Assessment of the metabolic changes in type 2 diabetes mellitus using magnetic resonance spectroscopy

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Introduction: Diabetes is a reduced insulin disorder in which the body either cannot produce insulin or cannot effectively use the insulin it produces. Type 1 diabetes occurs when the body's own immune system destroys the insulin-producing cells of the pancreas (called beta cells) [1]. In type 2 diabetes, also called Diabetes Mellitus (DM2), the beta cells produce insulin but it is either not enough or the body is unable to recognize the insulin and use it properly [2-4]. Since autoimmune disorders co-exist, many of our subjects turned out to be affected with both DM2 and Hypothyroidism. We studied the metabolic changes associated with DM2 and DM2+Hypothyroidism using MRS in brain (^{1}H) and calf muscle (^{31}P). We also compare the results with our earlier ^{1}H and ^{31}P MRS studies on hypothyroidism.

Materials and methods: Six patients (4M, 2F with mean age 45±SD 9.04) with DM2, five patients (3M, 2F with mean age 48±SD 10.29) with DM2 and hypothyroidism and six age and sex-matched controls were recruited for study. Spectra were acquired with a circularly polarized Head coil using 1.5 T whole body MR system (Magnetom Vision, Siemens, Germany). Single voxel (1.5x1.5x1.5cc) proton MRS (PRESS) was carried out (TR 2000ms and TE 135ms) in right and left frontal lobe white matter, left parietal white matter and left occipital gray matter. ^{31}P spectrum was taken from the right calf muscle using FID-NOE (TR 3000ms, TE 1ms) sequence. Spectra were post-processed using vendor provided software. The ratios of the metabolites were calculated from the integral values of metabolite peaks.

Results and Discussion: In DM2 a statistically significant reduction in NAA/Cr was observed in the white matter region of left frontal lobe and the left occipital gray matter as compared to controls. Increased Cho/Cr value was also observed in the occipital gray matter (Table 1). Figure 1(a, b) shows representative spectra in controls and DM2. Micro vascular dysfunction occurs early in diabetes and is associated with hypoxia and sometimes neuronal ischemia. NAA is a neuronal marker; therefore a reduced NAA/Cr may be due to the neuronal loss. Moreover, some cognitive and psychiatric studies suggest that diabetes may be associated with cognitive or functional impairment [5, 6]. Reduced NAA/Cr ratio in left frontal white matter and left occipital gray matter also correlates with this fact. An increased Cho/Cr value in the diabetic patients may be due to hyperosmolality, as a result of diabetes. In DM2+Hypothyroid cases, reduced NAA/Cr was observed in left frontal white matter as compared to controls.

^{31}P muscle spectrum shows a statistically significant reduction in PCr/Pi and an elevation in PDE/ATP values in DM2 patients (figure 1c) as compared to controls. Decreased PCr/Pi ratio and increased PDE/ATP values at rest, suggests impairment of the skeletal muscle energy metabolism in these patients. In DM2+Hypothyroid patients there was a statistically significant reduction in PCr/Pi value and an increase in PDE/ATP and PCr/ATP values. However, no statistically significant change in the metabolite ratios was observed between DM2 and DM2+Hypothyroid subjects.

Conclusion:

The present study shows that patients with Diabetes Mellitus and hypothyroidism have similar deficit in muscle metabolism but proton MRS is indicative of neuronal loss in DM2 alone.

Abbreviations used: PDE- phosphodiester, ATP- adinosinetriphosphate, Pi- inorganic phosphate, PCr- phosphocreatine, NAA- N-acetlyaspartate, Cr- creatine, Cho- choline

References:

1. K Sarac, A Akinci, A Alkan, et.al. Brain metabolite changes on proton magnetic resonance spectroscopy in children with poorly controlled type 1 diabetes mellitus. Neuroradiology, 2005; 47:562-565.
2. A Geissler, R Frund, J Scholmerich, et.al. Alterations of cerebral metabolism in patients with diabetes mellitus studied by proton magnetic resonance spectroscopy. Exp. Clin. Endocrinol. Diabetes, 2003; 111:421-427.
3. R Kreis and B D Ross. Cerebral metabolic disturbances in patients with subacute and chronic diabetes mellitus: detection with proton MR spectroscopy. Radiology, 1992; 184:123-130.
4. M Scheuermann-Freestone, P L Madsen, A M Blamire, et al. Abnormal cardiac and skeletal muscle energy metabolism in patients with type 2 diabetes. Circulation, 2003; 107:3040-3046.
5. N Awad, M Gagnon and C Messier. The relationship between impaired glucose tolerance, type 2 diabetes, and cognitive function. J. Clin. Exp. Neuropsychol., 2004; 26:1044-1080.
6. C Geroldi, G B Frisoni, G Paolisso, et al. Insulin resistance in cognitive impairment: the InCHIANTI study. Arch. Neurol., 2005; 62:1067-1072.

Table 1: ^{1}H metabolite ratios

Metabolite ratios	Controls (N=25)	DM (N=6)	DM+HYPO (N=6)
Rt Frontal			
Cho/Cr	1.25±0.44	1.11±0.19	1.13±0.45
NAA/Cr	1.97±0.68	1.51±0.22	1.68±0.63
Lt Frontal			
Cho/Cr	1.04±0.34	1.02±0.22	1.18±0.23
NAA/Cr	1.84±0.39	1.39±0.25	1.37±0.22
Lt Parietal			
Cho/Cr	1.06±0.25	1.02±0.20	0.92±0.14
NAA/Cr	1.98±0.45	1.87±0.47	1.67±0.27
Lt Occipital			
Cho/Cr	0.46±0.06	0.72±0.21	0.50±0.13
NAA/Cr	2.07±0.13	1.68±0.36	2.02±0.58

(Values in red are statistically significant as compared to controls)

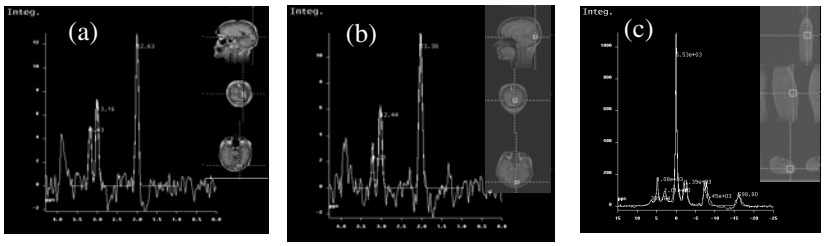

Figure 1. (a,b) ^{1}H Spectra from occipital gray matter in DM2 patients and controls respectively, (c) ^{31}P MRS from calf muscle of a DM2 patient

Table 2: ^{31}P metabolite ratios

Metabolite ratios	Controls (N=25)	Hypo (N=32)	DM (N=6)	DM+HYPO (N=6)
PCr/Pi	6.08±0.38	4.78±0.84	5.35±0.62	5.19±0.53
Pi/ATP	1.04±0.13	1.53±0.62	1.35±0.48	1.46±0.60
PCr/ATP	6.27±0.78	7.07±1.50	7.19±1.09	7.67±1.11
PDE/ATP	0.84±0.21	1.21±0.43	1.38±0.26	1.56±0.41