Drug-Impaired Driving

Introduction

Every year more than a million people in the world are killed in traffic crashes and many millions more are injured. Beside the heavy and tragic burden on those directly affected, there is an enormous economic impact, costing countries between 1 and 4% of their gross national product. Driving is a very complex task, requiring the cooperation of several different cognitive and psychomotor functions at once. Crashes can be the consequence of many different factors, which can be classified into three categories: the road, the vehicle, and the driver. A crash is rarely attributable to only one factor, indicating that it is very difficult to precisely determine in what percentage of crashes alcohol or drugs have contributed.

Influence of Drugs on Performance

The effects of drugs on performance can be studied by means of experimental studies, in which different doses of a certain drug are administered to volunteers, and the effects on performance are measured and compared to a placebo or a positive control. The performance of the volunteers can be evaluated by means of tests that assess the different psychomotor and cognitive functions, by means of tests in a driving simulator, or by "real" driving tests [1–3].

Alcohol

Alcohol is a central nervous system depressant. Many studies have already been performed to determine the effects of acute alcohol ingestion on cognitive functions and driving performance. These studies found that numerous driving-related skills are degraded beginning at low blood alcohol concentrations (BACs). Several skills have been shown to decrease with increasing BAC, such as prolongation of reaction time performances and lowering of coordination performance [4, 5]. (For further information *see also* **Alcohol**.)

Cannabis

A cannabis user feels euphoria, relaxation, and increased social interaction with frequent laughing and experiences changes in perception (visual, audible, sensory, or time perception). The users are aware of the effects of the drug, and this awareness increases with higher doses. Cannabis acutely reduces some cognitive and psychomotor skills such as learning, equilibrium, coordination, tracking ability, memory, perception, motor impulsivity, and vigilance, and these effects are mostly dose dependent [6, 7].

Cannabis can also have an effect on behavior. The influence of cannabis on human risk taking is unclear. The results of experiments in laboratory settings are contradictory, while in some driving studies (with rather low doses) users are aware of the impairment and often compensate their driving style by driving more slowly, overtaking less, or keeping longer distances from other vehicles. Nevertheless the driver is still unable to completely compensate for the loss of capability in some psychomotor skills [8].

Some deleterious effects of cannabis appear to be additive or even synergistic with those of alcohol, and the combination of both substances results in a prolongation as well as enhancement of their effects. Driving studies revealed that drivers under the influence of both alcohol and cannabis were less attentive to traffic approaching from side streets, while the use of either cannabis or alcohol (at low doses) had no effect [9], and that the combination of cannabis and alcohol generated an additional decrement in control of lateral deviation on top of the decrement caused by either cannabis or alcohol [10]. The detrimental effects of other drugs such as cocaine can also be reinforced by additional intake of cannabis [11]. (For further information *see also* **Cannabis**.)

Amphetamines

Amphetamine causes a strong central stimulation and euphoria. The user thinks he can do everything and will take more risks. In addition, amphetamine widens the pupils (mydriasis) and reduces sleepiness leading to insomnia, but after some time (hours or days depending on the pattern of use), the subject is exhausted and falls asleep (crash phase). Amphetamine can improve some cognitive functions such as divided attention performance and verbal

interaction [12]. However, tests in driving simulators reveal that the intake of amphetamine causes a decrease in overall simulated driving by inducing problems such as incorrect signaling, failing to stop at a red traffic light, and slowing reaction times. The decrease in simulated driving ability is only observed during daytime, which is consistent with the tunnel vision associated with amphetamine consumption [12, 13]. It is also important to note that the doses of amphetamine administered in these experimental studies were very low (10–30 mg) and thus not representative of the doses that are generally taken by abusers (100–1000 mg/day) [1].

Studies investigating the effect of amphetamine in sleep-deprived persons revealed a positive effect on psychomotor functions [14, 15]. The effects of amphetamine on cognitive functions in sleep-deprived persons are less obvious. Both positive and negative effects as well as no effects have been assessed [12, 14].

Methamphetamine like amphetamine is a central nervous system stimulant that may cause restlessness, euphoria, dizziness, dysphoria, tremor, and insomnia.

Ecstasy (methylenedioxymeth(yl)amphetamine, MDMA, XTC) is a "designer" amphetamine, indicating that it is synthesized to resemble the effects of amphetamine. It causes a weaker stimulation of the central nervous system than amphetamine, but it can also cause sensory disturbances, nausea, dizziness, ataxia, muscular rigidity, sweating, restlessness, and tremor.

Ecstasy acutely causes decreases in attention, short- and long-term memory, verbal memory, visuospatial skills, executive functioning, and prediction of object movement under divided attention [16–18]. It also leads to improved psychomotor performance on a battery of tests, such as movement speed and tracking performance in a single, as well as in a divided attention task [16]. Tests in driving simulators however revealed that the intake of ecstasy can decrease performance by increasing speed and speed variation, and inducing problems in car following, while some tasks are not influenced (reaction time, lateral control), and may even be improved (e.g., lateral control) [17, 19].

Other psychoactive substances such as alcohol can reinforce the deleterious effects of ecstasy, and cause some additional negative effects [20]. On the other hand, the use of ecstasy can diminish some, but not all detrimental effects of alcohol, while other negative effects of alcohol can be reinforced [17].

During the crash phase following the use of amphetamines, the subject feels very tired, unable to combat sleep and depressed. This phase can last for several days [21]. (For further information *see also* **Amphetamine**.)

Cocaine

Cocaine is extensively metabolized to a variety of compounds. The major metabolites are benzoylecgonine, ecgonine, and ecgonine methyl ester and they are often targeted in analyses.

The desired effects of cocaine are similar to those of the amphetamines, but the onset is slower and the duration is longer. The use of cocaine can partially reverse performance decrements in sleep-deprived persons [22]. In rested persons, some studies found no effect of the use of cocaine on psychomotor or cognitive skills [23], while other studies assessed an improvement in psychomotor performance (decreased reaction time), attention, and learning [24].

Cocaine can partially diminish performance decrements caused by alcohol consumption. The use of a combination of alcohol and cocaine decreases psychomotor impairment and improves performance on cognitive tests when compared to the use of alcohol alone. Cocaine also decreases the subjective feeling of drunkenness caused by alcohol [11, 25]. Detrimental effects of other drugs such as cannabis can be reinforced by cocaine [11].

A depressive phase follows the use of cocaine, with the subject feeling very tired, depressed, nervous, and unable to combat sleep [1]. (For further information *see also* **Cocaine**.)

Heroin

The user generally feels intense euphoria ("rush") accompanied by a warm flushing of the skin, dry mouth, and heavy extremities, and alternates between a wakeful and drowsy state. Few experimental studies have investigated the acute effects of heroin in humans. Several studies confirmed the acute effect of heroin on subjective sedation and miosis [26, 27]. One study found a trend toward a decreased performance on the circular lights task, which measures psychomotor performance [28]. In another study the

administration of heroin impaired performance on a reaction time task [26]. However the doses used in these experimental studies ranged from 2 to 20 mg, while average daily doses in a chronic, tolerant user range from 300 to 500 mg of heroin [1]. (For further information *see also* **Opioids**.)

Epidemiology and Risks

Prevalence of Drugs in the General Driving Population or in a Subset of Drivers

The prevalence of drugs in the general driving population can be estimated by means of roadside surveys, in which samples of randomly stopped drivers are analyzed. Results of roadside surveys have shown that about 1–2% of drivers stopped during roadside surveys tests positive for drugs in saliva. Higher prevalence rates were found in studies using urine as sample (6–12%) or in studies where samples were only collected during weekend nights (6–15%) [29].

In some studies, samples of a subset of drivers are analyzed. Such studies have shown that drugs are prevalent in 19–50% of drivers injured by a traffic crash, 6–35% of drivers killed by a traffic crash and 55–99% of drivers suspected of driving under the influence of drugs (DUID) [29]. These figures can vary strongly, because the methodology used in the different studies can differ in many aspects. For example, some studies used blood as biological matrix, while others used urine or saliva. As these matrices have different detection times, this can have an influence on the results [30]. Furthermore, the methodology of the studies can differ in the type of drugs included in the analysis and the kind (and sensitivity) of analysis method used.

The most prevalent drug in most of these studies is cannabis. Other important drugs are amphetamines, benzodiazepines, and opiates.

Besides analyzing biological samples of drivers, the prevalence of DUID can also be assessed by interviewing persons. A disadvantage of this method is the possibility of underestimation of the prevalence. Such interviews have shown that about 3.6% of the general population, 15% of the young people, and 85% of drug users state ever to have driven after having used drugs [29]. In the United States in 2005, an estimated 10.5 million persons aged 12 or older reported driving under the influence of an illicit drug during the past year [31].

Risks Associated with DUID

By comparing the prevalence of a certain drug in the general driving population to the prevalence in drivers who were involved in a traffic accident, some studies tried to estimate the accident risk. Several studies have already shown that an increasing BAC is associated with increasing accident risks [32, 33]. Other studies have calculated the accident risks associated with other psychoactive substances. The impaired motorists, methods of roadside testing and assessment for licensing (IMMORTAL) study in the Netherlands revealed that drivers under the influence of benzodiazepines alone have a relative risk for an accident that is three times greater than the risk of a drug-free driver. The highest risk was associated with the use of drugs in combination with alcohol ($\geq$0.8 g l^{-1}), namely a 179 times higher risk [34]! A study that was performed in Canada, for example, showed that the crash risk associated with driving under the influence of cocaine, benzodiazepines, and cannabis is respectively 5, 2.5, and 2.2 times higher than that of a person who has not consumed these drugs [33].

Some studies have made a more thorough analysis than calculating the risk of being involved in a traffic crash, and have estimated the risk of being responsible for a traffic crash while DUID. The results of these types of studies indicate that increasing BACs are associated with increasing risks of being responsible for an accident [35]. They also show that driving under the influence of cannabis increases the risk of being responsible for a crash. The risk of being responsible for an accident even increases with increasing cannabis concentration in the blood, indicating a causal relationship between cannabis and crashes. The risk of being responsible for a fatal accident when driving under the influence of cannabis and alcohol is approximately equal to the multiplication of the risks when driving under the influence of cannabis or alcohol alone [35]. Responsibility analyses have also shown that benzodiazepines and cocaine are associated with increased risks of being responsible for an accident, and that the risk is higher for a combination of alcohol and benzodiazepines than for benzodiazepines alone [36, 37].

Legislation

Each developed country has its specific legislation to deal with DUID. There is a lack of uniformity in the way in which nations approach the drugged driving problem. Generally there exist two major types of DUID legislation, namely "impairment" legislation and "*per se*" legislation [38].

Impairment Legislation

In impairment legislation, the prosecution must demonstrate that the driver was impaired, not fit to drive or "under the influence" depending on how the law is interpreted. The analysis of drugs in body fluids only provides corroborating evidence as to the cause of the impairment. This kind of legislation is subjective and requires the assessment by a medical doctor or a specially trained police officer. As a consequence many of the countries with this kind of legislation experience difficulties in obtaining convictions. Examples of countries with "impairment" legislation are Norway and the United Kingdom.

"Per se" Legislation

A "*per se*" law prohibits driving if drugs are present in blood, serum, plasma, or oral fluid above a certain threshold. Since the prosecution does not have to prove that the driver was impaired, this kind of legislation facilitates the enforcement process. The threshold concentrations, or cut-offs, used are analytical detection limits, meaning that any detectable concentration of a drug constitutes an offense. Therefore these laws are sometimes called *zero-tolerance* laws. Presently, Germany, Belgium, Sweden, France, Finland, Luxembourg, Switzerland, Denmark, a number of Australian states, and 14 states of the United States have introduced "*per se*" legislation in addition to the "impairment" legislation. The analytical cutoffs of Germany, Belgium, France, Sweden, and Switzerland are given in Table 1.

There is no consensus on the analytical cutoffs between the different countries. This lack of consensus can be partially attributed to the use of different biological matrices (serum in Germany, plasma in Belgium, and whole blood in Australia, France, Sweden, and Switzerland) and the different consequences of a positive result: for example, in Belgium there is a penal sanction that follows a positive result, while in Germany there is an administrative sanction. The effectiveness of "*per se*" legislation in increasing the number of prosecutions has already been demonstrated in some countries. For example, in Finland there was a slow increase in the number of samples that were investigated until 2002. However since the introduction of "*per se*" legislation in 2003 there was a cumulative monthly increase in the number of samples (Figure 1) [39].

In Sweden, immediately after the zero-limit law came into force, the number of cases of DUID submitted by the police for toxicological analysis

Table 1 Analytical cutoff limits in blood, plasma, or serum as agreed upon or proposed in different countries (all concentrations in ng ml^{-1}, except Sweden where it is in ng g^{-1})

	Germany[a]	Belgium	France	Sweden	Switzerland
Sample type	Serum	Plasma	Blood	Blood	Blood
Amphetamine	50	50	50	30	15[b]
MDMA	50	50	–	20	15
MDEA	50	50	–	20	15
MDA	–	–	–	20	–
MBDB	–	50	–	20	–
Cocaine	–	50	50	20	15
Benzoylecgonine	150	50	50	20	–
Morphine (free)	20	20	20	5	15
THC	1	2	1	0.3	1.5

MDMA, 3, 4-methylenedioxy-*N*-methylamphetamine; MDEA, 3, 4-methylenedioxy-*N*-ethylamphetamine; MDA, 3, 4-methylenedioxyamphetamine; MBDB, 3, 4-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine; THC, Δ9-tetrahydrocannabinol

[a] Lower cutoffs have been proposed, but they are not yet used everywhere

[b] For Switzerland also the cutoff is 15 ng ml^{-1} for methamphetamine; for all analytes, an error margin of 30% is added to the cutoff

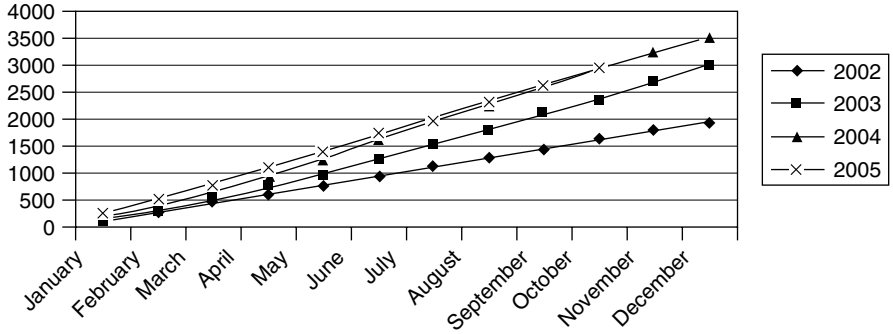

Figure 1 The cumulative monthly increase in the number of samples after introducing the zero-tolerance law in 2003 in Finland [Reproduced with permission from Ref. 39. © P. Lillsunde, 2005.]

increased sharply and was 10 times higher in 2005 than before the new legislation. Nevertheless it was found that Sweden's zero-concentration limit has done nothing to reduce DUID or deter the typical offender because recidivism is high in this population of individuals (40–50%). Many traffic delinquents in Sweden are criminal elements in society with previous convictions for drunk and/or drugged driving as well as other offenses. The spectrum of drugs identified in blood samples from DUID suspects has not changed much since the zero-limit law was introduced [40].

Detection of Drugs in Drivers

Roadside Detection

Since many years, police officers involved in road safety have expressed the need for a rapid and reliable roadside screening test for drugs, similar to an alcohol breathalyzer. This would help them to determine which drivers have to provide a blood sample, or to take immediate administrative measures like confiscating the driver's license or impounding the vehicle. As illegal drugs are not released in measurable amounts in the breath, roadside drug testing must be based on other specimens (*see* **Oral Fluid Toxicology**).

Roadside detection tests are mostly immunoassays, which are read visually or by a small electronic reader. At first, urine was used for roadside drug testing because of the high drug concentrations. Unfortunately for some substances such as cannabis, the metabolites can be detected for a long time after chronic use. Consequently, the presence of drugs in urine does not necessarily indicate impairment. Another disadvantage of urine is the necessity of sufficient privacy during the sample collection. Nevertheless, roadside urine screening in Belgium significantly decreases the number of unnecessary confirmatory blood analyses for DUID [41]. An example of an on-site urine test for drugs is given in Figure 2.

In recent years, the interest in the use of oral fluid as biological matrix has increased significantly, as this matrix displays some particularly interesting properties. First of all, oral fluid can be obtained easily by nonmedical personnel in a relatively noninvasive and observable way. There is also some correlation with impairment. The results of the European project roadside testing assessment (ROSITA) indicated that for most drugs of abuse the correlation with blood is better for oral fluid than for urine. Nevertheless, the results of ROSITA and the follow-up project ROSITA 2 indicated that none of the currently available on-site oral fluid drug testing devices is reliable enough to be recommended for roadside screening for drivers [42]. However, the experience in the state of Victoria in Australia shows that random roadside oral fluid testing of drivers for methamphetamine, ecstasy, and cannabis has a deterrent effect: the level of awareness of drivers of random oral fluid testing increased from 78 to 92%, 33% of illicit drug users stated that the drug tests had influenced them (primarily to avoid taking drugs when they are going to drive) and the proportion of drug-using respondents who drove while under the influence of drugs dropped in the after period from 45 to 35% (Swann, P. 5-12-2005. Baltimore, Maryland, USA. Rosita 2 meeting. *Personal Communication*). On the other hand, the oral

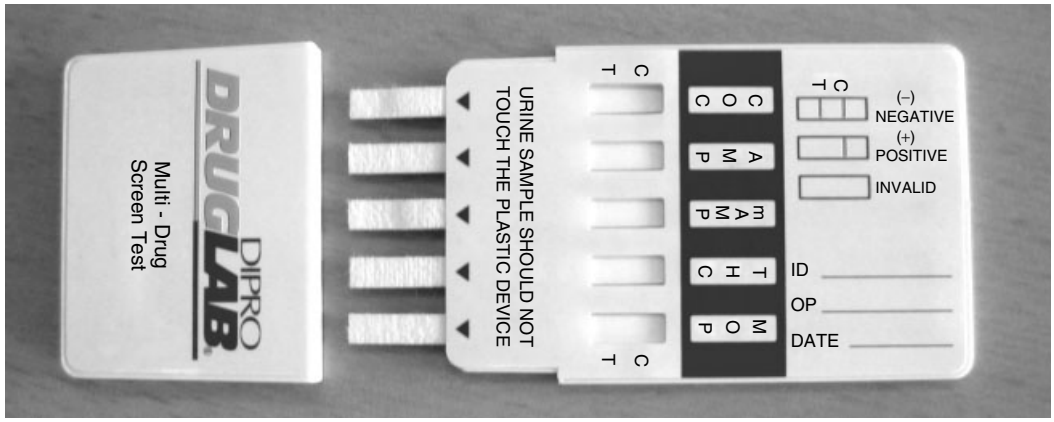

Figure 2 An example of a multidrug on-site urine test: the tips should be placed in the urine sample (urine should not touch plastic device). At the C level, a line should appear, indicating that the test is valid. At the T level, the presence of a line indicates a negative result and the absence a positive result

cavity can be contaminated by intranasal and smoked drug use, leading to extremely high concentrations in oral fluid. It is also difficult to obtain sufficient sample volume for the analysis, and the concentrations of 9-tetrahydrocannabinol (THC) and benzodiazepines in this matrix are low [43].

Evidentiary Analysis

Blood is considered to be the best matrix for confirmation analysis, because the presence of drugs in blood corresponds best with recent use and impairment. In many countries with "*per se*" legislation, the only legally allowed evidence for DUID is confirmation of the presence of drugs in blood. A review on drugs of abuse monitoring in blood for control of DUID was recently published [44]. The most widely used method is gas chromatography coupled to mass spectrometry (GC-MS) because of its sensitivity and specificity. However, the procedure is labor intensive and time consuming, as solid phase extraction and derivatization are necessary for sample preparation. In addition, different methods are often needed to quantify different drug classes. Therefore, liquid chromatography (tandem) mass spectrometry (LC-MS(MS)) procedures have been introduced for different classes of drugs for confirmatory analyses or even for screening and confirmation in one step. Several laboratories are developing methods that detect a large series of different drugs in one procedure in a small sample volume [45].

Another biological specimen that is used for evidentiary analysis in the context of DUID is hair. In Germany, Italy, and other countries, hair analysis is used for license (re)granting to drug dependent persons. The hair samples are first screened by immunoassay and positives are then confirmed by high pressure liquid chromatography (HPLC), capillary electrophoresis (CE), GC-MS, or LC-MS. The major practical advantage of hair testing compared with urine and blood testing for drugs is its larger detection window, which is weeks to months, depending on the length of hair shaft analyzed. Other advantages of hair are its stability and ease-of-transportation. A disadvantage of the use of hair as biological matrix is the possible contamination by exposure to drugs in the air and the absence of correlation with recent use because of the delayed appearance of drugs in hair [46–48]. (For further information *see also* **Hair: Toxicology**.)

Conclusion

There is an increasing knowledge regarding the influence of drugs on performance, and the prevalence of drugs other than alcohol in road traffic. Experimental studies clearly show that many drugs can have a detrimental effect on driving performance. These negative effects are often even more pronounced when drugs are combined with alcohol. Results of epidemiological studies confirm the detrimental effects of drugs on driving performance. These studies show that DUID

is associated with increased crash risks and increased risks of being responsible for a traffic crash. They also show that these risks increase even more when drugs are taken in combination with alcohol compared to when drugs are taken alone.

Regarding DUID there is a clear move toward "*per se*" legislation, although some countries at this time have decided to stay with impairment legislation, and some have both (e.g., Australia, Germany etc.). The detection by the police of drivers under the influence of drugs can be done by means of screening tests. In recent years, the interest in oral fluid screening tests has grown significantly. Studies however have shown that none of the currently available on-site devices are reliable when used alone. More recent methods developed for confirmation analysis use HPLC with tandem mass spectrometry.

It is possible that future developments could lead to on-site screening of capillary blood obtained by a finger prick and confirmation of the presence/absence of drugs by analyzing dried blood spots. Possible advantages of this approach would be the easy transportation (no need for refrigeration or shipping on dry ice necessary), the stability of parent substances at ambient temperature, and less risk of loss of sample (e.g., breakage of glass tube of blood) or of infection.

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