Mapping of brain metabolite distribution by short echo time Echo Planar Spectroscopy Imaging (EPSI)

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Target audience: MR spectroscopy community and people interested in using whole brain MRSI in clinical research protocol

Purpose: In order to obtain normative metabolic templates of N-Acetyl-Aspartate, Choline and Creatine, we acquired short TE (20ms) whole brain Echo Planar Spectroscopy Imaging (EPSI) in a population of 10 healthy volunteers. We evaluated the regional variance of these maps and mean values of metabolites derived from these templates. This work is a preliminary step in order to perform robust statistical mapping onto metabolite maps to demonstrate focal or diffuse metabolic cerebral abnormalities in various neurological or psychiatric pathologies.

Methods: Ten young healthy subjects (mean age=23.7±2.4, age range = [19-26], 5 women and 5 men) gave written and informed consent before participating to the protocol. All MR data were acquired with 3T MR system (Siemens, Verio system) with a 32-channel receiver head coil. The imaging protocol included 3D EPSI [1] and T1-weighted magnetization prepared rapid gradient echo (MPRAGE) with similar localization parameters. Imaging was applied along a tilted orientation of 15° with respect to the anterior commissure posterior commissure (AC-PC) line. ***EPSI*** was performed with a TR/TE=1710/20ms, a covered region of 280x280x180 mm^3, a matrix of 50x50x32. The sequence included an interleaved water reference realized with a 10° excitation angle and TE=6.3ms.
After processing data in the Midas software package [2], water reference images derived from EPSI sequence were normalized on T1-template on SPM8 with the VBM8 toolbox. The transformation matrix was then applied on EPSI signal normalized metabolites images. Using the data from all subjects, voxel-wise mean signal normalized maps and voxel-wise normalized standard deviation maps defined as $nSD=\frac{\sigma}{mean}$ with $\sigma=\sqrt{\text{var}iance}$, were computed for each major metabolites, N-Acetyl-Aspartate (NAA), Choline (Cho) and Creatine (Cre). In order to remove outlier pixels from metabolite maps, we selected pixels showing nSD values below 1 for each metabolite map obtained. After segmentation of normalized T1 images, we applied the corresponding gray matter and white matter masks (threshold 75%) to obtain GM and WM metabolite maps. Mean values and SD were extracted from these maps.

Results: 1-Table.1 showed metabolite global values obtained in whole brain gray matter and white matter. Similar values were obtained while mean inter-subject standard deviation was 6 % of the mean with a maximum of 9.6% for NAA values in the whole brain white matter.
2- At the regional scale, figure 1 showed nSD maps (thresholded at 1) derived from NAA, Cho and Cre maps from the 10 volunteers acquired in the AC-PC+15° plane. Most of the brain can be observed. The largest standard deviations were observed in the upper slices and in the orbitofrontal region where the magnetic resonance susceptibility is higher than in the other brain areas.
3-Figure.2 showed voxel-wise mean signal normalized maps of NAA, Cho and Cre obtained from the whole brain. Metabolite signal drop out was observed in the upper slices and the orbitofrontal regions. Nevertheless, outside these regions robustness of the EPSI appeared compatible with statistical mapping analyses to locate focal metabolic abnormalities.
4- Whole brain GM and WM metabolite values extracted from these data showed standard deviations ranging from 3.8% to 9.6%; allowing to evidence diffuse metabolic abnormalities within metabolite variations between 8% and 20%.

Institutional unit (IU)	NAA	Cho	Cre
Whole brain GM	12.5±0.9	2.2±0.1	10.3±0.4
Whole brain WM	13.5±1.3	2.3±0.1	9.6±0.6

Table.1. Average metabolite values and metabolite ratios (Institutional Unit) over all subjects, for gray and white matters.

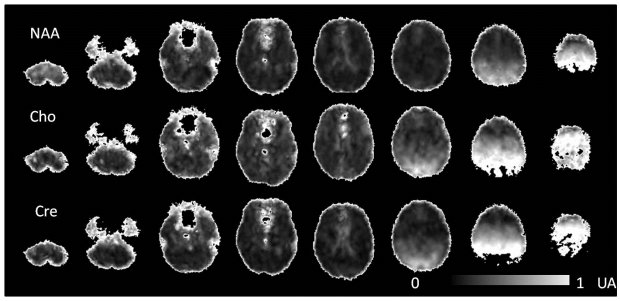

Figure.1. NAA, Cho and Cre metabolite normalized standard deviations (nSD) (Arbitrary unit UA) maps with the threshold of 1

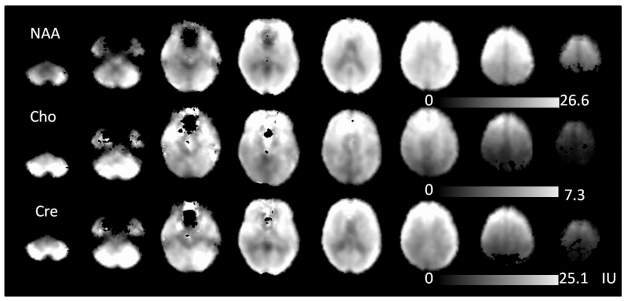

Figure.2. NAA, Cho and Cre metabolite signal normalized means (Institutional units IU) maps across the brain after applying the threshold

Conclusion: This work provides global normative values in the whole brain gray matter and white matter and spatial values distributions of NAA, Cho and Cre obtained with EPSI at 20ms on a cohort of young healthy adults. Due to magnetic susceptibility artifact, the tilted orientation of 15° with respect to the AC-PC line (abstract ISMRM 2013 n°1970), metabolites values and nSD spatial distributions were heterogeneous in the upper slices and the orbitofrontal region. Procedures to limit susceptibility artifacts such as proton density mapping accounting for B0 and B1 corrections (abstract ISMRM 2013 n°1877) might help to minimize these differences and to really obtain accurate metabolic templates to be used to perform statistical mapping analysis on short TE MRSI data. A larger cohort of volunteers has to be included in this study to improve the statistical power. In addition, the same approach has to be conducted on others metabolites observed at short TE such as myo-inositol, glutamine or glutamate.

References: [1] Ebel and al, MRM, 53: 465-469 (2005) [2] Maudsley et al, NMR Biomed, 19:492-503 (2006)