966;94:478–84.
(17) Rosenfeld G. Potentiation of the narcotic action and acute toxicity of alcohol by primary aromatic monoamines. Q J Studies Alcohol 1960;21:584–96.
(18) Newman HW, Newman EJ. Failure of dexedrine and caffeine as practical antagonists of the depressant effect of ethyl alcohol in man. Q J Studies Alcohol 1956;17:406–10.
(19) Garriott JC. Interpretive toxicology. Clin Lab Med 1983;3(2): 367–84.
(20) Winek C. Drug and chemical blood level data 1994. Allegheny County Department of Laboratories, Pittsburgh PA, 1994.
(21) Änggard E, Gunne LM, Jönsson LE, Niklasson F. Pharmacokinetic and clinical studies on amphetamine dependent subjects. Euro J Clin Pharmacol 1970;3:3–11.
(22) Toxicology. The basic science of poisons. Casarett LJ, Doull J (eds.) first edition, 1975. Macmillan New York, NY.
(23) Drugs and drug abuse, a reference text. Second edition, Jacobs MR, Fehr KO (eds). Addiction Research Foundation, Toronto, 1987.
(24) Logan BK, Weiss EL, Harruff RC. Case report: tissue distribution of methamphetamine following a massive fatal ingestion. J Forensic Sci, March, 1996.
(25) Smith DE, Fischer CM. An analysis of 310 cases of acute high dose methamphetamine toxicity in Haight-Ashbury. Clin Toxicol 1970;3(1):117–24.
(26) Smith DE. The characteristics of dependence in high-dose methamphetamine abuse. Int J Addictions 1969;4(3):453–59.
(27) Caldwell J, Sever PS. The biochemical pharmacology of abused drugs I. Amphetamines, cocaine and LSD. Clin Pharm Ther 1974;16(4):625–38.
(28) Kramer JC. Introduction to amphetamine abuse. J Psychedelic drugs 1969;2:1–16.
(29) Elinwood EH, Nikaido AM. Stimulant induced impairment: a perspective across dose and duration of use. Alcohol Drugs and Driving 1987;3(1):19–24.
(30) Gawin FH, Kleber HD. Abstinence symptomatology and psychiatric diagnosis in cocaine abusers. Clinical observations. Arch Gen Psychiatr 1986;43:107–13.
(31) Logan BK, Friel PN, Case GA. Analysis of sertraline (zoloft®) and its major metabolite in postmortem specimens by gas and liquid chromatography. J Anal Tox 1994;18:139–42.
(32) Logan BK, Friel PN, Peterson KL, Predmore DB. Analysis of ketorolac in post mortem blood. J Anal Tox 1995;19(2):61–64.
(33) Cook CE, Jeffcoat AR, Hill JM, Pugh DE, Patetta PK, Sadler BM, White WR, Perez-Reyes M. Pharmacokinetics of methamphetamine self administered by smoking s-(+)-methamphetamine hydrochloride. Drug Met Disp 1993;21:717–23.
(34) National Transportation Safety Board safety study: Fatigue, alcohol, other drugs, and medical factors in fatal-to-the-driver heavy truck crashes (vol I and II). Accession# PB90-917002, report# NTSB/SS-90/01/02, National Transportation Safety Board, Washington DC, 1990.
(35) Yamamura T, Hisida S, Hatake K. Alcohol addiction of methamphetamine abusers in Japan. J Forensic Sci 1991;36(3):754–64.
(36) Summala H, Mikkola T. Fatal accidents among car and truck drivers: effects of fatigue, age, and alcohol consumption. Hum Factors 1994;36(2):315–26.
(37) Brown ID. Driver fatigue. Hum Factors 1994;36(2):298–314.

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