Binge Ethanol Induced Structural and Neurochemical Changes in the Rat Brain Detectable at 3T

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Introduction
Human and animal studies indicate that chronic alcohol intoxication resulting in dependence damages the brain. That only a few days of intoxication can also lead to brain insult thus far has only been demonstrated in vitro in animals1. Binge drinking in humans is associated with high blood alcohol levels (BALs, e.g., over 500mg/dL) modeled in rodents with intragastric injections of 15% ethanol (EtOH) every 6h for 4d. In rodents, this intoxication protocol leads to neuronal damage in corticolimbic areas including perirhinal and entorhinal cortices and hippocampal dentate gyrus2. Our current study was conducted to provide in vivo structural and biochemical magnetic resonance (MR) evidence in rodents for brain damage resulting from binge EtOH exposure and potential recovery with abstinence.

Methods
The study group consisted of 19 wild-type, male, Wistar rats weighing 264.04±3.99g at the baseline scan. After the baseline scan, 11 rats were assigned to the EtOH group and received a loading dose of 5g/kg EtOH via oral gavage, then 3g/kg every 8h for 4d, for a total average cumulative EtOH dose of 45.1±1.74g/kg. Control (Con) animals received equivalent doses of 5% dextrose. The EtOH animals had average BALs of 257.84±13.18mg/dL, peak BALs of 417.16±20.68mg/dL, and lost 16% of their body weight (p=.0065) after 4d of EtOH exposure. Animals were scanned after EtOH exposure within 10h of their last dose (post-binge scan), and again after 7d of abstinence from EtOH (recovery scan). MR data were acquired on a 3T GE Signa MR scanner equipped with a high-strength insert gradient coil (500mT/m, 1800 mT/m/ms) and a custom-built RF coil (2). MR spectroscopy was performed with a CT-PRESS sequence (\(T_E=139\)ms, \(T_1/2=0.8\)ms, \(n=129\), TR=2s, 6 averages). A second acquisition without water suppression (\(T1/2=6.4\)ms, \(n=17\)) was performed to determine tissue water content used as a reference for metabolite quantification.

Results
MR spectroscopy, in vivo microscopy, and white matter diffusiontensor imaging (DTI) were used to detect neurochemical, biochemical, and structural changes in the EtOH group. Biochemical changes detected at 3T were compared with in vitro (1H-NMR of rat brain) and in vivo (13C-MRS of mouse brain) studies in the literature. A group-by-time interaction (F(2,34)=10.79, \(p<.0001\)) was computed images was used to calculate lateral ventricular cerebral spinal fluid (CSF) volume across a defined region of interest in 5 axial slices. A 2-group, repeated-measures ANOVA yielded a group-by-time interaction (F(2,34)=10.79, \(p<.0001\)), indicating that cerebral spinal fluid (CSF) volume was modified by EtOH exposure. At the post-binge scan, CSF volume in the EtOH group had significantly increased from baseline (t(17)=3.9, \(p<.0029\)), and was higher than the Con group at the post-binge scan (t(10)=3.9, \(p=.0029\)) and was higher than the Con group at the post-binge scan (t(10)=3.9, \(p=.0029\)). After binge EtOH exposure, the baseline post binge recovery scan (t(10)=3.9, \(p=.0029\)), and was higher than the Con group at the post-binge scan (t(10)=3.9, \(p=.0029\)). After binge EtOH exposure, the EtOH group had lower NAA (t(17)=5.23, \(p=.0001\)) and tCr (t(17)=3.24, \(p=.0048\)) and higher Cho (t(17)=3.48, \(p=.0002\)).

Discussion and Conclusion
We have previously used MR methods to detect the effects of chronic (24wks) EtOH exposure on the wild-type Wistar rat brain and demonstrated that BALs of -293mg/dL result in ventricular expansion and increases in Glx, Glu, and Glu. The current study was designed to determine whether brain changes induced by acute binge EtOH exposure could be detected using in vivo MR methods. In agreement with in vitro findings1 and our chronic EtOH experiment, binge EtOH exposure results in brain insult detected in FSE images as an increase in ventricular CSF volume. That CSF volume returns to baseline after 7d of abstinence supports the concept of the brain’s ability to recover from acute EtOH damage. In agreement with studies in recently detoxified human alcoholics, lower NAA levels in the frontal lobes generally resolve with longer abstinence. The decline and recovery of NAA argues for a transient effect of EtOH on neuronal integrity. Corroborating previous evidence, EtOH exposure is associated with an increase in Cho that may be interpreted as inflammation, demyelination, or abnormally high glial density. To our knowledge, this study is the first to provide evidence of EtOH effects on tCr. The EtOH induced decrease in tCr may be interpreted as a compromise in the brain’s energy reservoir (in the form of ATP). Recovery of tCr levels in the absence of the causative agent again argues for transient effects on the brain of binge EtOH exposure.

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References