Neurochemical profile of Patients with Type 1 Diabetes Measured by 1H-MRS at 4 T

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Introduction

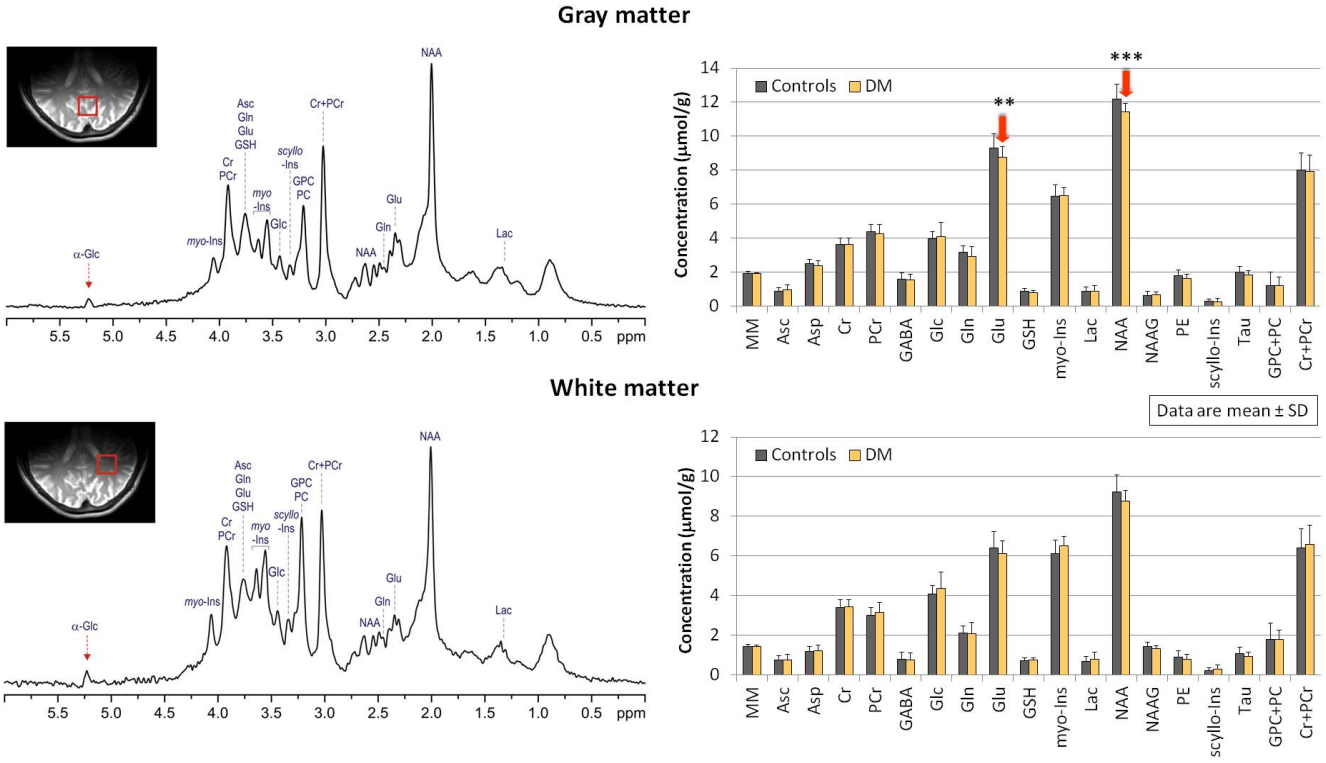
Decreased N-acetylaspartate (neuronal marker) and increased *myo*-inositol (osmolyte) have been observed in subjects with type 1 diabetes (T1DM) using ^{1}H MRS [1,2]. However, the impact of the disease on a comprehensive neurochemical profile has not been reported yet. Our previous ^{1}H MRS studies 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

^{1}H 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 ^{1}H MR spectra with Cramer-Rao lower bound CRLB < 10% for Cr, PCr, Glc, Gln, 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 ^{1}H MRS at 4T were not observed.



References: References [1] Heikkilä et al. Diabetologia 52:534 (2009) [2] Northam et al. Diabetes Care 32:445 (2009) [3] Seaquist et al. Diabetes 50:2203 (2001) [4] Seaquist et al. Metabolism 54:1008 (2005) [5] Criego et al. J Neurosci Res 82:525 (2005) [6] Tkac et al. App Magn Reson 29:139 (2005) [7] Provencher MRM 90:672 (1993). **Acknowledgments**: NIH Grants BTRR - P41 RR008079, P30 NS057091, NIH R01 DK62440, S10 RR023730, S10 RR027290.