Lactate-edited 3D MRSI and Rapid Automated Processing for Neonatal Brain Injury Studies

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Abstract

In term neonatal encephalopathy, increased brain lactate (LAC) levels and decreased N-acetylaspartate (NAA) levels, measured by proton MR spectroscopy in specific brain regions, are associated with adverse neurodevelopmental outcome. Lactate-edited 3D MRSI now allows the assessment of these metabolite levels throughout the newborn brain. In this study, new automated processing methods were developed to rapidly analyze the 1024 spectral arrays acquired in neonatal MRSI in order to better quantify the presence and extent of abnormal metabolite levels. These methods were investigated in a preliminary study of term neonatal encephalopathy. The rapid post-processing methods allowed the analysis of all spectra in <0.5 hours and provided metabolite ratios for specific anatomic ROIs. In this study, LAC/NAA and LAC/choline (LAC/CHO) were increased and NAA/CHO decreased in widespread regions, in neonates with fatal outcome relative to those with normal neurodevelopmental outcome at 1 year of age.

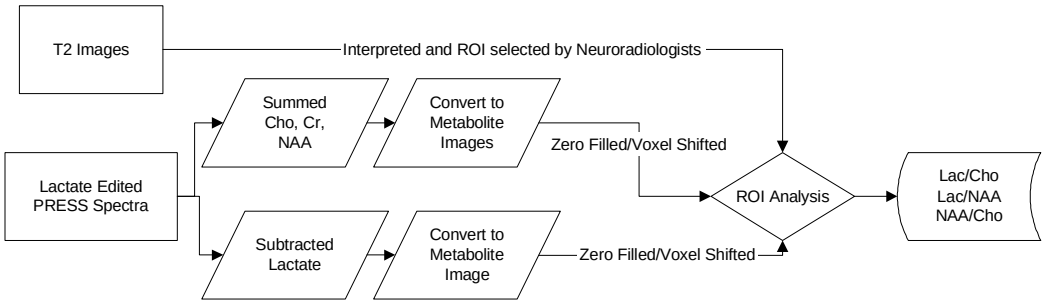
Introduction

Recent studies have demonstrated the important diagnostic value provided by anatomic, diffusion, and spectroscopic MR imaging, especially in assessing neonates with brain injury [1-3]. In this study, a lactate editing method was employed together with 3D point-resolved spectroscopic imaging (PRESS-MRSI) to provide accurate measurements of metabolite levels throughout the neonatal brain [4]. Novel post-processing methods were developed to analyze the large volume of complex MRI/MRSI data with the goal of being minimally interactive, several orders of magnitude faster, and less prone to human subjectivity.

Methods

Patients: A total of 10 newborn patients were studied early after birth at a median post-partum age of 24 hours ± (range =24hrs-30.5hrs). The studies were performed in an MR compatible incubator with a specialized neonatal head coil to provide a temperature-controlled, well-monitored, safe environment and to improve image quality [5]. Motor outcome was assessed at 1 year of age using a neuromotor score (NMS) of 0-5 as previously defined [6]; cognitive outcome was measured using the mental development index (MDI) of the Bayley's Scales of Infant Development II. For this technical development study, we included the newborns with normal neurological outcome (NMS=0; MDI>85) (N=4) and those who died in the neonatal period (N=6).

MRI/MRSI Acquisition: The neonatal MR studies performed on a 1.5 T GE Signa Echospeed scanner included: 1) T1 weighted sagittal and axial images 2) T2 weighted axial dual echo, spin-echo with TR of 3sec, TE of 60 and 120ms. A multivoxel 3D MR spectroscopy scan was performed to obtain metabolite levels covering most of the brain using PRESS acquisition with BASING lactate editing method [4, 7]. The uniformity of the selected region was obtained by slightly overexciting the prescribed region and shaped with very selective saturation (VSS) pulses [8]. The acquisition parameters are 144ms/1s TE/TR, 1cc resolution, 8x8x8 array, and an acquisition time of 17 minutes.



Analysis Methods: Seven ROI's were positioned on the T2 weighted images by an experienced pediatric neuroradiologist and then used to obtain metabolite levels in the MRS data. The graphical image viewer and ROI tools were custom developed using Interactive Data Language (IDL). The selected ROIs were basal ganglia (BG), thalamus (THAL), optic radiation (OR), calcarine gray matter (CGM), corticospinal tract (CST), posterior white matter (PWM), and frontal white matter (FWM). Custom software was developed to integrate and analyze the spectroscopy data according to the corresponding metabolite peak file. The reconstruction started with an apodization of the k-space data and followed by a Fourier transform to produce the spectral arrays. Then, the spectra were corrected for phase and frequency variations. The resultant spectra were also baseline corrected for the incomplete water suppression [9, 10] and metabolite images were generated to depict the three-dimensional distributions of metabolite levels. An automated program was developed to zero-fill the MRSI data to 256x256 and select the center value corresponding to each ROI in the spatial domain. The program calculated the height of the metabolites in each ROI, and outputted the information into a comma delimited text file for automated statistical analysis. The left and right ROI for each region was compared using the Wilcoxon rank-sign test. Metabolite ratios of normal and deceased patients were compared in each ROI using Kruskal-Wallis rank-sign test in JMP (SAS, Cary, NC).

Results and Discussions

For individual patients, these rapid post-processing methods allowed the analysis of all spectra in <0.5 hours and provided metabolite ratios for several specific anatomic regions of interest. LAC/NAA and LAC/CHO were significantly higher in the deceased patients relative to those with normal outcome in each of the regions (Table 1). NAA/CHO was lower in the deceased group in the THAL, OR, PWM, and FWM. In this preliminary study of term neonatal encephalopathy, the elevated lactate levels and lower NAA levels in deceased newborns relative to newborns with normal neurodevelopmental outcome, supports the validity of this approach, and suggests that metabolic abnormalities are widespread in severely affected newborns.

Table 1. P Values comparing DECEASED vs. Normals by ROI

	BG	THAL	OR	CGM	CST	PWM	FWM
LAC/NAA	**0.0002**	**0.002**	**0.05**	**0.0003**	**0.001**	**0.0002**	**0.0004**
LAC/CHO	**0.0004**	**0.005**	**0.02**	**0.0004**	**0.005**	**0.0002**	**0.0008**
NAA/CHO	0.6713	**0.005**	**0.03**	0.07	0.2	**0.05**	**0.03**

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