Arterial Spin Labeling in Young Adults during Alcohol Infusion

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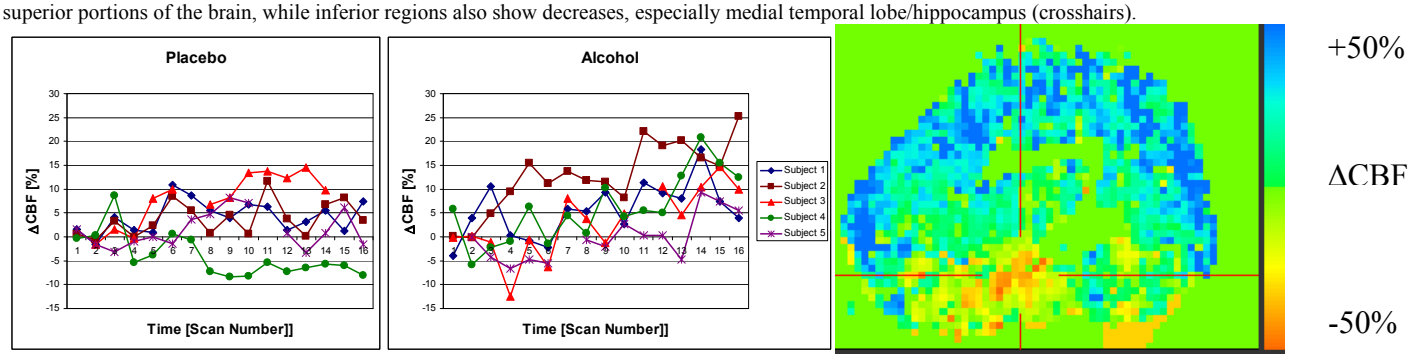
Introduction: Within a larger Study of effects of alcohol consumption on Young Adults, the influence of alcohol on the brain is studied on a number of levels including behavior, fMRI tasks, and perfusion. The perfusion measurements may clarify confusing findings in the literature on the effects of alcohol on the brain and will aid in the interpretation of potential differences in BOLD fMRI signals between alcohol and placebo conditions. A SPECT study [1] found that oral alcohol administration increased total cerebral blood flow (CBF) by 4% but also reported a negative correlation with blood alcohol levels. A Xenon-133 study [2] reported an increase in global CBF of 12% with a low dose of ethanol (0.7 g/kg) and 16% with a high dose (1.5 g/kg) with the strongest effects in the prefrontal lobe for the low dose and in the temporal lobe with the high dose. A recent ASL study 2 hours after alcohol administration only found CBF changes in the cerebellum [3].
Within our study, subjects are tested at ages 18 and 20. MRI is conduced only at age 18. The protocol includes Arterial Spin Labeling (ASL) scanning during the infusion of alcohol or placebo to measure perfusion and bolus arrival time (BAT). We are presenting here initial findings from the first five subjects.

Methods: Subjects were studied on two different days. During one session, an ethanol infusion was administered to reach a target blood alcohol level of 0.06% 15min after the start of the infusion. In the other session, a placebo saline solution was administered. ASL data was acquired before and during the infusions using a pulsed ASL sequence with a 3D GRASE readout [4] with ¾ slice partial Fourier was utilized with TR /TE /Flip (refocusing pulse)/#slices /gap /BW /Turbo Factor = 3s /18ms /130° /26 /0 /20 2790Hz/Px with 5x5x4 mm voxels. ASL series with inversion/inflow times TI from 300ms - 2500ms and from 400ms – 2600ms with 200ms increments are alternated as a compromise between resolution in infusion time and inflow time. Two series are acquired before the start of the infusion, 12 series during infusion, and two series after reaching the target level. The acquisition time for one series with selective and non-selective saturation images is 1:12 min. One selective saturation image from each series with TI = 2000ms or 2100ms from both scan sessions is used for motion correction using SPM8. The determined transformation matrices are applied to all difference images. Images are normalized to MNI space and resampled to a 3x3x3mm resolution. A 1-compartment perfusion model [5] is applied to the difference data for each series in gray matter voxels only with T1(blood)=1500ms, T1(tissue)=1300ms, λ=0.9 and a bolus length=1s [6]. The magnetization of arterial blood is determined as half the average over all series of the signal from the voxel with the maximum difference signal after correcting for T1 decay. Perfusion and BAT were fitted. Total gray matter (GM) perfusion and BAT changes with respect to the average pre-infusion values were calculated and correlated with infusion time. A map of average perfusion changes over 5 subjects was calculated.

Results: Time courses of global perfusion changes are shown for 5 subjects. The correlation coefficients R between ΔCBF and scan number were (0.28, 0.41, 0.84, -0.68, 0.21) for the placebo and (0.55, 0.83, 0.75, 0.78, 0.71) for the alcohol infusion. In 4 of 5 subjects the correlation is much higher for the alcohol condition. These differences could not be seen in the BAT measurements. The observed increase in total perfusion ranged from approximately 5-25 %. As an example for the group average local distribution of perfusion a sagital slice at MNI coordinate 39mm left at time point 16 of the alcohol condition is shown. Increases in perfusion are seen in superior portions of the brain, while inferior regions also show decreases, especially medial temporal lobe/hippocampus (crosshairs).



Discussion and Conclusion:
The initial analysis indicates that alcohol increases global perfusion in agreement with the Xenon study[2]. However, local perfusion in specific areas such as the medial temporal lobe decreases, which has not yet been reported to our knowledge. No effects were seen for the BAT. These preliminary results indicate that baseline blood flow cannot be assumed to be constant for studies that investigate activation changes under the effect of alcohol. Techniques that rely on a vascular response such as BOLD fMRI may require spatially dependent correction. It is not clear whether perfusion changes correlated with neural activity and what the driving mechanisms are behind different local responses.
Future work will include the determination of the power of the changes using a general linear model. Using the ASL measurements, correlations between the perfusion response and behavioral (e.g. visually guided saccades) or fMRI measures (e.g. stop signal task response) can be investigated.

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Ref.: [1] Schwartz, J.A. et al. (1993), Alcohol Clin Exp Res 17(6):1119; [2] Sano M. et al. (1993),J Stud Alcohol 54(3):369; [3] Khalili-Mahani, N. et al. (2010) ISMRM, Stockholm; [4] Guenther, M. et al. (2005), MRM 54:491; [5] Buxton, R.B. et al. (1998), MRM 40:383; [6] MacIntosh, B.J. et al. (2009), MRM 63:641.