

Press Release: European College of Neuropsychopharmacology

[Research shows club drug GHB associated with brain and cognitive changes.](#)

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Type of study: partially peer-reviewed/observational study/people

Scientists have discovered that regular use of the party drug GHB, and especially unconsciousness following GHB use, is associated with brain changes including negative effects on long-term memory, working memory, IQ, and higher levels of stress and anxiety. This work is presented at the ECNP conference in Barcelona, following partial peer-review publication*.

GHB (gamma-hydroxybutyrate), also known as 'G', 'liquid ecstasy' (etc), is a central nervous system depressant. It is used extensively in clubs, but also in private house parties. It produces an initial feeling of euphoria in users, but it can also cause sleepiness, and users easily tip into a coma. Some regular recreational users will often fall into a coma, which can require hospital treatment: it is not unusual that regular GHB users have experienced more than 50 GHB-induced comas. Despite its limited recreational use, GHB overdose and coma is the third** most common drug-related cause for emergency medical attendance in Europe, after heroin and cocaine, and this trend is increasing.

To understand the effects of GHB on the brain, a team of scientists from the Amsterdam UMC, recruited 27 GHB users who had experienced multiple GHB-induced comas (with a minimum of 4 comas), 27 GHB users who had never had a coma, and 27 volunteers who had used drug combinations (polydrug), but had never used GHB. Each person was asked to complete an adult reading test as proxy for IQ, anxiety, depression and stress questionnaires and they performed different neurocognitive tasks while undergoing a brain scan (fMRI, functional Magnetic Resonance Imaging).

There were two main findings. Firstly, GHB use, even in those who did not undergo a coma, was associated with alterations in identification of negative emotions. Secondly, the presence of GHB-induced comas, but not the use of GHB per se, was associated with lower IQ (despite similar educational level), and altered brain processes during verbal long-term memory and working memory. Additional analyses showed that these findings could not be attributed to group differences in the use of drugs other than GHB.

Lead researcher, Filipa Raposo Pereira, said

“Surprisingly little is known about the effects of GHB in humans, and as far as we know, these are the first functional MRI scans to gauge the effect of the regular GHB use and multiple GHB-induced comas. Our results indicate that there may be risks involved in regular GHB use. This is particularly relevant to regular users with multiple GHB-induced comas; we

found that these users show differences in cognition to either those who don't fall into a coma, or drug users who have never used GHB.

In an as yet unpublished study, we show that those with multiple GHB-induced comas also have 63% more stress and 23% more anxiety, and alterations in long-term memory. MRI scans also show that there are changes to the brain, with some areas showing altered brain activity and connectivity between memory-related cerebral pathways. These results show that there are brain and cognitive changes associated with multiple GHB-induced comas. Most users experience only the feeling of elation followed by drowsiness or sleep, so they don't see that there might be any negative effects. This work indicates that might not be the case”.

Commenting, Professor David Nutt (Imperial College, London) said:

“This research is interesting and recreational users should be made aware of these findings. They probably reflect periods of hypoxia due to excessive GHB concentrations in brain. When GHB is used in a regulated fashion as a medicine – for example, for narcolepsy – there doesn't appear to be a similar risk, so patients on this medicine should not worry”.

Professor Nutt was not involved in this research, it is an independent comment.

Study limitations

According to Filipa Raposo Pereira “There are a couple of points to note about her study. Firstly the study was conducted exclusively in male volunteers, so the results may not be generalizable to female GHB users. A second thing to bear in mind is that we have found an association between GHB use and brain and cognitive changes, so we need to be careful with causal interpretations; we would need a different type of study to confirm this”.

*This work includes new preliminary material, not presented elsewhere. It includes research from the peer-reviewed papers: *Adverse effects of GHB-induced coma on long-term memory and related brain function*, Filipa Raposo Pereira et al (published in *Drug and Alcohol Dependence*, Sept 2018) <https://doi.org/10.1016/j.drugalcdep.2018.05.019> and *Effect of GHB-use and GHB-induced comas on dorsolateral prefrontal cortex functioning in humans*, Filipa Raposo Pereira et al (published in *Neuroimage: Clinical*, Sept 2018) <https://doi.org/10.1016/j.nicl.2018.09.022> Other parts of the work have not yet been published.

**See European Drug Report, 2017, <http://www.emcdda.europa.eu/system/files/publications/4541/TDAT17001ENN.pdf> Figure 3.8.

Background information on GHB (from the European Monitoring Centre for Drugs and Drug Addiction, 2008) can be found at: http://www.emcdda.europa.eu/system/files/publications/505/TP_GHB_and_GBL_107300.pdf

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Notes for Editors

Please mention the ECNP Congress in any story resulting from this press release.

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The European College of Neuropsychopharmacology (ECNP)

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe. Website: www.ecnp.eu

The 31st annual ECNP Congress takes place from 6th to 9th September in Barcelona. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting between 4,000 and 6,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: <https://2018.ecnp.eu/>

Conference Abstract P718: The influence of GHB-use and GHB-induced coma on affect and the affective network

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Introduction: GHB is a popular drug of abuse which despite its relative low prevalence of use, it is currently the fourth most common drug of abuse presented at emergency rooms [1]. The observed increase in emergency rooms attendances is mainly associated with the presence of GHB-induced comas and paralleled by equally growing numbers of GHB users who seek treatment for their GHB addiction [1][2][3]. Moreover, GHB has been seen to increase anxiety and decrease emotional discrimination capacity in rodents[4]. Animal studies have also shown that regular use of GHB is associated with oxidative stress incident in highly sensitive brain areas such as the hippocampus or amygdala [5]. However, little is known about the effects of GHB-use and GHB-induced comas on affect regulation in humans.

Aims: Here we tested the following hypothesis: (a) GHB users with multiple GHB-induced comas report more negative affect and show altered amygdala and hippocampus activity and functional connectivity when compared with the GHB users without GHB-induced comas and polydrug users who never used GHB; (b) GHB users without GHB-induced comas report more negative affect and show altered amygdala and hippocampus activity and functional connectivity when compared with the polydrug users who never used GHB.

Method: We recruited 27 GHB users with ≥ 4 GHB-induced comas (GHB-Coma), 27 GHB users who never had a GHB-induced coma (GHB-NoComa) and 27 polydrug users who never used GHB (No-GHB). Participants completed self-report questionnaires to assess negative affect, and performed an emotional face matching task during functional magnetic resonance imaging (fMRI) known to probe amygdala and hippocampus activity.

Results: The findings of the current study suggest an association between exposure to GHB and disruptions of the affective network, which are largely driven by the presence of multiple GHB-induced comas and not so much by GHB use per se. When considering the effect of multiple GHB-induced comas, the GHB-Coma group reported higher levels of stress and anxiety, showed a decrease in hippocampus activity and an increase in functional connectivity between the hippocampus and the left fusiform gyrus and a cluster located on the left temporal-parietal-occipital junction with three peak regions on the angular gyrus, the middle occipital gyrus and on the middle temporal gyrus when compared with the two other groups. When considering the effect of GHB use per se, the GHB-NoComa group showed decreased functional connectivity of the hippocampus with the amygdala in comparison with the No-GHB group.

Conclusion: These results suggest that GHB use is not without risk. Society is faced with increasing numbers of emergency attendances related to GHB overdose and individuals seeking treatment for GHB dependence. This suggests that awareness campaigns directed at recreational GHB users are warranted to highlight the lasting adverse effects of GHB, despite the absence of immediate apparent side effects.

References

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[5] Pedraza C, Belén García F, Navarro JF, 2009. Neurotoxic effects induced by gammahydroxybutyric acid (GHB) in male rats. *12*, 1165–1177.

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