3T MRS observations of acetone and beta-hydroxybutyrate in an epileptic patient under ketogenic diet

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Introduction

Although the mechanism is not fully understood, ketogenic diet (KD, high-fat, low-protein, and low-carbohydrate diet) has been shown to be an effective way of controlling intractable epilepsy. Ketogenic diet is known to induce production of ketone bodies (mainly β-hydroxybutyrate (BHB), and to lesser extent, acetoacetate and acetone), which have been implicated in the mechanisms of seizure control. It is believed that the biochemical changes associated with KD mimic that of fasting or starvation and the brain is forced to switch to ketone bodies as alternate fuel for brain metabolism. ^{1}H MRS has become a powerful non-invasive tool for evaluating various brain disorders and would be an ideal tool for monitoring ketone bodies in the brain and help define the roles they play in controlling seizures. There are only a few reports of ketone bodies measured with ^{1}H MRS in the literature due to the nature of their low sensitivity and narrow spectral window. Low concentration metabolites such as acetone and acetoacetate and others can be difficult to detect, especially when they are overshadowed by neighboring strong metabolites (such as glutamate, glutamine and γ-aminobutyrate). Techniques such as multiple-quantum, multiple dimension and various spectral editing methods have been devised to overcome the spectral overlapping problem and many sensitivity enhancement techniques have also been developed. A simple and obvious solution for ketone body detection is to go to higher magnetic field, which provides higher sensitivity and wider spectral window.

We studied a five year-old patient with a history of developmental delay and glucose-1 transport deficiency who was on ketogenic diet to control his seizures. Single and multi-voxel MRS studies reveal normal levels of NAA, creatine, choline and myo-inositol in the brain parenchyma. Prominent peaks observed in the moderately enlarged ventricular spaces appear to be that of the acetone, beta-hydroxybutyrate (BHB) and lactate (Fig.1). A smaller amount of acetone was also detected in the brain parenchyma but no BHB or lactate was detected in the parenchymal regions (Fig.2). Unlike BHB which have been reported in MRS studies of diabetic ketoacidosis and fasting induced ketosis (1-3), direct detection of cerebral acetone at 1.5T is difficult due to its low concentration (~0.7 mM, (4)) and spectral overlap as mentioned above. To our knowledge, there is only one MRS report in the literature (4) demonstrating acetone detection at 1.5T. Here we demonstrated the increases in SNR and resolving power at 3T improve the detectability of this and possibly other low concentration metabolites.

Methods

In addition to routine MRI sequences (sagittal T1 weighted, dual echo axial T2, coronal and axial FLAIR, coronal TSE T2, and axial diffusion with ADC), 2D MRSI (PRESS localization technique) study with TE/TR of 135 /1700 msec was conducted through the level of basal ganglia with a Siemens Trio (3T) scanner. VOI =6.0 (A/P) x 6.0 (L/R) x 1.5 (S/I) cm, 16x16 weighted phase encoding steps. Total acquisition time (NA=4) is 8.03 min. A SVS (STEAM localization technique) study with a TR/TE of 1700/20 msec (NA=256) was also conducted with a VOI centered at the right basal ganglia region. Size of the VOI is 2.0x2.0x2.0 cm. Prior to Fourier transform and phase correction the raw spectral data was multiplied with an exponential function corresponding to a 2 Hz line broadening. No baseline correction was performed.

Results and discussion

MRI reveals moderately enlarged ventricle, abnormal CSF dynamics and thinning of corpus callosum. Spectroscopy studies indicate normal NAA, creatine, choline and myo-inositol patterns. Spectra from the ventricular regions indicate a prominent peak at 2.22 ppm (Fig. 1, sharp singlet, line width ~ 4Hz) which resembles that of the acetone. This is distinct from the resonances expected of methyl peak of acetoacetate (at 2.26 ppm), for which we would expect to see an additional singlet at 3.46 ppm with 2/3 of the intensity. Inverted doublet peaks at 1.36 and 1.20 (out of phase with NAA, Cr and Cho) are consistent with that of lactate and β-hydroxybutyrate. NAA, Cho, Creatine peaks in this spectrum arise from the partial volume effect. Spectrum from voxel in left basal ganglia (Fig.2) appears normal as the ratios of NAA and choline to creatine are within normal ranges. Although small, acetone peak is present in this region. Short TE SVS study (Fig.3) appears to be normal also, with additional resonances from that of myo-inositol, glutamine/glutamate and lipids. Our results demonstrate the advantages of MRS in a higher field.

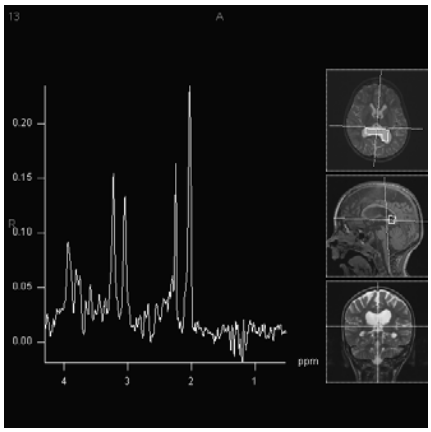

Figure 1

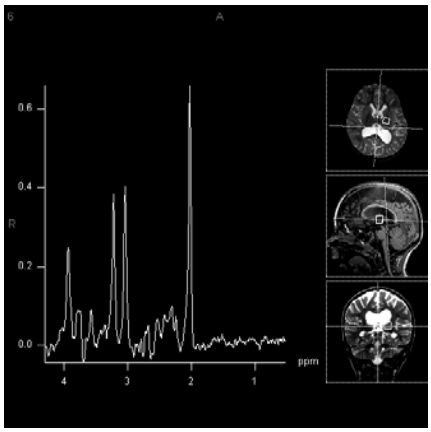

Figure 2

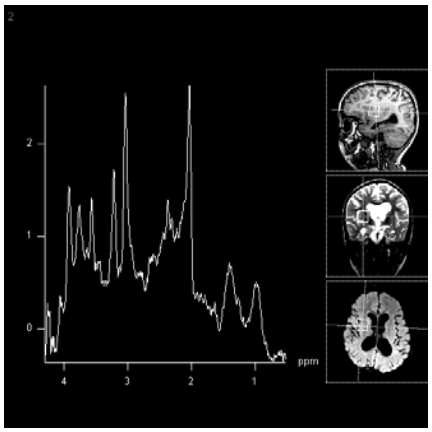

Figure 3

References

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