Compressed Sensing Based J-Resolved Spectroscopic Imaging in Obstructive Sleep Apnea
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Target audience: Researchers interested in obstructive sleep apnea syndrome and compressed sensing reconstruction.

Purpose/Introduction: Obstructive sleep apnea syndrome (OSAS) is a common sleep disturbance affecting approximately 10% of the adult population and leads to numerous health problems, including symptoms and comorbidities involving CNS impairments and cerebrovascular risk factors. The causes of OSAS seem to be multifactorial. Chronic intermittent hypoxic episodes, hypercapnia and transient blood pressure elevation in OSAS may damage neural structures and induce cerebral metabolic changes. Many structural imaging studies have shown brain tissue changes at the voxel level describing the nature of neural and axonal changes in OSAS, but to date, only a limited number of MRS based studies can be found. The MRS studies based mainly on 1D spectroscopy have reported differences in N-acetylaspartate (NAA), choline (Ch), and myo-inositol (mI) relative to creatine (Cr) in frontal, hippocampal and occipital regions in OSAS. Combining the speed advantage of EPSI readout and increased spectral dispersion offered by 2D JPRESS, 4D echo-planar J-resolved spectroscopic imaging (EP-JRESI) enables recording better-resolved 2D spectra from multiple voxels in a single recording. Implementation of non-uniformly undersampling (NUS) and compressed sensing (CS) reconstruction will further shorten the total acquisition time of EP-JRESI making it clinically applicable. In this study, we examined neurochemical changes in multiple brain regions of OSAS patients using CS based EP-JRESI and quantify the metabolites using prior knowledge fitting (ProFit) algorithm.

Materials and Methods: Study participants consisted of eleven OSAS patients (54.55±10.6 years) and fourteen age matched healthy volunteers (50.66±8.48 years). OSAS patients were recruited following a diagnostic sleep study at the UCLA Sleep Disorders Center, based on full overnight polysomnography scoring according to current American academy of Sleep Medicine criteria. Any evidence of clinical brain pathology was cause for exclusion. All data were collected on a 3T Trio-Tim MRI scanner. The basic 4D EP-JRESI sequence was modified to accommodate for the 25% NUS of the fully sampled data. The following parameters were used for CS EP-JRESI: TR/TE = 1.5s/30ms, 1.5x1.5x1.5 cm³ voxel for VOI localization, 64Δt increments, 256 bipolar echo pair, FOV= 24x24x24cm³, 2 averages, F1 and F2 bandwidths of 1000 Hz and 1190 Hz, respectively. The undersampled data was reconstructed using a modified Split Bregman algorithm which solves the unconstrained optimization problem, arg minₜₐₜᵋ₈,∥ₐ₈ₜₐᵋ₈−ₐ₈₁ₗₜₐᵋ₈∥ + 1₂∥₄ₗₚₜₐᵋ₈−ₚₜ₇ₗₚₜₐᵋ₈∥ where V is the gradient operator, α is the reconstructed data, ∥ₐ₈ₜₐᵋ₈∥ is the l₁ norm, a, β are positive parameters, Fₜ is the undersampled Fourier transform, and α is the undersampled data. Before applying the NUS based EP-JRESI sequence, 3D high resolution T₁-weighted images for localization were collected using a MPRAGE pulse sequence. EP-JRESI was performed over two slices: 1) an axial slice covering frontal, basal ganglia and occipital regions and 2) a coronal slice covering the hippocampus, thalamus, etc. Acquired data were post-processed with a custom MATLAB-based program, which applied spatial Hamming and spectral apodization filters to smooth the data. Modified ProFit algorithm was applied to process the extracted data and to calculate metabolite ratio with respect to the 3 ppm creatine peak (S/Sc). Prior knowledge generated for EP-JRESI included 20 metabolites including, Cr, NAA, phosphorylcholine (PCh), free choline (Cho), aspartate (Asp), γ-aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glutathione (GSH), lactate (Lac), mI, NAcetylaspartylglutamate (NAAG), phosphoethanolamine (PE), and taurine (Tau). The metabolite differences between OSAS patients and healthy controls were tested with a two-tailed t-test using SPSS software.

Results and Discussion: Fig. 1(a) shows the spatial map of 2D diagonal peaks of NAA from the CS reconstruction of the undersampled data of a 40-year-old OSAS patient brain overlaid onto T₁-weighted axial MRI covering the frontal/occipital regions. A representative spectrum extracted from the frontal gray matter region is shown in Figure 1(b). The overall quality of the spectra was good with minimal leakage and many metabolites were visible. Table 1 and Fig. 1(c) show the metabolite ratios with respect to Cr in the right hippocampus, occipital gray, medial frontal gray and left frontal white regions of OSAS patients and healthy controls. Significantly reduced metabolite differences were observed between OSAS and healthy controls in multiple brain regions: tCho/Cr and Glx/Cr in right hippocampus, tNAA/Cr and NAA/Cr in the medial frontal, tNAA/Cr, Tau/Cr, sICr, PCh/Cr and tCho/Cr in the occipital gray and Tau/Cr, tCho/Cr, PE/Cr in the left frontal white matter region.

Reduced NAA/Cr and Cho/Cr ratios agree with previous MRS studies obtained in the frontal WM of OSAS patients. Reduced NAA/Cr ratio is indicative of neuronal dysfunction and axonal damage in those regions, presumably consequent to known repeated episodes of hypoxia in OSAS patients. Decreased Cho/Cr and tCho/Cr ratios may result from loss of myelin lipids or dysfunction of phospholipid metabolism. Alchanatis et al. reported increased mL/Cr in OSAS subjects in agreement with our study. Increased mL/Cr ratio may be a reflection of membranal breakdown and reactive gliosis. Studies with more number of OSAS patients and controls are required to follow the results of decreased sICr, Tau/Cr, Glx/Cr ratios and PE/Cr ratio as these has not been reported in any of the OSAS single voxel studies. We also calculated the metabolite ratios in the right frontal WM, left and right occipital WM, and right and left Thalamus and found similar trend.

Conclusion: This study demonstrates clearly that several cerebral metabolites can be quantified using 4D EP-JRESI and the ProFit algorithm that has not been clearly demonstrated using 1D MRS studies of OSAS. Our findings using multi-voxel 2D MRS are in broad agreement with the literature and are consistent with the known phenomenon of oxidative stress in OSAS. Acknowledgement: This research was supported by NINR 013693.


Table 1: ProFit-adjusted metabolite ratios (Means±SD) calculated from different regions of 11 OSAS patients and 14 healthy controls (HC).

<table>
<thead>
<tr>
<th>S/N</th>
<th>Right hippocampus</th>
<th>Medial frontal gray</th>
<th>Occipital gray</th>
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<tbody>
<tr>
<td>OSAS</td>
<td>HC</td>
<td>OSAS</td>
<td>HC</td>
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<tr>
<td>tNAA</td>
<td>1.66±0.20</td>
<td>1.85±0.25</td>
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<tr>
<td>Glx</td>
<td>1.29±0.31*</td>
<td>1.72±0.39</td>
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<td>tCho</td>
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<td>0.36±0.04</td>
<td>0.31±0.09</td>
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<tr>
<td>NAA</td>
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<td>1.60±0.14</td>
<td>0.74±0.20*</td>
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<td>mL</td>
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<td>0.71±0.14</td>
<td>1.77±0.63</td>
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<tr>
<td>Tau</td>
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<td>0.49±0.15</td>
<td>0.63±0.24</td>
</tr>
<tr>
<td>sICr</td>
<td>0.04±0.01</td>
<td>0.05±0.02</td>
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<tr>
<td>OPC</td>
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<td>0.23±0.09</td>
<td>0.18±0.10</td>
</tr>
<tr>
<td>PCh</td>
<td>0.05±0.01</td>
<td>0.07±0.02</td>
<td>0.07±0.02</td>
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</table>

Fig. 1: (a) Spatial distribution of 2D diagonal peaks of NAA from a CS EP-JRESI scan of a 40-year-old OSAS patient overlaid on the T1-weighted localization image; (b) selected 2D J-resolved spectra extracted from the voxel labeled in (a); (c) Bar graphs showing mean metabolite ratios (±SD) in left frontal white matter.

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