Assessment of neurochemical alterations in rats exposed to long-term alcohol treatment

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Purpose: Chronic alcohol consumption causes a serious public health problem and can lead to the various brain disorders in the human [1]. Previous studies have investigated the cerebral metabolic alterations in chronic adolescent alcohol dependent patients [2,3]. However, cerebral metabolism of the chronic adolescent alcohol consumption is affected by many factors, such as the period of alcohol use, the pattern of drinking and types of alcohol [4]. Thus, the chronic adolescent alcohol consumption study is necessary to more quantitatively investigate the metabolic changes in an animal model. Therefore, the purpose of this study was to assess the neurochemical changes induced by long-term alcohol exposure in the adolescent rat.

Materials and Methods: Twenty, six-weeks-old, male, Sprague-Dawley rats were used in this study. All animals were divided into two groups (control group: N=9, ethanol group: N=11), and fairly fed with the Lieber-DeCarli ethanol and control liquid diets for 10 weeks. After 10 weeks, in vivo proton spectra were acquired from the twenty animals using 4.7 T BIOSPEC MR scanner (Bruker Medical GmbH) with a 400-mm bore magnet and 150 mT/m actively shielded gradient coils. All rats were anaesthetized by a gas mixture of O2 (50%) and N2O (50%) with 4-6 % isoflurane inhalation. The VOI (4 x 1.6 x 3 mm, volume: 19.2 ul) was positioned based on multislice axial T2-weighted MR images obtained using RARE sequence (TR/TE=5000/90 ms, NEX=4) as shown in Fig. 1. The VOI was adjusted to minimize intracranial lipid contamination. Water suppressed 1H-MRS spectra were acquired using PRESS sequence with (TR/TE=4000/20 ms, NEX=384, number of data points=2048). The unsuppressed water signal was also acquired. Spectra were analyzed using LCModel software.

Results: The representative in vivo 1H MRS spectrum obtained from the rat frontal cortex is shown in Fig. 2. Figure 3 shows that the metabolite concentration levels of the GPC+PCh (p = 0.005) were significantly increased in the ethanol treated group compared to control. However, Ins (p = 0.031) and Glx (p = 0.026) concentrations levels were significantly decreased. Fig. 4 indicate that the (GPC+PCh)/NAA ratio levels (p = 0.001) were significantly increased in the ethanol group. However, Gln/Glu ratio levels had no significant differences between two groups.

Discussion: This study was aimed to investigate the cerebral neurochemical effects of the long-term alcohol exposure on the adolescent rat frontal cortex. Our results show that the GPC+PCh, Ins, Glx concentrations and (GPC+PCh)/NAA levels were significantly differed in the frontal cortex of the ethanol group, compared to the control group. In particular, GPC+PCh concentrations and (GPC+PCh)/NAA levels showed the most significant differences in the ethanol group. Significantly increased GPC+PCh concentrations and (GPC+PCh)/NAA ratio levels may indicate that increased turnover rate of phosphatidylycholine and/or changed adaptive mechanism in the frontal cortex of the long-term alcohol exposure adolescent rats [5]. Therefore, increased GPC+PCh concentrations and (GPC+PCh)/NAA ratio levels of the frontal cortex might be utilized as the key marker in chronic adolescent alcohol intoxication.

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