Neurochemical profile of Patients with Type 1 Diabetes Measured by 1H-MRS at 4 T
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Introduction
Decreased N-acetylaspartate (neuronal marker) and increased myo-inositol (osmolyte) have been observed in subjects with type 1 diabetes (T1DM) using 1H MRS [1,2]. However, the impact of the disease on a comprehensive neurochemical profile has not been reported yet. Our previous 1H MRS studies on T1DM were focused exclusively on the assessment of brain glucose levels [3-5]. This study aimed at reanalyzing our previously acquired data to investigate differences between neurochemical profiles of T1DM subjects relative healthy controls of similar age.

Methods
1H MRS data from a group of 14 patients with long-standing T1DM (>10 years) and a group of 32 healthy controls studied during a hyperglycemic clamp ([Glc]plasma = 300 ± 15 mg/dl) clamp with somatostatin and insulin were selected from our database. Spectra were acquired in an interleaved manner from 16-ml VOIs located in gray matter-rich occipital cortex (GM) and periventricular white matter-rich tissue (WM) using ultra-short echo-time STEAM sequence (TE = 6 ms, TR = 5 s) with VAPOR water suppression [6]. Metabolite concentrations were quantified using LCModel [7] with the spectrum of fast relaxing macromolecules included in basis set. Unsuppressed water signal was used as internal reference assuming 80% and 72% brain water content in GM and WM, respectively.

Results and discussion
Seventeen brain metabolites were consistently quantified from GM and WM 1H MR spectra with Cramer-Rao lower bound CRLB < 10% for Cr, PCr, Glc, Gin, Glu, myo-Ins, NAA, GPC+PC, Cr+PCr and with CRLB < 30% for remaining weakly represented metabolites (representative spectra from a subject with T1DM are shown in the figure). Robustness of metabolite quantification was demonstrated by small inter-subject coefficient of variation (CV < 6%) of [Cr+PCr] both in GM and WM. Differences in [Cr+PCr] between T1DM patients and controls were not observed (< 2%, p > 0.3). Of all quantified metabolites in both brain regions, lower levels of NAA (6%, p < 0.005) and glutamate (6%, p < 0.05) were observed in GM of T1DM patients as compared to controls. A trend (p = 0.064) for decreased [NAA] in WM of T1DM patients was also observed. No difference was found in [Glc]brain between T1DM and controls under the same [Glc]plasma levels. In addition, [Glc]brain data demonstrate a uniform distribution of glucose within these brain regions. In conclusion, the small, but significant, decreases of NAA and Glu levels in gray matter-rich occipital cortex might indicate a partial neuronal loss or dysfunction as a consequence of long-term T1DM. Effects of T1DM on all other brain metabolites detectable by 1H MRS at 4T were not observed.