The Dynamics of Ethanol Uptake in the Brain by Whole Brain MRSI, ADC Mapping and BOLD fMRI

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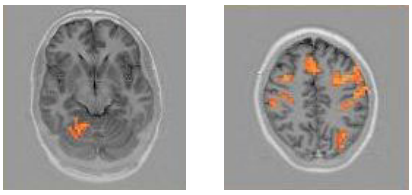
Introduction The effects of ethanol on brain function and metabolism are complex and have broad implications for biology, health, and society. Our purpose was to dynamically assess regional changes in detectable ethanol, ADC and BOLD motor response during acute alcohol intoxication. Previous dynamic MRSI studies, such as that by Hetherington *et al.* (1) were limited to single slices. In this study, we combine a fast multi-slice multi-echo MRSI methodology (TSI) (2) at 3T with BOLD fMRI and ADC measurements in order to provide a more comprehensive picture of acute alcohol intoxication.

Methods MRI and MRSI data were acquired from three normal adult male subjects using a 3T Philips Intera whole body system. Following initial baseline data acquisition, subjects drank a 1% bodyweight dose of ethanol (40% vodka diluted to 250ml with cordial). Blood alcohol content was monitored between data acquisitions using a breath analyzer fitted with an extension tube to reach the subject within the magnet bore. Multi-slice TSI data (6 slices, 20x20 voxels each, TE = echo spacing = 144 ms, echo train length = 6, acquisition time = 11 minutes) were acquired using a T/R-Head coil at t = 0, 29, 56, 86 and 126 min after intake. Auxiliary imaging studies were interleaved with the dynamic MRSI acquisitions to assess motor coordination and performance as a function of intoxication: (a) fMRI was acquired during a simple visually-guided right hand coordination task to assess changes in BOLD responses in the cerebellum and motor cortex (b) whole brain ADC maps. All MRSI spectra were analyzed using both naïve peak integration and a four-resonance model with an adaptive baseline (3).

fMRI at baseline (t = 0 min) (BAC = 0)



fMRI at t = 54 min (BAC = 0.69%)

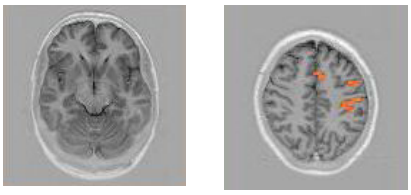


Figure 1: Two of 12 fMRI slices demonstrating the loss of BOLD response in cerebellum and motor cortex at peak intoxication

Results All subjects demonstrated a rapid rise in blood alcohol concentration (BAC) over 40 minutes to a maximum of approximately 0.65‰ from breath analysis. Dynamic TSI reveals the differential accumulation of visible ethanol (methyl triplet at 1.2ppm) in the cerebellum, cerebral cortex and CSF (Figures 2 & 3). The rise of detectable ethanol within the ventricles and CSF spaces is particularly pronounced. Regional differences in ethanol uptake kinetics between the cerebellum and cerebrum are also noted, but were not observed in all subjects. fMRI showed almost total loss of BOLD response at peak intoxication (Figure 1) but also demonstrated inter-subject differences which did not necessarily correlate with level of intoxication from breath analysis. ADC values in cerebrum and cerebellum showed slight, but significant reductions, on the order of 1-5% during peak intoxication.

Discussion Multi-slice, multi-echo TSI has sufficient spatiotemporal resolution to map the uptake kinetics of ethanol across a significant fraction of the adult human brain and can be interleaved with other functional experiments to provide a more comprehensive, multi-modal analysis of intoxication. The question of ethanol visibility in these images is an important one, since the differences in detected ethanol between the CSF spaces and parenchyma are striking. Further experiments specifically designed to quantify MRSI visible alcohol will be required. The fMRI results are consistent with previous reports of reduced BOLD response in the visual and auditory cortex during intoxication (4,5). ADC changes suggest a physiologic effect but the mechanism is unsettled. Potential pathophysiologic explanations include, but are not limited to: direct alcohol toxicity, recompartmentation of water secondary to systemic dehydration and ethanol induced changes in cell membrane properties.

References

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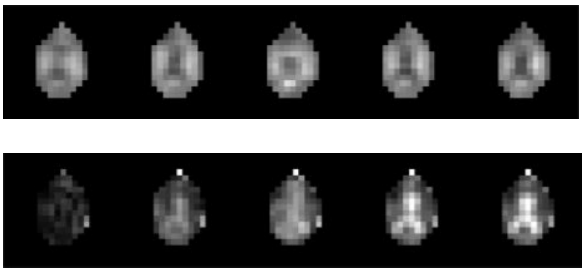

Figure 2: Masked spectral integrals for NAA and ethanol from one TSI slice demonstrating marked differences in detectable ethanol uptake dynamics between CSF and parenchyma.

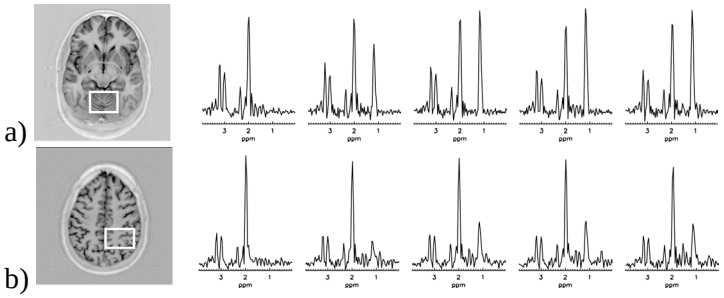

Figure 3: Representative time-courses (l-r) of averaged TSI spectra from (a) a region of the superior cerebellum and (b) superior cerebrum demonstrating regional differences in the detectable ethanol methyl resonance at 1.2ppm.