Preliminary Observation of Dynamic Changes in Alcohol Concentration in the Human Brain with Proton Magnetic Resonance Spectroscopy on a 3T MR Instrument

Hitoshi KUBO1**, Masafumi HARADA2, Minoru SAKAMA3, Tsuyoshi MATSUDA4, and Hideki OTSUKA1

Departments of 1Medical Imaging, 2Radiology, and 3Radiological Science, Institute of Health Biosciences, The University of Tokushima Graduate School
3–18–15, Kuramoto-Cho, Tokushima 770-8503, Japan
4Applied Science Laboratory Asia Pacific, GE Healthcare Japan Corporation

(Received September 3, 2012; Accepted April 3, 2013; published online July 12, 2013)

Purpose: Our purposes were to establish suitable conditions for proton magnetic resonance spectroscopy (MRS) to measure dynamic changes in alcohol concentration in the human brain, to evaluate these changes, and to compare the findings with data from analysis of breath vapor and blood samples.

Materials and Methods: We evaluated 4 healthy volunteers (mean age 26.5 years; 3 males, one female) with no neurological findings. All studies were performed with 3-tesla clinical equipment using an 8-channel head coil. We applied our modified single-voxel point-resolved spectroscopy (PRESS) sequence. Continuous measurements of MRS, breath vapor, and blood samples were conducted before and after the subjects drank alcohol with a light meal. The obtained spectra were quantified by LCModel Ver. 6.1, and the accuracy of the MRS measurements was estimated using the estimated standard deviation expressed in percentage (%SD) as a criterion.

Results: Alcohol peaks after drinking were clearly detected at 1.2 ppm for all durations of measurement. Good correlations between breath vapor or blood sample and MRS were found by sub-minute MRS measurement. The continuous measurement showed time-dependent changes in alcohol in the brain and various patterns that differed among subjects.

Conclusions: The clinical 3T equipment enables direct evaluation of sub-minute changes in alcohol metabolism in the human brain.

Keywords: alcohol, dynamic, ethanol, proton MRS, 3 tesla

Introduction
It is well known that many neuropsychiatric disorders are associated with alcohol use, and direct observation of alcohol metabolism in vivo is considered useful for evaluating the influence of alcohol on brain function. Magnetic resonance spectroscopy (MRS) is one of the most powerful tools to offer noninvasive and quantitative evaluation of the amount of metabolites, such as N-acetyl aspartate (NAA), N-acetyl aspartyl-glutamate (NAAG), choline-containing compounds (Cho), creatine and phosphocreatine (Cr), glutamate (Glu), glutamine (Gln), glucose (Glc), and lactate (Lac), in local brain tissues.1 Alcohol metabolism can also be evaluated using MRS, which can measure levels of local alcohol concentration in the brain.2-5

Although measurement of alcohol concentration in breath vapor is the most convenient method for determining alcohol concentration in the body, this...
method does not directly evaluate the concentration in the brain. The most accurate determination of alcohol concentration in the body is direct measurement from the blood, but continuous measurement is invasive because recurrent blood sampling is required for every measurement.

To the best of our knowledge, few studies have evaluated alcohol concentration in vivo with high temporal resolution and adequate reproducibility. The aims of this study were to establish suitable conditions for proton MRS to measure dynamic changes in alcohol concentration in the human brain, to evaluate these dynamic changes, and to compare the findings with data from analyses of breath vapor and blood samples.

Materials and Methods

We evaluated 4 healthy volunteers (3 men, one woman; mean age 26.5 years, range 21 to 38 years) with no neurological findings and no specific habit of high alcohol consumption or drug use, all carefully screened to rule out contraindications for MR measurement. Our local ethics committee approved the study, and informed consent was obtained from all participants.

All studies were performed using 3-tesla clinical equipment (Signa 3.0T HDx, General Electric, Milwaukee, WI, USA) with an 8-channel phased array head coil. All spectra were obtained using a single-voxel point-resolved spectroscopy (PRESS) sequence (repetition time [TR], 2,000 ms; echo time [TE], 35 ms) with a chemical shift suppression pulse for water suppression in automatic setup mode. Crusher pulses were modified in the PRESS sequence to improve spectral quality. In this study, we changed the number of scans and water references to control the total acquisition time of each spectrum as follows: 128 scans and 8 water references in 298 s; 32 scans and 4 water references in 106 s; 16 scans and 4 references in 58 s; and 8 scans and 2 references in 30 s. A set of MRS measurements included 4 spectra in 298, 106, 58, and 30 s of the total acquisition time. Prescanning took approximately 40 s and included center frequency adjustment, transmitter and receiver gain adjustments, and shimming for each measurement. A voxel of interest (8 mL) for the acquisition of the spectra was localized in the left parietal white matter.

We analyzed all spectroscopic data using commercially available linear combination of model spectra (LCModel) ver. 6.1 software, a user-independent fitting routine that uses a library of model spectra of all individual metabolites. We used the original basis-set consisting of 28 model spectra of metabolites including ethanol (provided by S.W. Provencher). For quantitative evaluation, we applied the internal water reference method in this study because we used a multi-channel receiver coil. The LCModel software expressed the precision of the curve fitting of the spectra as the standard deviation expressed in percentage (%SD). An increase in %SD denotes a decrease in the precision of the curve fitting.

To compare alcohol concentrations obtained by different measurement methods, we also determined alcohol vapor concentration in the breath using Intoxilyzer® S-D5 (CMI Inc., Owensboro, KY, USA) and measured blood alcohol concentration by gas chromatography. Physicians obtained blood samples (approximately one mL) using blood collection needles.

Figure 1 shows the time course of the study. After approximately 4 hours of fasting, the pre-intake examination (‘‘pre’’) included measurement of alcohol vapor concentration in the breath, sampling of blood for measurement of blood alcohol concentration, and acquisition of a set of MRS measurements comprising the above-mentioned 4 spectra with different acquisition times. After the pre-intake examination, the participants drank approximately 750 mL of alcoholic liquor (7% alcohol concentration) with a light meal for approximately half an hour.

After the intake of alcohol and the light meal, the post-intake examination (‘‘post’’) comprised measurements of alcohol vapor concentration in the breath, blood sampling for the measurement of alcohol concentration in serum, and acquisition of a set of MRS measurements comprising 4 spectra. In this paper, we describe the 4 sets of MRS measurements in the post-intake period as ‘‘post’’ 1, 2, 3, and 4. The approximate cumulative duration for each set of MRS measurements starting from the finish of alcohol intake were 10, 25, 40, and 55 min. Blood sampling to measure blood alcohol concentration was conducted in the period before ‘‘post’’ 1, between ‘‘post’’ 2 and 3, and after ‘‘post’’ 4.

We used Microsoft Excel function to evaluate the correlation between the concentrations of alcohol measured by MRS with the 4 different measurement times and alcohol vapor concentrations in the breath as well as the results of MRS measurement and alcohol concentrations in the serum. We compared the %SDs of the alcohol for each measurement time evaluated by LCModel and adopted Friedman’s rank test to test statistics using R software (version 2.15.2, http://www.r-project.org/).
Fig. 1. Time course of the study. After approximately 4 hours of fasting, pre-examination included measurement of alcohol vapor concentration in the breath followed by drawing of blood for measurement of blood alcohol concentration and then acquisition of a set of magnetic resonance spectroscopy (MRS) measurements with 4 different acquisition times. After the pre-intake examination, participants drank alcohol with a light meal for approximately 30 min. Measurement sets are denoted as “pre” and “post” 1, “post” 2, “post” 3, and “post” 4.

Results

Figure 2 shows the chronological spectra from “pre” to “post” 3 in one of the participants in the 298-s acquisition time. We observed all peaks of the major metabolites that with a high signal-to-noise ratio (SNR). Alcohol peaks were observed as ethanol (EtOH) at 1.2 ppm from “post” 1 to 3. Figure 3 shows the same participant’s spectra at “post” 2; each spectrum was acquired in 298 (a), 106 (b), 58 (c), and 30 (d) s. Although worsening SNR was related to decreased scan time, ethanol peaks could be recognized from “post” 1 to 3 in each spectrum at different acquisition times. A triplet peak of ethanol was observed only with 298-s acquisition time. Figure 4 shows the results of %SD of the 4 different acquisition times. The %SD increased as acquisition time decreased.

Figure 5a shows correlations between the results of MRS measurement and vapor alcohol concentration in the breath. Positive correlations were found in the data for acquisition times exceeding 58 s ($r > 0.80$). Figure 5b shows the correlations between MRS measurements and blood alcohol concentrations and similar positive correlations between MRS and blood sample concentration.

Figure 6 shows the time-dependent changes in alcohol concentration of the 4 participants. Each participant demonstrated a different pattern, such as a persistent high peak in Participant A, a lower peak with gradual decay in Participant B, and intermediate changes in Participants C and D.

Discussion

In this study, we used proton MRS to explore dynamic changes in the concentration of alcohol in the brain. Our results showed a tendency for deterioration of spectrum quality as acquisition time decreased, but the peak of alcohol could be recognized in all spectra with various acquisition times. They could also be analyzed by the LCModel software. The triplet peak of ethanol was clearly observed only in the spectra with 298-s acquisition time. Because the precision expressed as %SD was reduced in line with a decrease in acquisition time, long acquisition times may increase the quality of spectra. However, considering the balance between spectral quality and temporal resolution, 20%SD is usually considered an acceptable threshold in clinical settings. One-minute measurements could be used in future human alcohol studies because most of the spectra with 58-s acquisition time retained less than 20%SD.

We could observe concentrations of metabolites such as Glu, Gln, Glc, and Lac as well as EtOH.
Fig. 2. Spectra from a single participant obtained at “pre” (a), “post” 1 (b), “post” 2 (c), and “post” 3 (d), acquired with a total scan time of 298 s. All peaks of the major metabolites are seen, with an excellent signal-to-noise ratio. Ethanol peaks (1.2 ppm) are clearly apparent at “post” 1, 2, and 3.

Fig. 3. Spectra from a single participant obtained with scan times of 298 (a), 106 (b), 58 (c), and 30 (d) s, acquired at “post” 2. Although an ethanol peak (1.2 ppm) was observed with all acquisition times, a triplet peak was clearly observed only with the acquisition time of 298 s.
Fig. 4. Precision of curve fitting of the spectra, expressed as %SD. The %SD increased in line with a decrease in acquisition time. Significant differences are shown between each measurement time ($P < 0.05$).

Fig. 5. Relations between the results of magnetic resonance spectroscopy (MRS) measurement and vapor alcohol concentration in the breath (a) and relations between the results of MRS measurement and blood sample measurement (b). Positive correlations were found in both figures for measurement times exceeding 58 s ($r > 0.80$).

Fig. 6. Time course of change in alcohol concentration in each participant (A–D). The time of measurement just after drinking ("post" 1) is expressed as 0. Various patterns are apparent, including a persistent high peak in Participant A, a lower peak with gradual decay in Participant B, and intermediate changes in Participants C and D.

The other metabolites. Most of these metabolites, especially Glc and Lac, produced greater than 20%SD. Biller and colleagues reported the longitudinal change of Glc, inositol, and aspartate. In their study, Glc was infused and temporal resolution was over 2 min with almost double voxel size in comparison with our study. Gomez and colleagues also reported the longitudinal change of GABA, Glu, Gln, myoinositol, and scyloinositol. Their voxel size was almost double ours, and they employed 4-tesla equipment. Also J-editing was employed to isolate GABA in their study. Our measurement conditions, such as 8-mL voxel size and one-minute time resolution, were sufficient to evaluate EtOH but not the simultaneous evaluation of metabolites with small amounts in the brain. Our result suggested that one-minute observation was enough to evaluate the longitudinal change of alcohol in the brain, but adopting larger voxel size or using MR equipment with higher static magnetic field strength may be considered if the small amount of metabolites should be evaluated simultaneously.

Conclusion

Dynamic observation of alcohol in the brain can be successfully conducted with one-minute time resolution by proton MRS on a 3T device.

Acknowledgement

Part of this work was supported by a Grant-in-Aid for Encouragement of Young Scientists (B),
MEXT Kakenhi (16790733), and part was presented at the 91st Annual Meeting of the Radiological Society of North America.

References