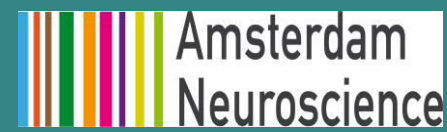


Effects of gamma hydroxybutyrate (GHB) induced coma on long-term memory and brain function



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Introduction

- GHB is a drug of abuse that may induce into temporary coma (GSC=3)^[1]
- Even though regular GHB users might experience multiple comas, they consider its use, safe ^{[2][3]}.
- Animal studies suggest that GHB can induce oxidative stress in the hippocampus and consequent memory impairments ^[4].
- Human self-reported surveys likewise suggest that regular GHB use leads to memory impairments^[5].

Effects of regular GHB use on long-term memory and underlying regions
NOT YET KNOWN

We used fMRI to answer the following:

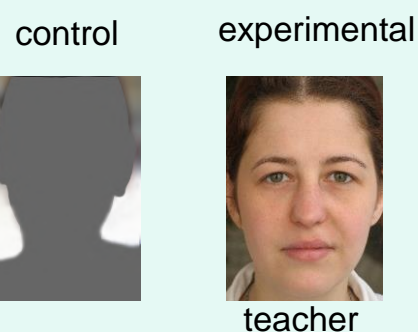
1. Does GHB use affect long-term memory in humans?
2. Do potential adverse effects result from GHB use, and/or GHB induced coma ?

Methods



27 GHB users >4 times coma (**GHB-Coma**)
 27 GHB users, never went into coma (**GHB-NoComa**)
 27 polydrug user controls (**No-GHB**)

- MRI data (Phillips 3.0T Ingenia MR scanner):
T1-weighted image → [TR/TE=7.0ms/3.2ms; 1x1x1mm isotropic voxels]
T2*-BOLD contrast image → [TR/TE=2000ms/27ms; 80 × 78matrix; voxel; 3x3.08x3]
- fMRI data preprocessing → **SPM12**
- Voxel-wise statistics → FWE rate corrected p<0.05 for multiple comparisons at cluster level p<0.001
 -whole brain
 -hippocampus ROI (WFUpickatlas defined).
- Group differences → **ANOVA**
- Functional connectivity (gPPI) → seed region = **Hippocampus**
- CANTAB recognition memory tests
 -**Verbal recognition memory**
 -**Spatial recognition memory**
- Verbal IQ → Dutch version of adult reading test (**DART**)
- fMRI **face-profession pair association memory** task → 2 conditions

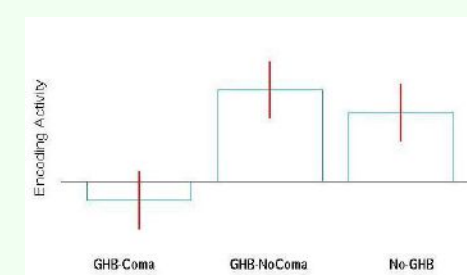


- **Experimental condition**
 -Encoding of face-professions pairs
 -Easy /difficult to establish face-profession pair
- **Control condition**
 -Shaded faces
 -whether right/left ear was closer to the bottom of the picture

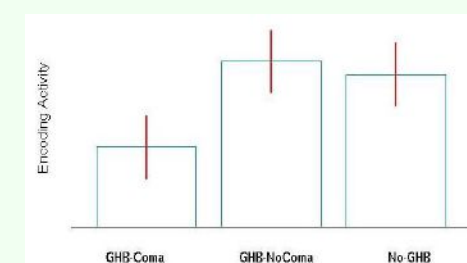
Results

- Verbal IQ → ↓ in GHB-Coma vs. GHB-NoComa and No-GHB groups
- Verbal recognition memory performance → ↓ GHB-Coma vs GHBNoComa and No-GHB groups
- Spatial recognition memory performance → No differences were found between groups.
- fMRI encoding activity → GHB-Coma < GHB-NoComa + No-GHB

Left lingual gyrus

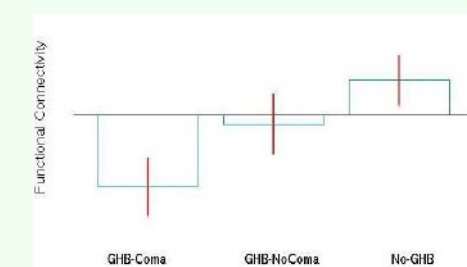
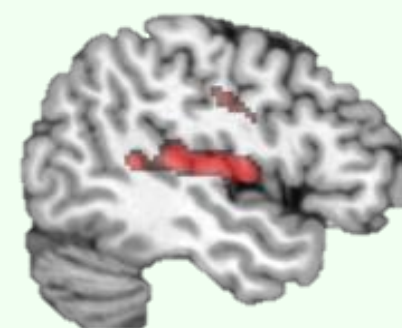


Left hippocampus



- Hippocampal Functional connectivity → GHB-Coma < GHB-NoComa + No-GHB

Superior Temporal Cortex regions (superior temporal gyrus, rolandic operculum, insula)



Conclusion

- GHB induced coma has a detrimental effect on long-term memory processing and performance.
- Likely not GHB use per se, but the multiple comas experienced by regular users induce these adverse effects

[1] van Laar, M., van Ooyen-Houben, M.M., Cruts, A.A., Meijer, R.F., Croes, E.A., Ketelaars, A.P. & Van der Pol, P.M., 2016. Nationale Drug Monitor: Jaarbericht 2015. Utrecht: Trimbos-instituut 2016

[2] European Monitoring Centre for Drugs and Drug Addiction, 2016. European Drug Report 2016: Trends and Developments, ed. Publications Office of the European Union, Luxembourg pp. 45-46;64

[3] Korf, D. J., Nabben, T., Benschop, A., Ribbink, K., & van Amsterdam, J. G., 2014. Risk factors of gamma-hydroxybutyrate overdosing. European Addiction Research, 20 (2), 66-74.

[4] Pedraza, C., Garcia, F. B., & Navarro, J. F., 2009. Neurotoxic effects induced by gamma-hydroxybutyric acid (GHB) in male rats. International Journal of Neuropsychopharmacology, 12(9), 1165-1177.

[5] Miotto K, Darakjian J, Basch J, Murray S, Zogg J, Rawson R. Gamma-hydroxybutyric acid: patterns of use, effects and withdrawal. Am J Addict 2001. DOI:10.1080/105504901750532111.

This study does not present any potential conflict of interest