Alcohol-induced changes in the hemodynamic response function in event-related fMRI : evidence for slow down of neurovascular coupling

M. Luchtmann[1], T. Moench[1], M. Hollmann[1], K. Jachau[2], S. Boettcher[2], and J. Bernarding[1]

[1]Institute for Biometrics and Medical Informatics, Otto-von-Guericke University of Magdeburg, Magdeburg, Germany, [2]Institute of Forensic Medicine, Otto-von-Guericke University of Magdeburg, Magdeburg, Germany

Introduction

Alcohol is a frequently and worldwide consumed psychoactive drug. Social behaviour as well as sensory perception and motor output may be significantly altered. Only few BOLD-imaging studies were performed which found significant changes between sober and alcohol conditions [1,2]. However, BOLD-related studies may suffer from the vasoactive effects of ethanol if using SPM's canonical HRF. In this study, we determined the individual hemodynamic response function (HRF) before and after intake of ethanol. Alcohol led to a significant drop of amplitude. In both motor cortices (MC) and the visual cortex (VC) this drop was counterbalanced by an increased full width at half maximum (FWHM) leading to an overall unchanged positive area under the curve, while in the supplementary motor area (SMA) the area under the curve was significantly reduced. This may be tentatively interpreted as a slowed down but on the whole unchanged neurovascular coupling in MC and VC while SMA was significantly altered. The findings lead also to the conclusion that significant changes in the HRF have to be taken into account when using statistical methods for evaluation of activated brain areas to avoid false positive reduction in the significance after intake of vasoactive substances.

Methods

Fifteen healthy and right handed volunteers (8 male, 7 female, 22.9 ± 1.3 years) were examined after written consent according to the local ethics committee. A test/re-test design was used to examine the effects of ethanol administration in each individual, i.e., all volunteers were examined before and after ingestion of alcohol. Alcohol was administered by mixing pure ethanol into 400 ml orange juice. The amount of alcohol was determined to reach an estimated maximum alcohol concentration of 1‰. Volunteers did not eat 6 hours before alcohol consumption. To evoke cerebral activities a visual event related paradigm with stimulus duration of one second was chosen, followed by 19 seconds black screen. The paradigm consisted of a flickering checkerboard (8Hz) and volunteers had to perform fingertapping for 1 sec as soon as the checkerboard appeared. The stimulus was repeated 60 times. FMRI experiments were conducted at 3 T (Magnetom Trio, Siemens, Germany). A GE EPI-BOLD sequence with TR=0.5s and TE=30ms was used to acquire functional images with 7 slices (6 mm) and a 64x64 matrix. Voxel size was 3x3x6 mm^3. All functional images were realigned with SPM2. To compare the HRF between sober and alcoholic conditions, regions of interests (ROI) were defined in each subject using SPM2 to depict the regions of activity. In the second step, the HRFs of these regions were averaged within the VC as well as in both motor areas (LMC/RMC) and the supplementary motor area (SMA) using custom-made software. The averaged HRF was fitted with a triple gamma variat function to account for the initial dip, the positive overshoot, and the negative undershoot. To estimate changes in the HRF between the positive parts of the fit, curves were analyzed regarding to amplitude, FWHM, and time to peak (TTP). As a parameter for the overall BOLD effect the area under the curve (AUC) of the positive signal part was calculated.

Results

Subjects reached a mean blood alcohol concentration of 0.82‰ (determined in venous blood samples, using an alcohol dehydrogenase based enzyme assay and a gas chromatographic method). The baseline signal did not differ significantly in the alcohol vs. sober condition. In each ROI the HRFs (averaged over all subjects) showed a clear change of amplitude, TTP, and FWHM after alcohol intake (fig. 1). The decrease of the amplitude was significant with a mean reduction between 20.7% and 28.3%, whereby the strongest amplitude decrease was found in the SMA. TTP as determined from the fit function also exhibited a delay under alcoholic conditions of up to 0.6 sec. The FWHM increased under alcohol conditions in both MC and the VC while the increase in the SMA was not significant. The increased FWHM counterbalanced the decreased amplitude in both MC and the VC leading to unchanged AUCs. However, in the SMA the AUC was reduced significantly under alcohol conditions, in average 21.8%. Interestingly, the negative undershoot was also less depicted under alcohol conditions.

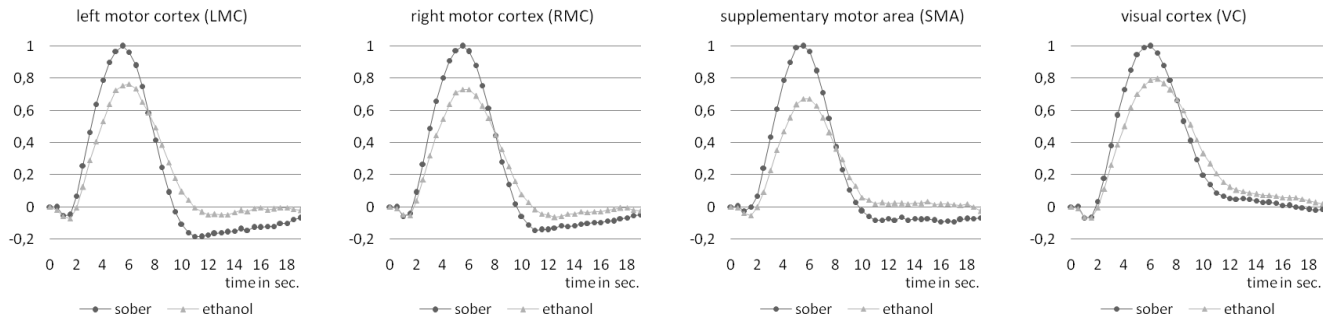

Fig. 1: HRFs averaged over all subjects before (black) and after (grey) alcohol intake. For comparison all HRF without alcohol were scaled to 1.

Conclusion

The study presents new results that may support the understanding of alcohol effects on human neurophysiology. It is well accepted that the BOLD HRF reflects the complicated interaction between increased regional cerebral blood flow (rCBF), neuronal activity, and oxygen extraction. However, depending on the local vessel architecture and other yet unknown parameters regions may be susceptible in a different manner to alcohol intoxication effects, e.g. as shown in the SMA. The stronger reduction of the BOLD in the SMA may be a hint for the known effect of alcohol to impair initiation of complex motor actions. These results also have widespread consequences to other studies, which observe cerebral effects of vasoactive substances.

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