A single-centre randomized double-blind, double-dummy, placebo-controlled, four-way crossover study in healthy subjects to investigate the effect of ethanol 0.5 and 1.0 g/L and alprazolam 1 mg on a driving simulator and to compare the results with the NeuroCart test battery.

Published: 07-10-2014
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ObjectivesPrimary:• To assess the effect of ethanol compared to placebo on a driving simulator performance tests;• To assess the effect of alprazolam compared to placebo on a driving simulator performance tests;Secondary:• To assess the effect of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41921

Source
ToetsingOnline

Brief title
Driving simulator study

Condition

- Other condition
- Environmental issues

Synonym

1 - A single-centre randomized double-blind, double-dummy, placebo-controlled, four- ... 13-05-2025

Sensitivity of driving simulators to assess drug effects

Health condition

safety

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Centre of Human Drug Research

Intervention

Keyword: Alprazolam, Driving performance, Driving simulator, Ethanol-clamping

Outcome measures

Primary outcome

NeuroCart assessment:

1.Adaptive tracking (average performance %);

2.Saccadic eye movements (saccadic reaction time (sec), saccadic peak velocity (deg/sec), and saccadic inaccuracy (%));

3.Smooth pursuit eye movements (percentage of the time that subject*s eyes are in smooth pursuit of the target (%));

4.Body sway (antero-posterior sway (mm/2min));

5.Visual verbal learning test (VVLT)

6.Visual Analogue Scales according to Bond and Lader (alertness, mood, and calmness subscales (mm)).

7. Stop signal task (mean response time on GO-trials, total correct responses on Go-trials, total missed responses on Go-trials, mean response time on Stop-trials, total correct responses on Stop-trials, mean stop signal delay

(SSD) of the Stop-trials and stop signal response time)

Driving simulator assessment:

1. Standard deviation of Lateral Position (SDLP in centimeters)

Questionnaire driving behaviour and safety:

1. driving behaviour questionnaire

Secondary outcome

Parameters to detect drug effects

1. Useful Field Of View test (UFOV)

2. Lapses of inattention

3. Standard deviation of speed

4. Mean Speed

5. Mean lateral position

6. Simple reaction time

7. Spatial perceptual-task

8. Standard deviation of throttle position

9. Steering wheel test

Safety driving performance parameters

1. Keeping safe distance

2. Car following

3. Driving failures

4. Gap acceptance

5. Drive safety score (DSS)

6. Reaction to unexpected events

7. Traffic violations

a. Traffic light scenario

Study description

Background summary

Pharmacological agents can induce fatigue and reduce vigilance leading to periods of inattention and as such poses a risk factor for usage during daily activities, especially in driving. Therefore it is important to determine whether the ability to drive a motorized vehicle is affected by a pharmaceutical agent.
Currently the ability to drive is assessed by using a standardized method, the Dutch on-the-road driving test (O*Hanlon, 1982). This test method has been used extensively to assess the sedative effects of numerous pharmacological substances (Verster, 201; O*Hanlon, 1982). During this test subjects are instructed to drive with a steady lateral position and constant speed on a public highway in normal traffic conditions and under supervision of a skilled instructor and continuous camera registration.
However some drugs are known to possess psycho-stimulant properties and drugs of abuse are known to lead to inactive, impatient or erratic behaviour, which poses risks for driving that are more difficult to assess under real driving circumstances. New medicines in general carry a larger risk for such unexpected behavioural effects but increasingly, knowledge about the effects of such medicines on risky daily activities is important early in development. Therefore, a public on-the-road test may not be the most suitable to measure drug-induced driving risks.
The purpose of the study is to determine the sensitivity of a driving simulator test battery to the effects of ethanol 0.5 and 1.0 g/L and alprazolam 1 mg, and to explore the relationships with historical results from actual driving performance. In addition, the results will also be compared with those of the NeuroCart, a validated test battery that quantifies a large range of drug-sensitive CNS-functions that are also relevant for every-day performance. Results from this study will allow us to determine whether a driving simulator is suitable to assess impairment in performance due to pharmacological agents in a laboratory setting.

Study objective

Objectives
Primary:
• To assess the effect of ethanol compared to placebo on a driving simulator performance tests;
• To assess the effect of alprazolam compared to placebo on a driving simulator performance tests;

Secondary:
• To assess the effect of alprazolam compared to ethanol on driving simulator performance tests;
• To establish the relationship between driving simulator and NeuroCart performances;
• To study the suitability of additional complex parameters of driving simulation on the assessment of drug effects.
• To explore the relationships between driving simulator and historical results from actual driving performance.

Study design

This is a single-centre, randomized, double-blind, double-dummy, placebo-controlled, four-way crossover study with ethanol 0.5 and 1.0 g/L and alprazolam 1 mg in 24 healthy subjects while performing neurocognitive and psychomotor tests on the NeuroCart and driving simulator.

Intervention

During the four occasions study subjects receive the following treatments in randomized order:
• Alprazolam 1 mg + placebo (sham clamp)
• Placebo (capsule) + ethanol clamping (0.5 g/L)
• Placebo (capsule) + ethanol clamping (1.0 g/L)
• Placebo (capsule) + placebo (sham clamp)

Study burden and risks

No exceptional severe adverse drug reactions are expected and burden/convenience for the subjects are considered relatively mild.
Side-effects alprazolam: - expected: daytime drowsiness, dizziness, muscle weakness, and ataxia. Side-effects ethanol clampling: -expected: sleepiness, headache, dizziness and drunken feeling. Placement of the cannula can be painful and sometimes causes bruizing, also the site of infusion can be painful during the start of dosing, preventative action is taken in the form of simultaneous glucose infusion.
Subjects have to perform an active task during the measurements. However, subjects get sufficient rest during the measurements. Therefore, the measurements will cost little effort. The risk of the measurements is

minimally. Safety is performed by software and hardware of the devices.

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

Eligible subjects must meet all of the following inclusion criteria:
1. Healthy subjects, aged 18 to 55 years, inclusive; healthy is defined as no clinically relevant abnormalities identified by a detailed medical history, full physical examination, including 12-lead ECG, and clinical laboratory tests.
2. Subjects are in possession of a valid driver*s license and are active and experienced drivers; this is to be determined by the investigators;
3. Evidence of a personally signed and dated informed consent form indicating that the study subject has been informed of all pertinent aspects of the study.
4. Willing and able to comply with scheduled visits, treatment plan, laboratory tests, and

other procedures.
5. Experienced alcoholic drinkers, with occasional well-tolerated self-exposure to eight alcohol-containing drinks per social occasion.
6. Female subjects of childbearing potential must have a negative (β-hCG) test (at screening and before the start of each occasion) and be willing and able to use one of the following double-barrier methods of birth control: hormonal intrauterine device with condom, or oral contraceptives with condom from the screening visit to the end of study

Exclusion criteria

Eligible subjects must meet none of the following exclusion criteria:
1. Confirmed or suspected myasthenia gravis, severe respiratory insufficiency, sleep apnoea syndrome, severe hepatic insufficiency or hypersensitivity to benzodiazepines;
2. Evidence or history of clinically significant haematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, psychiatric, neurologic, or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).
3. Any condition possibly affecting drug absorption (e.g., gastrectomy).
4. A positive urine drug screen for cocaine, amphetamine, morphine, benzodiazepine and THC.
5. Subject is not able to perform the drive simulator tests.
6. Treatment with an investigational drug within 3 months prior to screening or having participated in more than 4 investigational drug studies within 1 year prior to screening.
7. Use of (non-)prescription medications that are believed to affect subject safety or the overall results of the study following judgment by the investigator.
8. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening.
9. Unwilling or unable to comply with the Lifestyle Guidelines described in this protocol.
10. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.
11. Subjects who are investigational site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the Investigator, or subjects directly involved in the conduct of the study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-10-2014
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xanax
Generic name:	Alprazolam
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	13-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	19-02-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-003956-30-NL
CCMO	NL50821.056.14