Brain damage due to GHB-induced coma in GHB users.

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Addictive disorders affect a steady proportion of the population, and result in significant negative personal consequences(e.g. loss of jobs, psychosocial problems) and costs to society (absence from work due to hangover, treatment costs).GHB is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Structural brain disorders
Study type	Observational invasive

Summary

ID

NL-OMON40636

Source
ToetsingOnline

Brief title
GHB coma

Condition

- Structural brain disorders

Synonym
cognitive and memory damage

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van VWS

Intervention

Keyword: coma, GHB, illicit drugs, neurotoxicity

Outcome measures

Primary outcome

Cognitive skills and memory in the different groups (cross-sectional).

Changes in brain structures.

Secondary outcome

Not applicable.

Study description

Background summary

GHB has originally been developed as an anaesthetic drug, but is since the 1990s regularly used as a recreational drug (8). GHB increases feelings of euphoria, relaxation, sociability and sexuality (13). Users of GHB are generally young adults (18-30 years) who use the drug in clubs, dance parties or after parties (15,16). In addition, GHB use is also spread among other groups, such as bi- or homosexual men (2) and college students (3). In 2009 in The Netherlands, lifetime prevalence of GHB use was 1.3%, whereas last month use was 0.2%, indicating low GHB use continuation (14).
The initial stimulant-like effects of GHB are followed by sedation, but there is a narrow dose-response margin between subjective GHB effects and those related to overdose (1). Symptoms of GHB intoxication include drowsiness, sleep, confusion, convulsions, collapse, hypostatic pneumonia and coma with respiratory depression. Symptoms of GHB intoxication usually resolve within 4 to 8 hours. It is not known whether experiencing a GHB induced coma leads to residual long-term harm.
By 2009, 1200 cases of GHB related emergency visits to Dutch general hospitals were reported (6-fold higher compared to 2003) and the majority of these emergencies were caused by GHB-induced coma (4). Several other emergency department (ED) case studies have also reported GHB as one of the major reasons

for drug overdosing and drug-related ED presentations (6,7,9,10,12,16,18) and 72% of GHB-intoxicated patients scored * 12 on the Glasgow Coma Scale (GCS) (7).
GHB is generally considered by users as safe and non-toxic, although it has a lethal potential and GHB might be
addictive. One of the problems (and a hallmark) of a GHB induced coma is that victims awake next morning within 5
seconds from deep coma to full consciousness without any complaints (headache/hangover), which gives the user the
feeling that a GHB coma has no residual adverse effects (16). This also explains why the same users experience more
than one coma. There are indications that many GHB users experience a GHB overdose/coma during their lives (10). In a
survey among GHB users in the USA, 66% of 42 users reported loss of consciousness once or multiple times during GHB
use (11). Similar figures were found in a cross-sectional survey of 76 Australian GHB users where 40 subjects (53%) had
experienced a GHB overdose and a third had done so more than three times (5). A Swiss study reported that in a period
of three years, 7 out of 48 patients with GHB coma (15%) were presented two, three or even six times to the emergency
department (10).
In conclusion, GHB intoxication is an emerging problem in different countries, including The Netherlands, and this is
caused mainly by lacking awareness of the effects of overdose and co-ingestion with other drugs. The objective of this
investigation is to determine whether GHB intoxication/coma might lead to neurotoxicity (structural brain damage).
Because GHB acts as a general anaesthetic, it is anticipated that cognitive and memory disturbances occur in GHB users
who have experienced one or more coma*s (10).
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Study objective

Addictive disorders affect a steady proportion of the population, and result in significant negative personal consequences
(e.g. loss of jobs, psychosocial problems) and costs to society (absence from

work due to hangover, treatment costs).
GHB is becoming more popular and an increasing number of GHB users is presented at emergency departments of
general hospitals. The search for vulnerability factors and potential adverse effects of GHB use is therefore highly
relevant. The current literature on neurobiological indicators of brain damage by GHB use or GHB coma is very small.
However, the adverse effects of similar sedating drugs (general anaesthetics, ketamine and alcohol) on memory and other
cognitions have been described in the scientific literature.
The detection of severe adverse side effects of GHB overdosing (those leading to coma) might be helpful to readjust the
false belief among GHB users that GHB is a safe drug. The current study will provide better knowledge on the
neurobiological risk indicators of recreational GHB use. This may result in a wider awareness among GHB users and drug
policy makers about the health risks of GHB use. If confirmed that GHB is neurotoxic, this observation can be used in
objective counselling (information campaign*s) of recreational GHB users and the general public to explain that GHB is not
an innocent drug.
The main hypothesis to be tested is that one or more comas (*going out*) due to GHB overdosing is a prominent risk factor
of neurotoxic damage in distinct brain areas.
Specific research questions are:
a) Does exposure to high doses of GHB, known to induce coma result in structural brain damage according to MRI based
images (DTI)?
b) Is the effect of GHB comas dose-dependent i.e. do multiple experienced comas result in more damage than a single
experienced coma according to MRI based images (DTI)?
c) Does exposure to high doses of GHB, known to induce coma, impair memory and other cognitions as assessed via
validated psychological tests and MRI based images (DTI)?
d) Do the MRI findings match with psychological assessments of memory and other cognitions?
e) What are the clinical and socio-demographic characteristics of GHB users who repeatedly *go out*?

Study design

Open study using structured interviews, cognitive tasks, questionnaires, structural and functional brain scans.

Study burden and risks

The study will take place at the AMC in Amsterdam. The MRI scans that will be made while the subject is in the MRI scanner will be done by an experienced researcher. The study will take 2,5 hour for each test subject including 1 hour in the MRI scanner and including filling in several questionnaires.

For the patient groups (group 1 and 2) applies: the test subject will be picked up by car and brought back by car to the clinic where he resides by the researchers.

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

Males.
Age 18-40 years.

Expressed willingness to participate in experimental part at AMC (sign written informed consent).
Patients who experienced GHB coma (n<=27) are opgenomen in an addiction clinic for a GHB addiction during the time of the study.
Matched controls (n<=27) have used several illicit drugs in their lives but never used GHB.

Exclusion criteria

Epilepsy.
General anesthesia in the past two years due to a medical intervention.
Contra-indications for MRI: claustrophobia, presence of non-removable metal objects in the body.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-11-2014
Enrollment:	81
Type:	Actual

Ethics review

Approved WMO

Date:	25-07-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL49278.018.14