New Spectral Analysis of Short Echotime Multislice 1H MRSI in Human Brain using Eigen Spectra, Baseline Correction and Frequency Alignment.

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INTRODUCTION

Single voxel ^{1}H MRS studies consistently show increased myo-Inositol (MI, a glial marker) and decreased N-Acetyl Aspartate (NAA, a neuronal marker) in Alzheimer's disease (AD). Multislice MRSI studies in AD at long echo times (TE=135ms) found reduced NAA primarily in parietal gray matter but not in frontal gray matter and white matter. However, regional variations of MI, which is detected at much shorter values of TE (<25ms) could not reliably be determined as a result of complex signal contributions from variable macromolecular background signals and lipid contamination. To overcome these short TE MRSI limitations, we developed a new data analysis method that uses the complex eigen-spectra for regions of interest while accounting for problematic effects such as baseline and magnetic field variations. The new analysis method was examined for reproducibility in volunteer same-day test-retest studies and for sensitivity in AD patients and cognitive normal (CN) subjects.

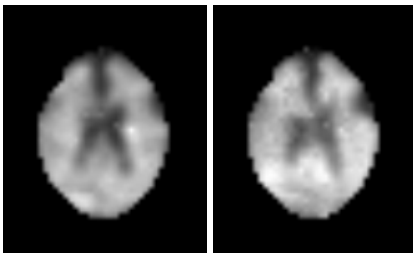

Fig 1. NAA (left) and MI (right) images.

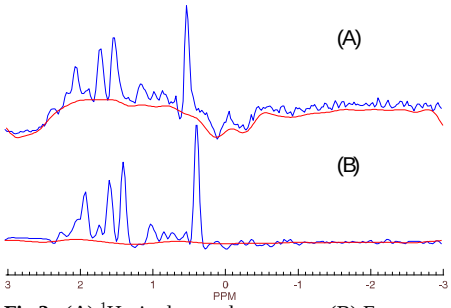

Fig 2. (A) ^{1}H single voxel spectrum; (B) E_1 spectrum after B_0, phase and baseline correction.

METHODS

Theory: A MRSI data set **A** is represented as a linear combination of an overall mean spectrum **m** and a **W**eighted eigen-spectra **E,**

$$\mathbf{A} = \mathbf{m} + \mathbf{WE} \quad (1)$$

Ranking all E's by their eigenvalues, the first eigen-spectrum E_1 represents the most coherent variation in the MRSI data set, while the last eigen-spectrum E_n represents noise [1]. Baseline residual fluctuations resulting from subtraction of a simulated baseline are normally distributed. Therefore, with proper spectral alignment, E_1 contains the most coherent information such as peak amplitude and area under the curve of metabolites, with minimum contributions from the independently, identically distributed (IID) noise and baseline residual fluctuations.

Subjects: For test-retest reliability, 10 healthy volunteers (age 22 to 84 y) were scanned twice on the same day in separate sessions. For testing sensitivity MRSI data from 22 CN subjects (age 72.1 ± 8.5y) and 14 AD patients (age 73.0 ± 6.21 y) were used.

Data acquisition and processing: 3 axially oblique MRSI slices with voxel size of 0.75 x 0.75 x 15 mm and TE/TR =25/1800 ms were acquired on a 1.5 T MR Siemens scanner. In addition, 3D MPRAGE and multislice DSE anatomical images were acquired and aligned with MRSI to determine the amount of gray matter, white matter, CSF, and other tissue in each MRSI voxel. ^{1}H MRSI data were automatically processed and metabolite resonances fitted using *a-prior* spectral information [2]. Wavelet shrinkage was used to remove baseline variations due to macromolecular resonances and lipid contaminations.

Spectral alignment and eigen spectra calculations: Spectral alignment was accomplished using cross-correlation and further Brent's method with parabolic interpolation [3]. Baseline corrected and frequency aligned spectra from regions of interest, e.g. parietal lobe gray matter, were pooled and Eigen-spectra computed and fitted to obtain NAA, Creatine (Cr), Choline (Cho) and MI. The new method was compared to results from standard MRSI analysis using linear regression [4].

Table 1. ICC of Metabolite peak areas (n=20).

	Method	NAA	Cr	Cho	MI
PG	**A**	0.73	0.74	0.33	0.11
	m	0.87	0.86	0.83	0.60
	$\mathbf{E_1}$	0.99	0.99	0.96	0.92
FG	**A**	0.85	0.82	0.33	0.22
	m	0.90	0.94	0.77	0.77
	$\mathbf{E_1}$	0.98	0.98	0.93	0.88

Footnotes: ICC values lower than 0.50 indicate unreliable measurements.

RESULTS

Figure 1 shows representative MI and NAA images from an 85 year old CN subject. Figure 2A shows a spectrum from a single voxel of parietal lobe gray matter (PG) region in an AD patient. Figure 2B shows an E_1-spectrum from the same region of interest but after B_0, phase and baseline corrections, revealing improved signal to noise ratio and reduced baseline fluctuation. Table 1 lists intraclass correlation coefficients [ICC] of test-retest MRSI measurements in parietal (PG) and frontal lobe gray matter (FG), where **A** are from standard MRSI analysis using linear regression. **m** and $\mathbf{E_1}$ are mean and Eigen 1 spectra from the new method after spectral alignment and baseline corrections. Table 1 demonstrates a considerable improvement for reliability when Eigen 1 spectra are used. Comparisons between new and standard MRSI analyses [4] are in separating AD from CN summarized in Table 2, indicating more robust observations of group effects when **m** and $\mathbf{E_1}$-spectra are used, especially for MI/Cr and NAA/Cr ratios in PG.

Table 2. Metabolite areas and ratios of PG.

	Method	AD (n=14)	CN (n=22)
NAA	**A**	8.00 ± 1.11	7.84 ± 1.19
	m	7.91 ± 1.17	8.78 ± 1.06 *
	$\mathbf{E_1}$	7.14 ± 1.82	8.55 ± 1.64 *
MI	**A**	4.79 ± 1.06	4.20 ± 0.77
	m	5.50 ± 0.76	4.99 ± 0.72 *
	$\mathbf{E_1}$	3.47 ± 0.79	3.37 ± 0.64
NAA/Cr	**A**	1.23 ± 0.14	1.35 ± 0.14 *
	m	1.30 ± 0.11	1.44 ± 0.12 **
	$\mathbf{E_1}$	1.34 ± 0.09	1.49 ± 0.11**
MI/Cr	**A**	0.73 ± 0.14	0.72 ± 0.11
	m	0.91 ± 0.12	0.82 ± 0.10 *
	$\mathbf{E_1}$	0.66 ± 0.07	0.59 ± 0.06 **

Footnote: significant (* p<0.05) and very significant (** p <0.01) differences between metabolites results of AD and CN using Wilcoxon Rank Tests).

DISCUSSION AND CONCLUSIONS

A new scheme to analysis of multislice MRSI data was introduced, which provides reliable results for MI in addition to NAA and other major metabolites. The result of improved reliability is consistent with the hypothesis that by ranking Eigen-spectra, coherent resonances (i.e. from metabolites) can be separated from random fluctuations or noise. The results further demonstrate that the new approach considerably improved sensitivity in separating AD patients from controls by MRSI. In conclusion, use of Eigen-spectra improves the analysis of MRSI data.

References: 1. Zhu et al, MRM 50:474-482, 2003; 2. Soher BJ et al, MRM 40:822-831, 1998; 3. Press WH et al, Numerical Recipe in C, p.402-405, 1988; 4. Schuff N et al, MRM 45:899-907, 2001.