Effects of Binge Acute Ethanol Intoxication on Cerebral Neurochemical Profile in Rats: Evidence from In Vivo Proton Magnetic Resonance Spectroscopy

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Introduction:

Binge alcohol consumption (heavy consumption of alcohol over a short period) is associated with various adverse consequences, including increased risk of developing alcohol dependence [1]. In particular, binge alcohol intoxication causes cerebral metabolite alterations and impairments [2]. In this study, the cerebral metabolite changes in vivo were quantitatively assessed in binge ethanol-intoxicated rats by using a 4.7-T proton magnetic resonance spectroscopy (^{1}H MRS).

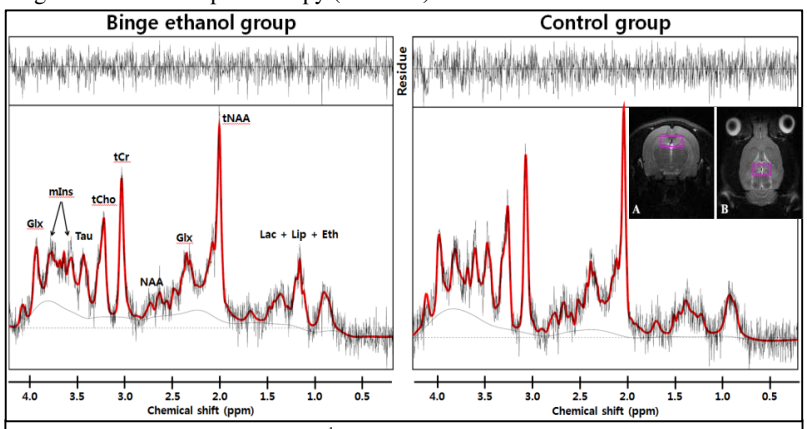

Fig. 1. Representative in vivo 4.7-T ^{1}H MRS spectra of the hippocampal region of a binge ethanol group rat (left) and control group rat (right). The original spectra and fitted LCModel spectra are represented by the black and bold-red lines, respectively. Inset are the T2-weighted images (A: axial; B: coronal) of the control rat brain. The rectangular boxes indicate the position of the volume of interest (VOI, 4 × 1.6 × 3 mm^3).

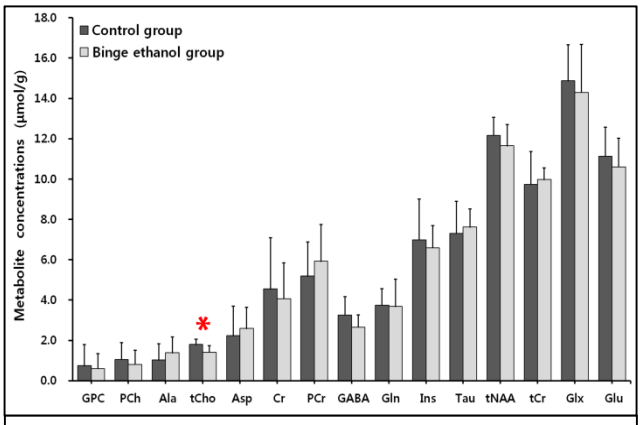

Fig. 2. Concentrations of cerebral metabolites in the hippocampal region, which were quantified by using an LCModel. The metabolite concentrations were expressed in micromoles per gram (μmol/g). Vertical lines on each of the bars indicate the standard deviation of the mean concentration values. Significance level: *, $p < 0.05$.

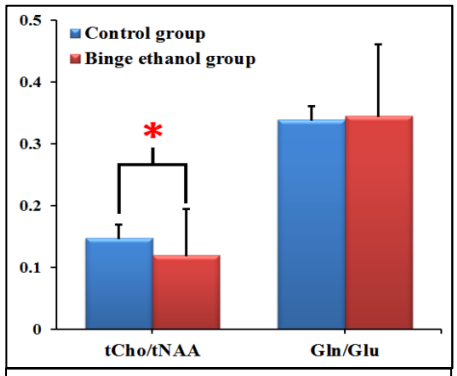

Fig. 3. Bar diagram showing the significance levels of total choline/total N-acetylaspartate (tCho/tNAA) and Glutamine/Glutamate (Gln/Glu) ratios between the control and the binge ethanol group rats. Vertical lines on the bars indicate the standard deviation of the mean values. Significance level: *, $p < 0.05$.

Materials and Methods:

In this study, thirteen 8-week-old, male Sprague–Dawley rats were used and divided into 2 groups (control group: n = 6; binge ethanol group: n = 7). The 7 binge ethanol group rats received an initial dose of 5 g/kg (30% w/v solution) via oral gavage method, followed by a maximum dose of 2 g/kg (25% w/v solution) every 8 h (at 1400, 2200, and 0600) for 4 days. The 6 control group rats simultaneously received equal volumes (about 3.55 ml) of normal saline (at 1500, 2300, and 0700). Oral gavage ethanol was administered based on the body weight, according to Majchrowicz binge alcohol protocol [3]. After 4 days of oral gavage, in vivo scanning was performed on all the animals by using a 4.7-T Bruker BIOSPEC. The volume of interest (VOI, 6 × 2 × 3 mm3; volume: 36 μL; Fig. 1 [A and B]) was positioned in the hippocampus based on multi-slice T2-weighted images obtained using Rapid Acquisition with Relaxation Enhancement (RARE) sequences (TR/TE = 5000/90 ms; number of acquisitions = 4; slice thickness = 1.0 mm). Thirteen water suppressed ^{1}H MRS spectra were acquired using Point-Resolved Spectroscopy (PRESS) sequences (TR/TE = 4000/20 ms; number of acquisitions = 384; number of data points = 2048). In addition, the unsuppressed water signal was acquired (TR/TE = 4000/20 ms; and number of acquisitions = 16). All spectra were analyzed using LCModel with simulated basis-set.

Results:

Figure 1 shows the representative fitted spectra from the hippocampus of the binge ethanol and control group rats. Our results showed that total choline (tCho; phosphocholine + glycerophosphocholine [GPC + PCh]) concentrations were significantly lower ($p = 0.038$) in the binge ethanol group than that in the control group (Fig. 2). Moreover, the tCho/total N-acetylaspartate (tNAA: NAA + N-acetylaspartylglutamate [NAAG]) ratios were significantly lower ($p = 0.043$) in the binge ethanol group than that in the control group (Fig. 3). However, Glutamine/Glutamate ratios showed no significant differences between the 2 groups.

Discussion:

This study aimed to quantitatively assess the cerebral neurochemical effects in the hippocampal region in binge ethanol intoxicated rats. Significantly reduced choline-containing signals could be observed in alcohol-dependent patients [4]. *Seitz et al.,* reported that the choline/creatine (Cho/Cr) ratios were significantly decreased in alcohol-dependent patients than that in healthy subjects. *Chang et al.,* reported also that the choline-containing compound is a marker of cell membrane turnover (from synthesis and degradation) [5]. Moreover, previous studies have shown that reduced choline-containing signals may reflect altered cell turnover rate of phosphatidylcholine and other phospholipids reflecting an adaptive mechanism of the brain [6,7]. According to our findings and from results in previous studies, significantly low tCho concentrations and tCho/tNAA ratios may indicate the cell membrane turnover abnormalities of phosphatidylcholine and changed adaptive mechanism in the hippocampus of binge ethanol intoxicated rats. Thus, we provide quantitative in vivo evidence that binge ethanol exposure causes cerebral neurochemical profile changes in rats, in the hippocampal region.

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