GHB neurotoxicity, brain damage due to GHB-induced coma in recreational 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** Will not start

Health condition type Structural brain disorders **Study type** Observational invasive

Summary

ID

NL-OMON37414

Source

ToetsingOnline

Brief titleGHB neurotox

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 en de nVWA

Intervention

Keyword: 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 and DTI-scanning of brain.

Study burden and risks

- 1. inclusion (various locations of hospitality industry).
- 2. group session about user profile. Location: (preferentially) Bonger Institute.
- 3. * day to fill in the questionnaires, and evaluate cognitive and memory function plus scanning (maximal 60 min. in the scanner).

Location: UvA Psychology, Roeterseiland. Subjects perform tasks inside and outside de scanner.

It is possible that contact moment 1 and 2 are combined.

Contacts

Public

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Scientific

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

- Age 18-40 years.
- Participants in groups 1-3 have a life time prevalence of GHB use of 25 times or more.
- Expressed willingness to participate to experimental part in AMC.

Exclusion criteria

- Subjects/patients with epilepsy.
- Heavy alcohol use (> 20 drinks) on at least one occasion in the last year.
- General anaesthesia in the last year.
- With respect to MRI imaging: claustrophobia; presence of non-removable metal objects, use of psychotropic

medication.

- . Pregnant or breast-feeding mothers
- Use of ketamine or speed is no exclusion criterion, but will be registered

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: Will not start

Enrollment: 60

Type: Anticipated

Ethics review

Approved WMO

Date: 10-07-2012

Application type: First submission

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 CCMO

ID

NL39337.018.11