Published: 25-11-2009
Last updated: 06-05-2024

To assess the effects of single dose of 100 mg (±) 3, 4-Methylenedioxymethamphetamine (MDMA, "ecstasy") and/ or a single dose of alcohol (0.5 %0) on simulated driving performance (in a controlled experimental design).To assess the effects...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Observational invasive

Summary

Source

ToetsingOnline

Brief title

MDMA , alcohol and simulated driving performance

Condition

- Other condition

Synonym

Influence of MDMA/ alcohol on driving performance

Health condition

gevolgen voor rijvaardigheid

Research involving

Human

Sponsors and support

Primary sponsor :	Rijksuniversiteit Groningen
Source(s) of monetary or material Support :	Europese Unie

Intervention

Keyword :	Alcohol, Driving performance, Driving simulator, MDMA

Outcome measures

Primary outcome

Study parameters/endpoints: Performance on the driving- and driving related

tasks.

Main study parameter/endpoint:Performance on the driving- and driving related

tasks.

Secondary outcome

Secondary study parameters/endpoints: Saliva, whole blood, blood plasma and

blood spot analyses for drug levels and breathe analyser measures of the

alcohol level, results from the questionnaires

Study description

Background summary

Movig et al., (2004) convincingly showed that drug use and especially multiple drug use and drug-alcohol combinations among drivers is an important risk factor for traffic accidents. Since drug- and medicine use is proportionally increasing over the years, special efforts have to be directed towards gaining

better knowledge of the various aspects of this problem and developing appropriate solutions. The objective of the recently started EU-project DRUID (Driving under the Influence of Drugs, Alcohol and Medicines) is to give scientific support to the EU transport policy (White Paper, 2001) by establishing guidelines and measures to combat impaired driving.
In this protocol, a study is proposed to assess the performance effects of single dose of (±) 3, 4-Methylenedioxymethamphetamine (MDMA, "ecstasy") and a single dose of alcohol (0.5 *), and a combination of the two, on simulated driving performance and driving related performance. A group of 20 experienced, healthy frequent MDMA-users aged between 21 and 40 will be administered MDMA (0 and 100 mg) and alcohol (0 and 0.5 %0) according to a 4- way, double-blind, placebo controlled, repeated measures, cross-over design. Performance assessments will consist of simulated driving tasks and laboratory tests of memory, response inhibition and impulsivity. The practical outcome of the present study is to generate recommendations for the definition of analytical and risk thresholds for driving under the influence of MDMA and the MDMA-alcohol combination.
Driving performance is assessed on three levels: the strategically level (general plans), manoeuvring level (controlled action patterns) and control level (automatic action patterns; Michon, 1985). It expected that alcohol will influence performance mainly on the control level expresed in an increase the amount of swerving. The main negative effect of MDMA is expected at the manoeuvring level. This will probably be expressed as an increase in the amount of risk a subject is willing to take. For the alcohol -MDMA combination it is expected that the stimulating effects of MDMA will moderate alcohol induced effects on the control level. However the combination of the substances will also lead to even greater impairment at the manoeuvring level as compared to when substances are taken separately by inducing greater risk taking.

Study objective

To assess the effects of single dose of 100 mg (±) 3, 4-Methylenedioxymethamphetamine (MDMA, "ecstasy") and/ or a single dose of alcohol (0.5 %0) on simulated driving performance (in a controlled experimental design).

To assess the effects of single dose of 100 mg (±) 3, 4-Methylenedioxymethamphetamine (MDMA, "ecstasy") and/ or a single dose of alcohol (0.5 %0) on driving related tasks (cognitive tasks).

Generate recommendations for the definition of analytical and risk thresholds for driving under the influence of MDMA alone or combined with alcohol for the EU project DRUID.

Study design

The study will be conducted according to a double-blind, placebo-controlled, 4-way cross-over design with treatment orders counter-balanced according to a Latin square. Driving tests will be conducted 1.5 hours post-drug oral intake and 20 minutes post-alcohol oral intake. Cognitive and psychomotor tests will be conducted directly after the driving tests approximately 2.5 hours post drug intake.
The study will be conducted during an eight period in which 20 paid volunteers will be subjected to four conditions. They will visit the UMCG four times with a wash-out period of one week in between, and an introduction session, including a dress-rehearsal test. The study will be conducted in a clinical laboratory equipped with driving simulator.

Study conditions:
1 Matching placebo + alcohol-free drink
2 100 mg MDMA + alcohol-free drink
3 0.5 g/kg Alcohol + placebo
4 100 mg MDMA + 0.5 g/kg alcohol

Study burden and risks

The most serious acute somatic adverse effects of MDMA are hyperthermia, hyponatermia and liver insufficiency. Hyperthermia can occur through inadequate compensation of the centrally induced rise of core body temperature after MDMA (Pennings et al., 1998). In a controlled experimental setting, it was shown that subjects* body temperature rose significantly during MDMA intoxication, independently of environmental temperature. However, the magnitude of elevation was modest (between 0.3°-0.6C) (Freedman, Johanson, & Tancer, 2005). Other factors though can cause an elevation of body temperature i.e. physical activity (dancing) and concomitant use of other hypothermic drugs (e.g. cocaine). Hyponatermia is also of central origin and is associated with the demonstrated anti-diuretic hormone response by MDMA (Henry et al., 1998). Hyponatermia is further facilitated by excessive fluid intake after MDMA. Hyponatermia can be prevented by ascertaining that fluid intake after MDMA is moderate and Natrium-containing (isotonic).
Liver insufficiency, hepatitis or fatal liver failure, appears to be a rare idiosyncratic response to MDMA, which can even occur after a single dose. The mechanism is unknown. Contamination of tablets, the origin of which is by definition unclear in the practice of its illegal usage, can not be excluded (de Man, Wilson, & Tjen, 1993; A. C. Parrott, 2004).
Transient subjectively experienced acute adverse effects of MDMA that are reported most frequently (62%) include bruxism (teeth grinding), lack of

appetite, difficulty concentrating and impaired balance (Baylen & Rosenberg, 2006; Vollenweider, Gamma, Liechti, & Huber, 1998). Stimulant effects and altered body sensations such as restless or heavy legs, paresthesias, increased sensitivity to cold and hot flashes are less frequent (23-46%). Further acute symptoms are thirst, palpitations and sweating. Compared to placebo, fatigue and worries are reported less. Symptoms that may persist up to 24 hours in 23-46% of users are suppressed appetite, thirst, bruxism, feelings of restlessness, difficulty in concentration and sweating, whereas after 24 hours new subjective adverse effects consist of lack of energy, insomnia and brooding in 23-46% of cases (Vollenweider et al., 1998).
It is known that in rats alcohol increases MDMA induced hyperactivity but attenuates MDMA related hyperthermia (Hamida et al., 2007). Furthermore plasma concentrations of MDMA can show a small increase after the use of alcohol (Hernandez Lopez et. al. 2002).
Any serious adverse event, whether or not related to the study treatment will be reported by the medical investigator immediately (within 24 hours) to the principal investigator, the Medical Ethics Committee (MEC), the general practitioner and the study subject. The exception to this rule is that serious adverse events that have already been treated by the general practitioner or medical specialist, or about which the general practitioner or medical specialist have already been informed, which situation is to be judged by the medical investigator, do not have to be reported to the general practitioner or subject. A written report on the event will be sent to the MEC within three working days.

Suspected unexpected serious adverse reactions

Advers events will be established by the principal investigator on basis of:
1. Answer to the open question: 'How are you feeling?'
2. Spontaneous reporting

Advers events will be classified under the responsibility of the medical investigator. He/she will register his/her findings, conclusions and actions. Intoxicated behaviour as a result of the intake of alcohol will not be reported as an Advers events.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Experience with the use of MDMA (at least 5 times in the past 12 months)
Experience with the use of alcohol (<2 or > 20 alcoholic consumptions a week)
Free from psychotropic medication
Good physical health as determined by examination and laboratory analysis Absence of any major medical, endocrine and neurological condition
Normal weight, body mass index (weight/length2) between 18 and 28 kg/m2
Valid driving license
Written Informed Consent

Exclusion criteria

History of drug abuse or addiction as determined by examination
Pregnancy, lactation or wishing to become pregnant in the period of the study
Cardiovascular abnormalities as assessed by standard ECG
Excessive drinking (> 20 alcoholic consumptions a week)
Hypertension (diastolic> 100; systolic> 170)
Current or history of psychiatric disorder
Participation in any clinical trial including blood sampling and/or administration of substances

up to 6 weeks before Day 01 of this study
History of malignant hyperthermia /serotonin syndrome
Susceptibility to simulator sickness (subjects will be pre-tested)
Heavy smoking: during the visit smoking is restricted to breaks.
Not having a general practitioner
Not willing to accept information-transfer concerning participation in the study, or information regarding his/her health, like laboratory results, findings at anamnesis or physical examination and eventual adverse events to and from his general practitioner

Study design

Design

Study type :	Observational invasive
Intervention model :	Crossover
Masking :	Double blinded (masking used)
Control :	Uncontrolled
Primary purpose :	Treatment

Recruitment

NL

Recruitment status :	Completed
Start date (anticipated) :	05-04-2010
Enrollment :	20
Type :	Actual

Ethics review

Approved WMO Date :	25-11-2009
Application type :	First submission
Review commission :	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date :	01-04-2010
Application type :	First submission
Review commission :	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2008-001359-23-NL
CCMO	NL26205.042.09