Responsibility Study: Main Illicit Psychoactive Substances Among Car Drivers Involved in Fatal Road Crashes

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ABSTRACT

In 1999, in France, before considering modifications in drug legislation, the government requested a study of the effect of illicit drugs on the risk of road crashes. It implemented a systematic screening of illicit drugs for all drivers involved in fatal crashes between October 2001 and September 2003. Within the European DRUID project, the study was restricted to car drivers.

The project reported here is a responsibility analysis and, as such, it belongs to the framework of case-control studies; the outcome of interest is "being responsible for a fatal crash". It was assessed with a method adapted from Robertson and Drummer. Cases are the 4,946 car drivers who are responsible for the crash; controls are the 1,986 car drivers selected from the non-responsible car drivers, in a way that makes the control group similar to the general driving population.

The effect of cannabis on fatal crash responsibility is significant after adjustment for age, sex and alcohol: adjusted odds ratio is 1.89 [1.43-2.51]. The dose-response effect is significant (p=0.0001). For alcohol (≥0.1 g/l), the adjusted odds ratio for responsibility is 8.39 [6.95-10.11]. No interaction was found between alcohol and cannabis. For amphetamine, cocaine and opiates, adjusted odds ratios were not significantly different from 1. However the statistical power is low.

The study finds similar odds ratios for alcohol as previously published. For cannabis, the significant odds ratio together with the significant dose-response effect indicates a causal relationship between cannabis and road crashes. A multiplicative effect between cannabis and alcohol was noted.

INTRODUCTION

In 1999 in France, before considering modifications in the drug legislation, the French Government requested reliable epidemiological evaluations on the role of cannabis in the occurrence of road crashes. Systematic screening of illicit drugs was therefore made compulsory in France, from October 2001 to September 2003 ("Gayssot Act"), for all drivers involved in fatal road crashes. This is the basis of the so-called SAM study (SAM=Stupéfiants et Accidents Mortels / illicit drugs and fatal crashes). A first responsibility analysis based on all drivers has already been conducted and published [Laumon, et

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al., 2005]. This effort, within the DRUID project (Driving Under the Influence of Drugs), was a responsibility study restricted to car drivers.

Cannabis intoxication of a driver may influence fatal crash occurrence in two ways: either by increasing the risk of causing a crash (resulting in death) or by increasing the risk of being killed (in a crash caused by that driver or by another driver) possibly because of riskier behaviour such as not wearing a seatbelt, and/or a reduced ability to avoid a crash. Our study only dealt with testing the first hypothesis. The second hypothesis implies that there is a selection bias in the non-responsible group. This is dealt with in the way of designing the control group.

In this research effort we evaluated the driver's risk of being responsible for a fatal crash. We assessed for association between cannabis concentration and responsibility, taking confounding factors into account (especially alcohol).

METHODS

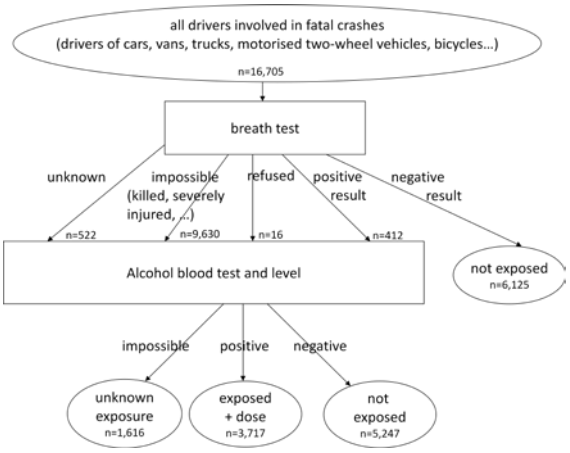
Data

Legal procedure for data collection on alcohol

For all drivers involved in injury and/or fatal crashes, the presence of alcohol must be tested using a breath test. If the breath alcohol concentration is lower than 0.25 mg/l (which is legally equivalent to a blood alcohol concentration of 0.5 g/l), then the driver is considered to be negative for alcohol; if the breath test is positive, it is followed by a blood test for alcohol concentration level.

If a driver refuses the test (rarely observed) or if the severity of the crash makes the test impossible (for someone killed or severely injured), then a blood test is performed.

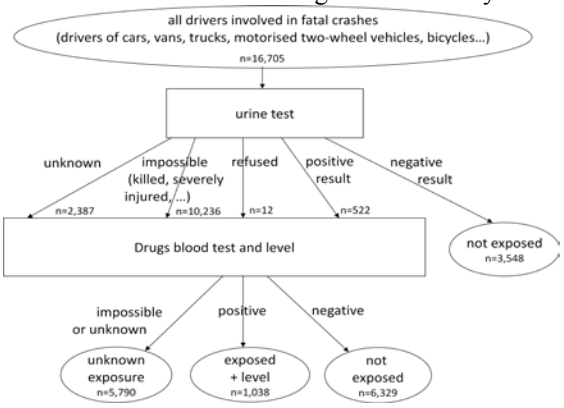
Figure 1 : legal police procedure (and frequencies) for the detection of alcohol in road fatal crashes



Legal procedure for data collection of illicit drugs

For each driver involved in a crash that is immediately fatal, there is an assessment for the presence of cannabis, amphetamines, opiates and cocaine. The first assessment is a urine test. If it is negative, the driver is considered negative. If it is positive, or if the testing is impossible or refused, a blood sample is obtained to assess for drug level. Drug blood levels were determined using gas-phase chromatography coupled with mass spectrometry.

Figure 2 : legal police procedure (and frequencies) for the detection of illicit drugs under the Gayssot act



Detection and impairment thresholds

The following thresholds for blood levels have been used within the DRUID project: alcohol 0.1 g/l, cannabis 1 ng/ml, amphetamines 20 ng/ml, cocaine 10 ng/ml, opiates 10 ng/ml [Gadegbeku and Amoros, 2010]. These are considered impairment thresholds; they are slightly lower than the French detection thresholds (except for cannabis) that were in use at the time the study was conducted. The procedure was precise about how to measure cannabis: measuring THC-tetra-hydro-cannabinol in the blood (and not THC-COOH in urine) but it was not specific about the compounds to be tested for opiates and amphetamines.

Police data

Over the study period from October 2001 to September 2003, 10,308 fatal crashes were recorded in the police data, involving 16,728 drivers.

Exclusion criteria

We excluded drivers with unknown age (there were 23) and drivers with unknown drug or alcohol status (35.6%; Please see later discussion). We were left with 10,748 subjects. We then selected all car drivers whatever the type of crash (single-vehicle crashes, or

against another car driver, a pedestrian, a cyclist, a motorised two-wheel vehicle user, a van/truck driver…). There were a total of 7,514. Among them, we kept only those above 18 years old; leaving 7,455 car drivers. The statistical unit was the driver (not the crash).

Analysis

Culpability and Responsibility studies

Within the DRUID project, Work Package 2 - Epidemiology, it was agreed that culpability should be defined in terms of legal regulation (and usually assessed by the police) whereas responsibility should be defined in terms of crash causation (and usually assessed by crash analysts). This study was a responsibility study.

Assessment of crash responsibility

Responsibility was assessed using an automated assessment procedure, adapted from Robertson and Drummer's method [Robertson and Drummer, 1994]. The original method consists in computing a responsibility score, based on information from 8 groups of characteristics: 1) condition of road, 2) condition of vehicle, 3) driving conditions, 4) type of crash, 5) witness observations, 6) road law obedience, 7) difficulty of task involved, and 8) level of fatigue.

It uses information on driving offences related to the crash, including the blood alcohol status. This is problematic because it leads to a direct relationship between alcohol status and responsibility status, and this relationship is of a legal sense. Since the interest of the study concerned only the possible relationship in terms of impairment, the item "alcohol status" must be excluded and was excluded from the responsibility assessment procedure.

Some other items were dropped from the method for other reasons: "comments from possible witnesses" as it is not part of the recorded police reports and "level of tiredness of the driver" since it is not reliable.

The adapted Robertson and Drummer's method has been applied on all drivers included in the study. The obtained responsibility score falls into 3 categories: (fully) responsible, partially responsible and non-responsible. In the analysis, partially responsible drivers were grouped together with fully responsible drivers.

In order to validate (or not) the adapted method, we compared it for a sub-sample with an assessment conducted by a group of crash analysts. This was done in a blind way i.e. the experts were not given the results from the adapted automated method. Information on alcohol/drug status was not provided to them; age and sex data were also blinded as they are correlated with alcohol and drug status.

These experts' assessments were conducted on a sub-sample of 3,024 drivers, who were involved in crashes with two or more vehicles. The two responsibility assessments were compared: we found a kappa score of 0.67 (agreement score), with 95% CI=[0.65-0.70]. They are similar enough to validate the adapted Robertson and Drummer method [Laumon, et al., in press].

Responsibility study = a case-control study

A responsibility study belongs to the framework of case-control studies [McGwin, et al., 2000 Sagberg, 2006]. The outcome of interest is, "being responsible for the crash". Cases and controls are defined according to it: cases consist of the responsible drivers and controls of the non-responsible drivers (or a selection thereof; see below). Cases (responsible drivers) and controls (non-responsible drivers) are compared in order to identify risk factors of being responsible for the crash.

Selection of cases and controls

The cases were the 4,946 car drivers responsible for the crash. The controls were selected as a sub-sample from the 2,509 non-responsible car drivers.

In a case-control study, in order to measure the association between a characteristic and the outcome (responsibility for a crash), one cannot estimate relative risks (RR) but only odds ratios (OR). While these may be difficult to interpret, they can be used as good approximation of relative risks if the following three conditions are all met: 1) the controls are a representative sample of the whole population, 2) the outcome of interest is a rare event, 3) the value of the odds ratio is rather close to 1. It implies here that the controls should be as close as possible to the whole driving population. In this population, the event "being responsible for a fatal crash" is a rare event.

The group of controls should be as close as possible to the whole car driving population. Of note is the following: preliminary analysis of the data on all drivers [Laumon, et al., in press] showed a significant increase in the risk of death of non-responsible drivers who tested positive to cannabis (the same was previously found for alcohol [Evans, 1991]). In other words, cannabis is a risk factor for a fatal outcome once a person is injured (all other things being equal). This may be because of a riskier behaviour such as not wearing a seat belt, and/or a reduced ability to avoid a crash. This phenomenon implies a selection

bias on the driving population: an over-representation of crashes in which the killed victim is a driver detected as cannabis/ alcohol positive. To avoid this, we excluded among non-responsible drivers, those who were the only fatally injured victim in the crash (there were 523.) This is because they may be the only fatality within the crash because of their higher propensity to be killed due to their intoxicated status; indeed among this sub-group the proportion of intoxicated drivers is higher than among the general driving population [Laumon, et al., in press]. Controls are therefore selected as non-responsible drivers, who were not the only fatality in the crash. The control group of car drivers therefore only included 1,986 subjects out of 2,509 non-responsible ones. In total, the analysis was conducted on 6,932 car drivers (1,986 controls and 4,946 cases).

Confounding factors

One major confounding factor is alcohol, as it is associated with both the exposure of interest (cannabis) and the outcome. On the one hand, alcohol consumption is positively correlated with cannabis consumption. Among drivers who are positive to cannabis, a high proportion, 50% [Amoros and Gadegbeku, 2010] are also positive to alcohol. On the other hand, alcohol consumption is correlated with being responsible for a fatal road crash. This has been documented in numerous studies [Drummer, et al., 2004 Dussault, et al., 2002 Longo, et al., 2000].

We tested whether there was an interaction between cannabis and alcohol consumption.

Age and gender were adjusted for. Age is a confounding factor, because younger age is positively correlated with higher risk of fatal crash, and at the same time, younger age is associated with higher consumption of cannabis [Amoros and Gadegbeku, 2010]. Note: the common DRUID cut-points defined for age are: 18, 25, 35 and 50 years old. Gender is a confounding factor as, on the one hand, it is associated with fatal crashes: men are more likely to be responsible for a crash than women [Martin, et al., 2004]. On the other hand, gender is associated with cannabis consumption: men are more often cannabis consumers than women [Ravera and de Gier, 2008].

In this study data were analysed using logistic regression, which was fitted using SAS software, version 9.1, LOGISTIC procedure.

RESULTS

Cannabis

Crude and adjusted odds-ratios of cannabis are provided in table 1. Car drivers under the influence of cannabis have 1.89 times more risk of being responsible for a fatal crash than non-intoxicated drivers (all other things being equal). The adjusted odds ratio is lower than the crude odds ratio.

When we explore a dose-response relationship for cannabis intoxication, again, the adjusted odd ratios are estimated at a lower value than the crude odds ratios. The trend test rejects the null hypothesis (of equality of the odds-ratios associated with different drug level categories) at $p<0.001$: there is an increasing risk of responsibility for fatal crashes with increased cannabis levels.

Table 1 : OR for cannabis intoxication of the risk of being responsible for a fatal crash for car drivers above 18 years old, France, 2001-2003, n=6,932

THC (ng/ml)	Number of drivers	Crude OR	95% CI	Adj* OR	95% CI
THC yes/no	529	3.00	2.31-3.91	1.89	1.43-2.51
$0 \leq THC < 1$	6403	1.00	-	1.00	-
$1 \leq THC < 3$	220	2.26	1.57-3.26	1.53	1.03-2.27
$3 \leq THC < 5$	116	4.54	2.37-8.70	2.84	1.44-5.60
$THC \geq 5$	193	3.51	2.22-5.54	2.01	1.24-3.27

* adjusted for 5 alcohol levels, age, gender

However, one notes that the confidence interval for the 3 to 5 ng/ml category is wider than the other two, most certainly due to the small number of such drivers. In other words, the precision of the estimate is not very good for this category.

Alcohol

Crude and adjusted odds-ratios for alcohol are provided in table 2. Crude and adjusted odds ratios for alcohol (in a yes/no categorisation) are very similar, and are quite high, at around 8.

When alcohol is categorised according to its concentration in the blood, the odds ratios increase together with the dose of alcohol ($p<0.0001$).

The odds ratio for alcohol above 1.2 g/l is very high. However this last category is very wide. About one half of the drivers of this category are in fact above 2.0 g/l, where the odds ratio is extremely high:

OR=39.6, 95% CI=[22.7-68.9] [Laumon, et al., in press].

Table 2 : OR for alcohol consumption of the risk of being responsible for a fatal crash for car drivers above 18 years old, France, 2001-2003, n=6,932

Alcohol (g/l)	Number of drivers	Crude OR	95% CI	Adj* OR	95% CI
yes/no	1 997	8.28	6.89-9.95	8.39	6.95-10.11
0 ≤ Acl < 0.1	4935	1.00	-	1.00	-
0.1≤ Alc < 0.5	327	2.57	1.9-3.40	2.45	1.84-3.26
0.5 ≤ Alc < 0.8	162	6.35	3.66-11.01	6.14	3.52-10.69
0.8 ≤ Alc < 1.2	251	7.33	4.58-11.74	6.92	4.30-11.13
Alc ≥ 1.2	1257	18.26	13.26-25.15	19.32	13.99-26.69

*adjusted for 4 cannabis levels, age, gender

Association between alcohol and cannabis

The model does not indicate an interaction between cannabis and alcohol intoxication (p=0.13), 'only' a multiplicative effect. The odds ratio when being under the influence of both alcohol and cannabis of being responsible for a fatal crash (compared to drivers not exposed to cannabis nor to alcohol) is therefore estimated at 8.39*1.89=15.86.

Other illicit drugs: amphetamines, cocaine, opiates

Crude and adjusted odds-ratio for amphetamines, cocaine and opiates are provided in table 3.

Table 3 : OR for illicit drugs consumption (yes vs no) of the risk of being responsible for a fatal crash for car drivers above 18 years old, France, 2001-2003, n=6,932

Psychoactive substance	N positive	Crude OR	95% CI	Adj* OR	95% CI
Amphetamines yes/no	54	2.71	1.22-6.01	(1.54)	0.66-3.56
Cocaine yes/no	34	(1.87)	0.78-4.53	(1.17)	0.45-3.02
Opiates yes/no	69	(0.80)	0.48-1.33	(0.76)	0.44-1.32

*Adjusted for alcohol and cannabis levels, age, and gender

The crude odds ratio on the influence of amphetamines in responsibility for a fatal crash is significantly above 1. However, when adjusting for confounding effects from alcohol, cannabis, age and gender, the odds ratio is estimated at 1.5 and it is no longer different from 1. The confidence interval is rather wide. For cocaine and opiates, both the crude and adjusted odds ratio are not significantly different from the value 1.

Because of the very small frequency of car drivers involved in fatal crashes who are positive for one of these drugs, it was not possible to conduct a dose-response analysis on them.

DISCUSSION

Strengths and weaknesses

The study was made possible due to enactment of a specific French law that made it mandatory in case of fatal crashes to test all involved drivers for illegal drugs. Alcohol was already being tested on all drivers involved in any road crash resulting in injury.

Illicit drug status is missing on 35% of the subjects, and alcohol is missing on 10% of the subjects (36% altogether). Physicians reported that reasons for not conducting a urine or blood test were (apart from the severity of the casualty) most frequently a lack of appropriate equipment [Biecheler, et al., 2008]. We compared (not shown) drivers with known drug/alcohol status to drivers with missing drug/alcohol status, separately for killed drivers and for surviving drivers, in terms of age and gender. They seem rather similar. From these factors, we can say that the missing data mechanism is not "missing completely at random" (MCAR), but merely "missing at random" (MAR). Nevertheless this means that, excluding subjects of missing drug or alcohol status will not create bias in the estimation of odds ratios in the regression model where alcohol and drug are explicative variables [Allison, 2010].

The study was based on a large number of subjects, about 7,000 of them. The statistical power was good for alcohol and cannabis; it was low for amphetamines, cocaine and opiates, where the prevalence of use was very low.

Responsibility was assessed by the automated method of Robertson and Drummer [Robertson and Drummer, 1994]. The high level of concordance with the experts' responsibility assessment validates the automated method [Laumon, et al., in press].

The sub-selection of the control group (excluding non-responsible drivers who were the only fatality in the crash) may seem surprising. The only objective was to have a control group as close as possible to the driving population, and therefore to be able to use the estimated odds ratios as approximations of relative risks. The exclusion of some subjects is completely analogous to what is done in others fields of

epidemiology. In cancer epidemiology, cases are cancer patients, and controls are usually recruited among other hospitalized persons, but excluding some of them. For example, if a study aims at exploring the effect of tobacco on bladder cancer, the selection of hospital controls will exclude patients suffering from diseases known to be related with tobacco. Otherwise the controls will display a higher proportion of smokers than the general population.

The representativeness of our controls can be assessed on the basis of a comparison, between the estimated prevalences [Amoros and Gadegbeku, 2010 Gadegbeku and Amoros, 2010] and those estimated for the whole driving population using other methods. These comparisons are available for all driver types, but prevalences for car drivers are not very different from all drivers [Amoros and Gadegbeku, 2010]. For alcohol, in the same period, the prevalence of alcohol above 0.5 g/l in the driving population in France was found to be 2.5% [ONISR, 2004] whereas the corresponding estimation in our control group was equal to 2.7%. This strong similarity supports the design of the control group.

Odds ratio would be lower if the control group would include all non responsible drivers

If the responsible drivers were compared to all non responsible drivers, without a sub-selection on the controls, odds ratio would have been lower for cannabis and for alcohol than those obtained with the controls restricted to non-responsible drivers who were not the only fatality in the crash. Indeed, for all drivers (not only car drivers), adjusted OR of responsibility for cannabis (THC>0) were estimated at 1.43, 95% CI=[1.19-1.73] when responsible drivers to non-responsible drivers were compared (versus 1.78, 95% CI=[1.40-2.25] when comparing responsible drivers to a sub-selection of controls).

Testing and drug level

For each of the five psychoactive substances except cannabis, the DRUID impairment threshold is slightly lower than the French legal detection threshold. This implies that we might have missed some positive drivers: those who were in the range between the DRUID threshold and the French legal threshold. As a consequence, the prevalences using the DRUID thresholds are under-estimates of the true prevalences. Because of this misclassification effect, (more precisely this dilution effect), the odds-ratios (for this particular small doses category) are probably under-estimates of the true odds-ratios.

Also, it may be that drug levels are somewhat over-estimated for killed drivers, because of blood loss, post-mortem redistribution, and the body region from which blood was taken. For non-killed drivers, it may be that levels are somewhat under-estimated because of the elapsed time between the crash and blood sampling (when known, it is mostly between 1 and 4 hours).

Similarity of our alcohol results with previous studies

We used alcohol as an indicator of plausibility for the results obtained. Our study yielded results consistent with previous studies on crash risk related to alcohol [Drummer, et al., 2004 Dussault, et al., 2002 Longo, et al., 2000]. These results support our study methodological choices.

We confirmed the confounding role of alcohol on cannabis. No interaction was detected among alcohol and cannabis. This implies that consumption of both cannabis and alcohol merely multiplies the risks related to consumption of either cannabis or alcohol alone. The evidence of no interaction was even greater when drivers of all vehicles types were studied [Laumon, et al., in press]. These results confirm previous experimental and epidemiological studies [INSERM, 2001].

Similarity of our results on cannabis with studies using detection of THC in the blood

Our results on the effect of cannabis (OR=1.89, 95% CI=[1.43-2.51] are consistent with the findings of Drummer et al [2004] (OR=2.7, 95% CI=[1.0-7.0]) which assessed cannabis status from the presence of THC in the blood, and not from THC-CCOH in urine. THC in the blood is a good indicator of being under the influence of cannabis when a crash occurs, whereas THC-COOH is only an indicator of past-exposure to cannabis, which may be up to several days ago. In other words, THC in the blood allows for the identification of people who were under the influence of cannabis at the time of the crash. THC-COOH in urine identifies users of cannabis, whom may not have been under the influence of cannabis at the time of the crash.

Study population=involved in fatal crashes versus fatally injured involved drivers

We found higher odds ratios than in studies that only included fatally injured drivers [Drummer, et al., 2004 Dussault, et al., 2002]. The reason is probably that in such studies the control groups were quite close to the case group in terms of proportions of intoxicated drivers. Indeed we mentioned that being under the influence of alcohol or drugs seems to increase the risk of dying in two ways: being

responsible for a fatal crash and dying from one's own injuries.

Cannabis drug level and fatal crash responsibility

Analysis showed a dose-response relationship between cannabis and the risk of responsibility for fatal traffic crashes. This finding strongly favours a causal relationship between cannabis and road crashes. The same dose-response effect was found when the analysis was not restricted to car drivers, but using drivers of all vehicles types [Laumon, et al., 2005].

CONCLUSION

The study found an increased risk of being responsible for a crash when driving under the influence of cannabis. The significant dose-response relationship indicates a causal relationship between cannabis and road crashes. The effect of cannabis on the risk of being responsible for a fatal crash is however not as strong as the effect of alcohol. Lastly, there is merely a multiplicative effect between cannabis and alcohol.

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