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Detection with Proton MR Spectroscopy of cerebral metabolic changes in children with type I Diabetes Mellitus

Mina Ramzy Emanuel Yacoub [1a,b]

1 a. PhD, Faculty of Medicine , Cairo University , Egypt, b. FRCR, East Suffolk and North Essex NHS foundation trust, United Kingdom.

Corresponding author : Mina Ramzy Emanuel Yacoub

Email: minaramzy_89@hotmail.com

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Abstract: ***Background:*** Magnetic resonance spectroscopy (MRS) is an imaging diagnostic method that allows non-invasive measurement of metabolites in tissues. MRS may demonstrate metabolic changes in normal appearing MRI examinations. Long term impairment of cognitive function can occur in patients with type I diabetes mellitus (DM).

Objective: In this study, we used MRS to investigate the impact of DM on brain neuro-chemical profile.

Patients & Methods: MR spectroscopic analysis was performed on 12 children diagnosed with type I DM and 12 age-matched volunteer healthy subjects. The duration of the disease, number of diabetic keto-acidosis episodes (DKA), number of hypoglycemic events and the level of hemoglobin A1C (HbA_{1C}) in the patients were noted. Voxels were placed in the right posterior parietal white matter, the occipital gray matter and the right basal ganglia. Single-voxel MRS with intermediate TE (144 ms) was performed in all 3 regions of interest plus short TE (34.5 ms) done only in the right posterior parietal white matter. N-acetylaspartate (NAA)/Creatinine (Cr) and Choline (Cho)/Cr ratios were recorded and compared between diabetic children and control subjects. The ratios collected from the diabetic group were correlated with the clinical data obtained. The presence of a significant lactate peak was also recorded.

Results: Type 1 diabetic subjects had lower NAA/Cr ratio in the white matter than control subjects. Longer duration of DM and increased number of DKA episodes predicted lower NAA/Cr ratio. The study also revealed slightly higher Cho/Cr ratios in the gray matter and basal ganglia in diabetic patients. No other significant differences in the metabolite ratios between the diabetic and control groups. Significant lactate peaks were detected in some diabetic patients performing the exam post recovery from DKA.

Conclusion: The decrease in NAA indicates reduced neuronal density or neuronal dysfunction as a consequence of long term poorly controlled type 1 DM. The explanation for the increase in Cho may be demyelination/gliosis or increased membrane turnover. The presence of lactate peaks suggest anaerobic metabolism during DKA.

Keywords: *Type 1 diabetes mellitus, Brain, MR spectroscopy*

Introduction

Type 1 diabetes mellitus (DM) affects about 1 in 500 children younger than 18 years. Type 1 DM is a metabolic disorder resulting from autoimmune destruction of the β-cells of the pancreas leading to insulin deficit and hyperglycemia. Type 1 DM can cause damage to multiple organ systems, either as a result of chronic hyperglycemia or acutely, in the setting of diabetic ketoacidosis (DKA). In recent years growing attention has been given to the effects of type 1 DM on the central nervous system (CNS). Long term impairment of cognitive function is known to occur in patients with type I DM and poor glycemic control ***(1)*.**

Because of the confounding effects of associated diseases with type 2 diabetes such as hypertension and hyperlipidemia & obesity, examination of the neurochemical profile of brains of type 2 diabetic patients doesn't necessarily provide insights into impact of the disease, however patients with type I diabetes mellitus generally do not have these associated conditions and examination of their brains does permit assessment of the unique effects of diabetes on cerebral metabolism ***(2).***

In vivo proton magnetic resonance spectroscopy (MRS) is a non invasive imaging method for monitoring chemical & metabolic changes in areas of interest within the brain. MRS can provide information about the concentration & relative levels of proton-including metabolites and may assist in discriminating normal & pathological tissues ***(3)***.

Proton MR Spectroscopy is a useful technique for functional interrogation of the brain in many neurological disorders. Prominent neurotransmitters and metabolites detected within the brain include N-acetylaspartate (NAA), choline compounds (Cho) and Creatinine/phosphocreatine (Cr). NAA is a neuronal-axonal marker and is not found in mature glial cells. Decreases in NAA may result from decreased neuronal viability, decreased neuronal function, or neuronal loss. Decreased NAA has been reported in seizure foci, brain metabolic disorders, neurodegenerative processes, ischemia and stroke. Reduction of cerebral NAA maybe reversible and thus it can be used as a dynamic marker of neuronal function & integrity ***(4)***.

MRS may demonstrate metabolic changes in normal appearing MRI examinations. Since Cr is relatively constant throughout the normal brain tissue and in different pathological conditions, it is often used as a reference resonance for the relative changes in NAA, Cho or both ***(3)***.

Metabolic abnormalities have been observed in the brain of poorly controlled type I DM children. These metabolic changes include a decrease in NAA indicating neuronal loss or functional impairment ***(3)***.

Lower levels of NAA in type1 DM subjects cannot be ascribed to possible bias in metabolite quantification, such as altered water content or partial volume effect resulting from brain atrophy because this type of systematic error in underestimating concentration should have been observed for all metabolites ***(2).***

Our aim was to investigate the impact of DM on brain neuro-chemical profile. This neuro-chemical profile can provide new information regarding the neurocognitive alterations that can occur in these patients

Patients and Methods

MR spectroscopic analysis was performed on 12 Children diagnosed with type I DM selected from endocrinology clinic and department in Abo El Reesh Pediatrics hospital. The control group included 12 volunteer healthy subjects, who were approximately age- and gender-matched to the group of patients with DM. An informed consent from each child's guardian was obtained before performing the study.

Inclusion criteria:

Patients with the following criteria: They were younger than 18 years of age, were diagnosed with type I diabetes mellitus. Control subjects without known neurological or biochemical disease.

Exclusion Criteria

History of stroke, seizures, or neurosurgical procedures, History of other chronic illness affecting cognitive function. Use of drugs other than insulin. Presence of congenital brain anomalies or signal abnormality on standard MRI.

Each patient was subjected to thorough data collection including:

Demographic data: Patient's name**,** Age, Sex

Clinical data: Duration of diabetes, Medications used & the average number of daily insulin injections, Level of HbA_{1C} (couldn't be obtained for all patients), Number of episodes of hypoglycemia requiring admission, Number of episodes of DKA requiring admission, Cause of admission (if inpatient), Presence of any neurological symptoms or any other systemic manifestation.

MR technique

Magnetic resonance imaging were performed on a 1.5 T MRI system (Philips Medical Systems, Netherlands) using a head coil. Combined magnetic resonance imaging (MRI) and spectroscopic imaging protocol was performed in all patients in one session. Total study time ranged from 45 to 60 minutes.

Conventional MR

The routine imaging studies included 6mm axial T2- weighted (TR/TE= 3733/100 ms), 6mm axial fluid-attenuated inversion recovery (TR/TE= 6000/120 ms; inversion time= 2000 ms), 6mm coronal T1-weighted (TR/TE= 487/15 ms) and 5mm sagittal T2-weighted (TR/TE= 3614/100 ms) images through the entire brain. The routine images were used to identify anatomical structures and to confirm the absence of any structural or signal abnormality.

No contrast or anesthesia was administered.

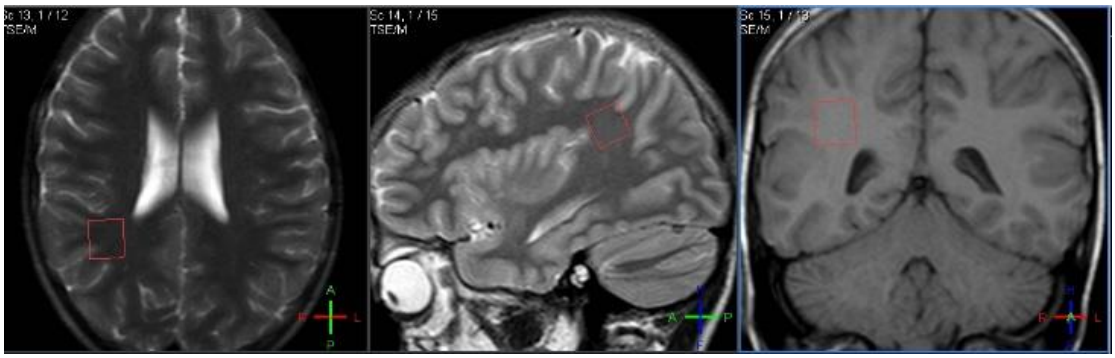

Fig. 1: Routine MR images (Axial T2, Sagittal T2 and Coronal T1 weighted images) used for voxel localization in the region of interest (in this case the right posterior parietal white matter)

MR spectroscopy

T1- and T2- weighted imaging were used for voxel localization. The exact anatomical location was determined visually by examining the MR images in three orthogonal planes (sagittal, coronal, and axial) to define the volume of interest. Voxels were placed in three regions of interest; the right posterior parietal white matter, the occipital gray matter and the right basal ganglia. For convenience, we will subsequently refer to these regions as white matter, gray matter and basal ganglia. A voxel of 1.5x1.5x1.5 cm^3 was used. Contact with the cerebrospinal fluid and the skull bone was avoided.

Single-voxel MRS was applied by using the method of point-resolved spectroscopy (PRESS). After automated transmitter and receiver adjustment, the signal intensity over the volume of interest was automatically shimmed. Optimal water resonance suppression was achieved by irradiation of the water resonance with chemical shift selective pulse sequences and spoiled gradients.

Four spectroscopic sequences where taken from all patients as follows:

- Intermediate TE (TR/TE= 2000/144 ms) at the white matter.
- Intermediate TE (TR/TE= 2000/144 ms) at the gray matter.
- Intermediate TE (TR/TE= 2000/144 ms) at the basal ganglia.
- Short TE (TR/TE= 2000/34.5 ms) at the white matter.

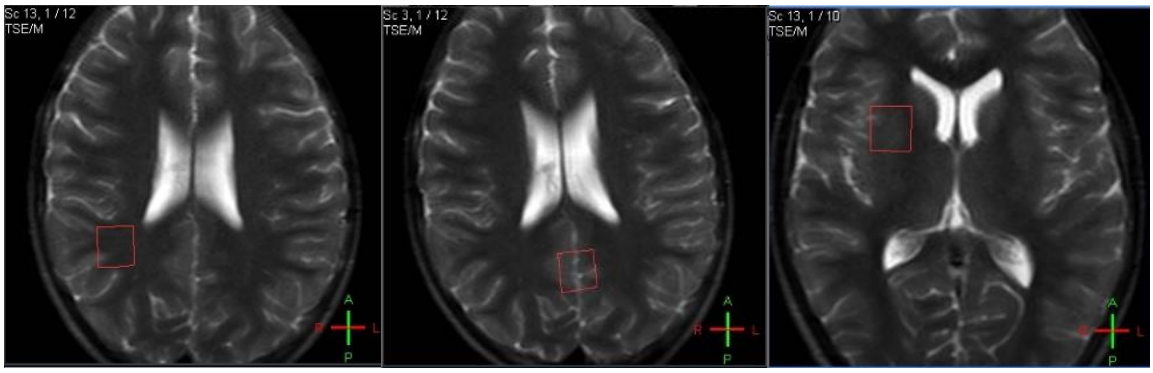

Fig. 2: Axial T2-weighted images showing the regions of interest (ROI) chosen for voxel placement in this study. (A): right posterior parietal white matter, (B): occipital gray matter and (C): right basal ganglia. Single-voxel MRS with intermediate TE (144 ms) was performed in all 3 regions of interest plus short TE (34.5 ms) done only in the right posterior parietal white matter region (A).

In vivo spectroscopy data were analyzed using the commercially available processing software provided by Philips Medical Systems, Netherlands. The magnitude spectra were processed automatically by baseline correction and curve-fitting procedures to determine the resonance areas of various metabolites.
The resonances of major metabolites detected were: the N-acetylaspartate (NAA) peak at 2.02 ppm, the creatine (Cr) and phosphocreatine peak at 3.02 ppm and the choline (Cho) peak at 3.20 ppm. The peak area metabolite ratios NAA/Cr and Cho/Cr were recorded for the three regions of interest. The presence or absence of a significant lactate peak was also recorded. In addition, the peak area ratios mI/Cr and Glx/Cr were recorded for the spectroscopic sequence with short TE (in the white matter). All the ratios recorded were compared between diabetic and normal subjects. The ratios collected from the diabetic group were correlated with the clinical data obtained.

Statistical methods:

Data were coded and entered using the statistical package SPSS version 24. Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test when comparing 2 groups and analysis of variance (ANOVA) with multiple comparisons post hoc test when comparing more than 2 groups. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations between quantitative variables were done using Spearman correlation coefficient**.** P-values less than 0.05 were considered as statistically significant.

Results

MR spectroscopic analysis was done on 12 patients with type 1 DM. Mean age of the patients was 12.8 ±1.0 years (range 11-15 years). The control group included 12 volunteer healthy subjects with mean age 12.7 ±1.5 years (range 10-15 years). No significant differences between the mean ages of the groups were discovered. Data is demonstrated in **Table 1**.

Table 1: Analysis of age in diabetic patients and normal subjects

	Diabetic group					**control group**				
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**
Age (in years)	***12.79***	***1.03***	***13.00***	***11.00***	***15.00***	***12.67***	***1.51***	***12.50***	***10.00***	***15.00***

Table 2 and **Chart 1** demonstrate the distribution of males and females among the diabetic and control groups.

Table 2: Sex distribution among the diabetic patients and normal subjects.

		Diabetic group		control group	
		Count	%	Count	%
Sex (M or F)	F	*3*	*25.0%*	*2*	*16.7%*
	M	*9*	*75.0%*	*10*	*83.3%*

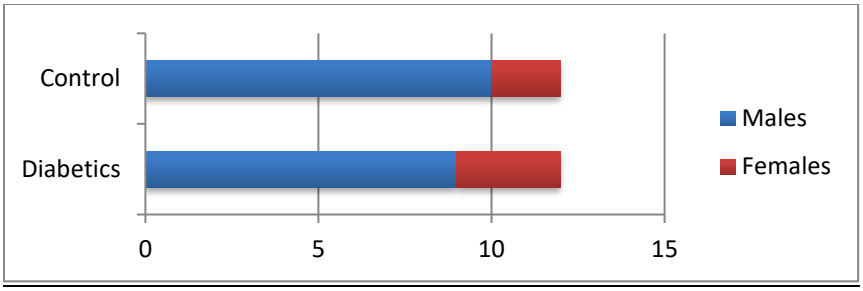

Figure 3: Sex distribution among diabetic patients and normal subjects.

In this study, the diabetic patients had a history of DM for 1.5-12 years (mean duration of DM was 4.5 ±3.3 years). The mean HbA_{1c} level was 9.7 ±1.2 %. The average number of DKA episodes requiring admission was 4.6 ±3.0 and the average number of hypoglycemic events requiring admission was 0.8 ±1.0. 41.7% of the diabetic patients selected performed the MRS examination after recovery from DKA.

Routine MR imaging of the diabetic patients and control subjects did not reveal any anatomical or signal abnormality.

In 24 subjects, a total of 96 spectra were sampled. Comparison between the different metabolite ratios in the diabetic and control groups is given in **Table 3** and **Chart 2**. MRS revealed lower NAA/Cr ratio in the white matter of DM patients than in control subjects by 22%. Cho/Cr ratio was found to be 17% higher in the gray matter and 19% higher in the basal ganglia of DM patients when compared with normal subjects. No other significant differences in the metabolic ratios between these groups were seen.

Table 3: Comparison of metabolic ratios between diabetic and control subjects.

	Diabetic group		control group		P value
	Mean	SD	Mean	SD	
NAA/Cr (white matter)	*1.89*	*.13*	*2.43*	*.23*	*< 0.001*
Cho/Cr (white matter)	*1.30*	*.28*	*1.33*	*.34*	*0.812*
NAA/Cr (gray matter)	*1.86*	*.12*	*1.91*	*.17*	*0.433*
Cho/Cr (gray matter)	*.95*	*.14*	*.81*	*.18*	*0.046*
NAA/Cr (basal ganglia)	*1.47*	*.18*	*1.44*	*.09*	*0.659*
Cho/Cr (basal ganglia)	*1.05*	*.22*	*.88*	*.15*	*0.031*
mI/Cr (white matter)	*.94*	*.07*	*1.11*	*.32*	*0.104*
Glx/Cr (white matter)	*.62*	*.10*	*.67*	*.06*	*0.137*

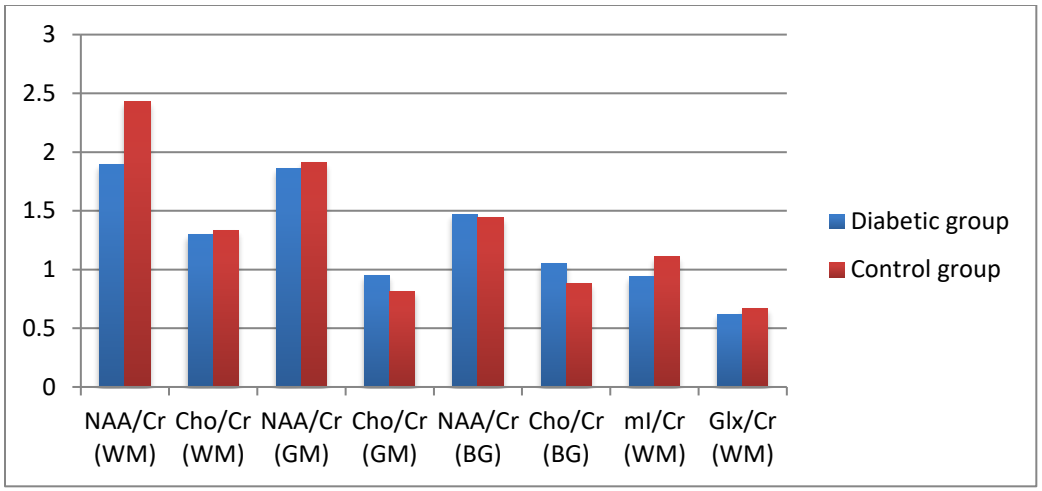

Figure 4: Comparison of the neuro-chemical profiles (mean value of the metabolite ratios) of type 1 diabetes mellitus patients relative to non diabetic controls. WM= white matter, GM= gray matter, BG= basal ganglia.

Table 4 demonstrates the correlation between the clinical data of diabetic patients (including the duration of diabetes, number of episodes of DKA requiring admission and number of episodes of hypoglycemia requiring admission), and the different metabolite ratios recorded in the diabetic group. Statistical analysis revealed significant inverse relation between the duration of diabetes and the NAA/Cr and Cho/Cr ratios in the white matter of diabetic patients. In addition, significant inverse relation was also found between the number of DKA episodes and the NAA/Cr and Cho/Cr ratios in the same region.

Table 4: Correlation of different diabetic metabolic ratios with the clinical data obtained from diabetic patients.

		Duration of Diabetes (in years)	Number of episodes of DKA	Number of hypoglycemic events
NAA/Cr (white matter)	Correlation Coefficient	*-.859-*	*-.845-*	*-.200-*
	P value	*< 0.001*	*.001*	*.534*
	N	*12*	*12*	*12*
Cho/Cr (white matter)	Correlation Coefficient	*-.724-*	*-.845-*	*-.147-*
	P value	*.008*	*.001*	*.648*
	N	*12*	*12*	*12*
NAA/Cr (gray matter)	Correlation Coefficient	*-.434-*	*-.133-*	*-.183-*
	P value	*.159*	*.681*	*.569*
	N	*12*	*12*	*12*
Cho/Cr (gray matter)	Correlation Coefficient	*-.244-*	*-.251-*	*-.139-*
	P value	*.445*	*.432*	*.665*
	N	*12*	*12*	*12*
NAA/Cr (basal ganglia)	Correlation Coefficient	*.101*	*.181*	*.321*
	P value	*.755*	*.574*	*.309*
	N	*12*	*12*	*12*
Cho/Cr (basal ganglia)	Correlation Coefficient	*-.230-*	*-.324-*	*.178*
	P value	*.472*	*.304*	*.581*
	N	*12*	*12*	*12*
mI/Cr (white matter)	Correlation Coefficient	*-.209-*	*-.066-*	*-.386-*
	P value	*.514*	*.839*	*.215*
	N	*12*	*12*	*12*
Glx/Cr (white matter)	Correlation Coefficient	*.459*	*.563*	*.395*
	P value	*.134*	*.057*	*.204*
	N	*12*	*12*	*12*

The presence or absence of a significant lactate peak was recorded in all regions in diabetic and control groups. No significant lactate peaks were detected in the control group. **Table 5** shows the relation between performing the spectroscopic analysis after recovery from DKA and the presence of a significant lactate peak in diabetic patients. Significant lactate peaks were detected in the basal ganglia in 60% of patients examined post recovery from DKA.

Table 5: Relation between performing the MRS after recovery from DKA and presence of a significant lactate peak in diabetic patients.

		Patient post recovery from DKA (yes or no)				
		yes		no		P value
		Count	%	Count	%	
Lactate (white matter)	absent	*5*	*100.0%*	*7*	*100.0%*	---
Lactate (gray matter)	absent	*4*	*80.0%*	*7*	*100.0%*	*0.417*
	present	*1*	*20.0%*	*0*	*.0%*	
Lactate (basal ganglia)	absent	*2*	*40.0%*	*7*	*100.0%*	*0.045*
	present	*3*	*60.0%*	*0*	*.0%*	

Table 6, 7, and **8** and **Chart 3** show comparisons regarding the distribution of NAA/Cr and Cho/Cr ratios across the different regions of interest in control subjects.

Table 6: Comparison of NAA/Cr ratio across different brain regions in control subjects.

	control group					P value
	Mean	SD	Median	Minimum	Maximum	
NAA/Cr (white matter)	*2.43*	*.23*	*2.43*	*2.02*	*2.80*	*< 0.001*
NAA/Cr (gray matter)	*1.91*	*.17*	*1.93*	*1.61*	*2.15*	
NAA/Cr (basal ganglia)	*1.44*	*.09*	*1.45*	*1.29*	*1.59*	

Table 7: Comparison of Cho/Cr ratio across different brain regions in control subjects.

	control group					P value
	Mean	SD	Median	Minimum	Maximum	
Cho/Cr (white matter)	*1.33*	*.34*	*1.28*	*.87*	*1.92*	*< 0.001*
Cho/Cr (gray matter)	*.81*	*.18*	*.81*	*.48*	*1.10*	
Cho/Cr (Basal ganglia)	*.88*	*.15*	*.90*	*.60*	*1.11*	

Table 8: Post hoc pairwise comparison of NAA/Cr & Cho/Cr ratios across different brain regions in control subjects.

Dependent Variable	(I) area	(J) area		
		white matter	grey matter	basal ganglia
NAA/Cr	white matter		<0.001	<0.001
	grey matter	<0.001		<0.001
	basal ganglia	<0.001	<0.001	
Cho/Cr	white matter		<0.001	<0.001
	grey matter	<0.001		1.000
	basal ganglia	<0.001	1.000	

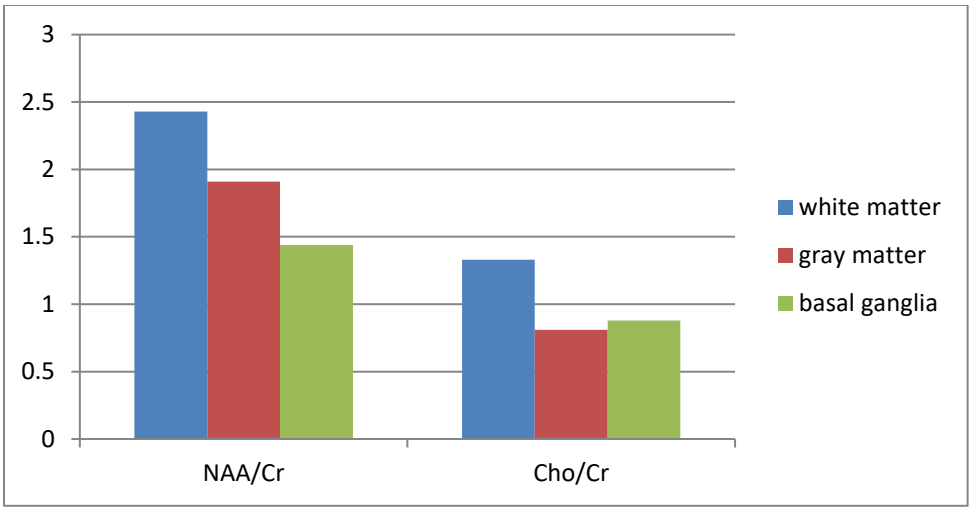

Figure 5: Comparison between the mean values of the NAA/Cr and Cho/Cr ratios across different brain regions in control subjects

Male patient, 12 years old, control subject. No history of stroke, seizures, or neurosurgical procedures. No history of neurological or biochemical disease or chronic illness. ***MRI:*** Routine MRI images showed absence of any anatomical or signal abnormality. ***MRS:*** NAA/Cr ratio in the white matter was 2.71**.** Cho/Cr ratio in the gray matter was 0.88**.** Cho/Cr ratio in the basal ganglia was 0.81**.** No significant lactate peaks were present in all regions of interest. (Fig 6: 9)

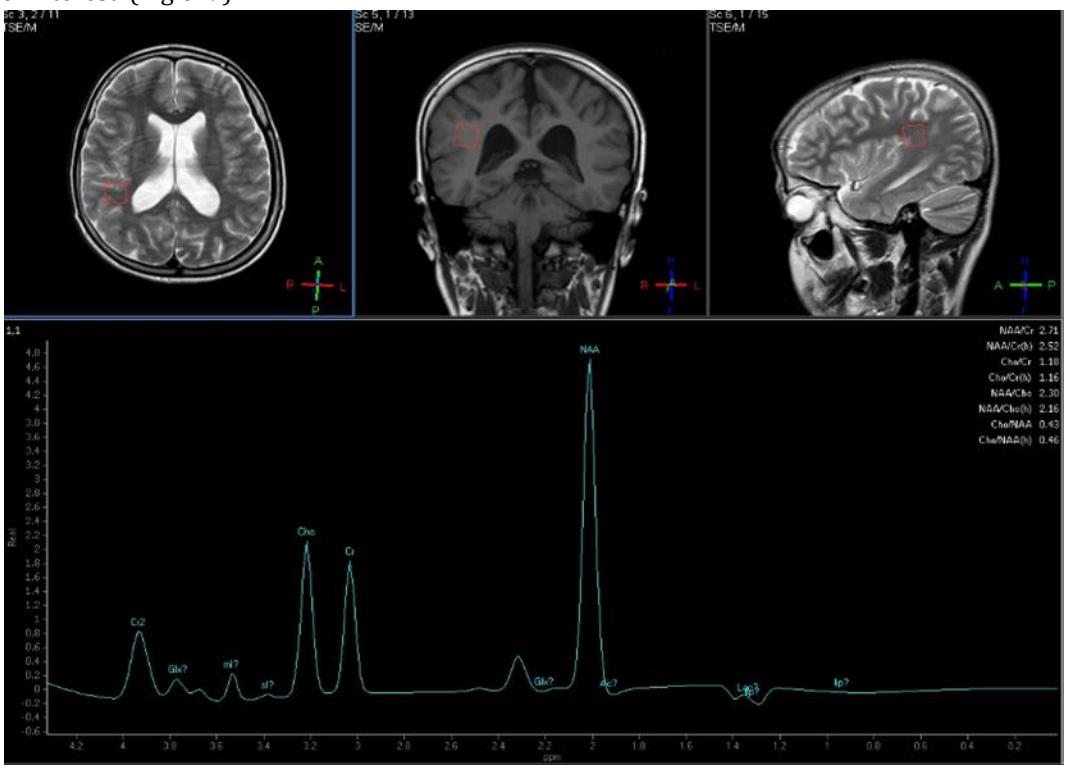

Fig. 6: MRS with intermediate TE (144 ms) performed on the right posterior parietal white matter. NAA/Cr ratio= 2.71, Cho/Cr ratio= 1.18.

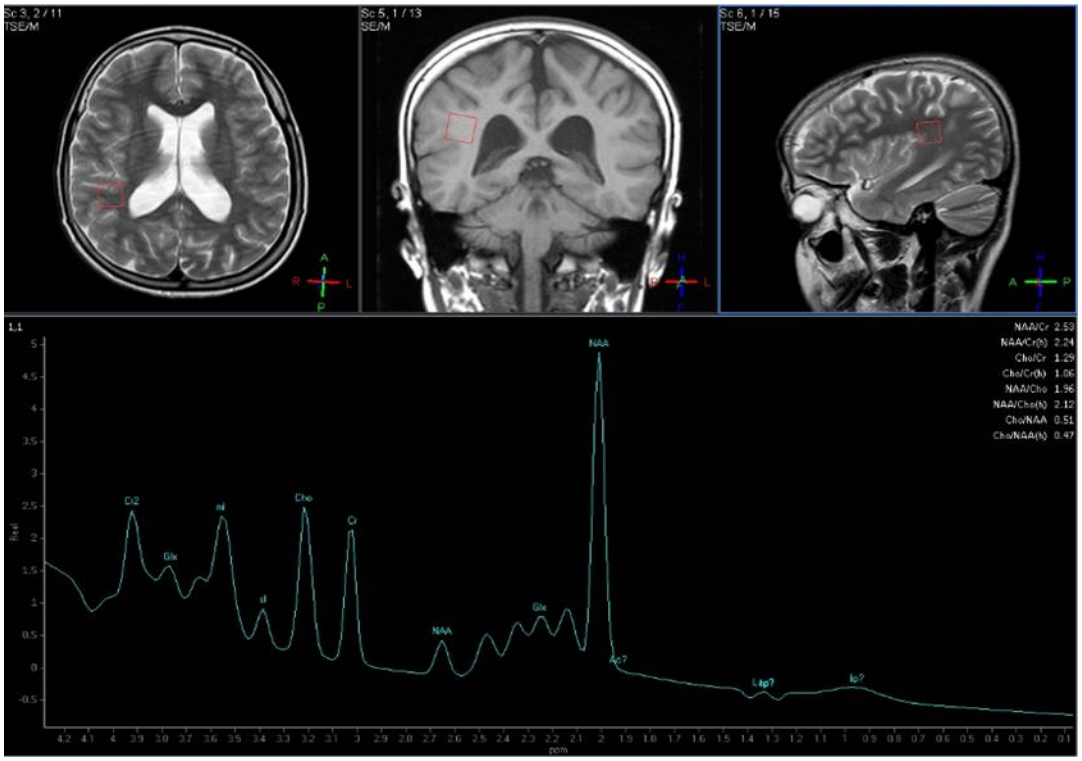

Fig. 7: MRS with short TE (34.5 ms) performed on the right posterior parietal white matter. mI/Cr ratio= 1.47, Glx/Cr ratio= 0.75.

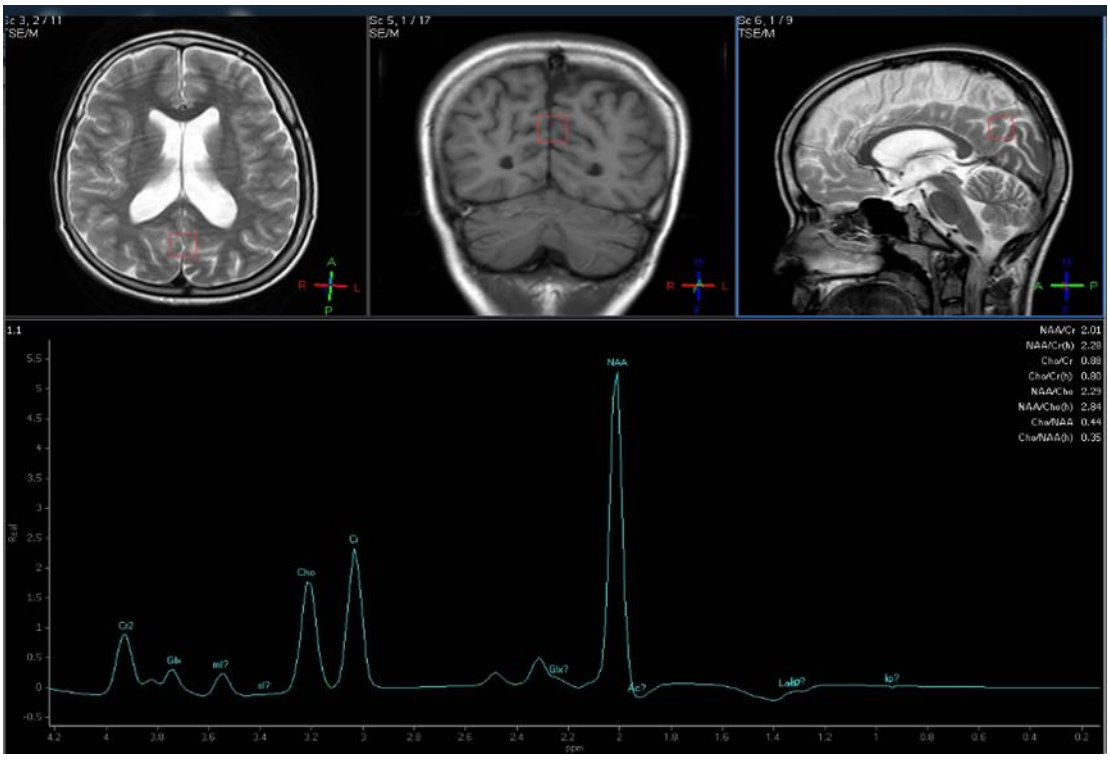

Fig. 8: MRS with intermediate TE (144 ms) performed on the occipital gray matter. NAA/Cr ratio= 2.01, Cho/Cr ratio= 0.88.

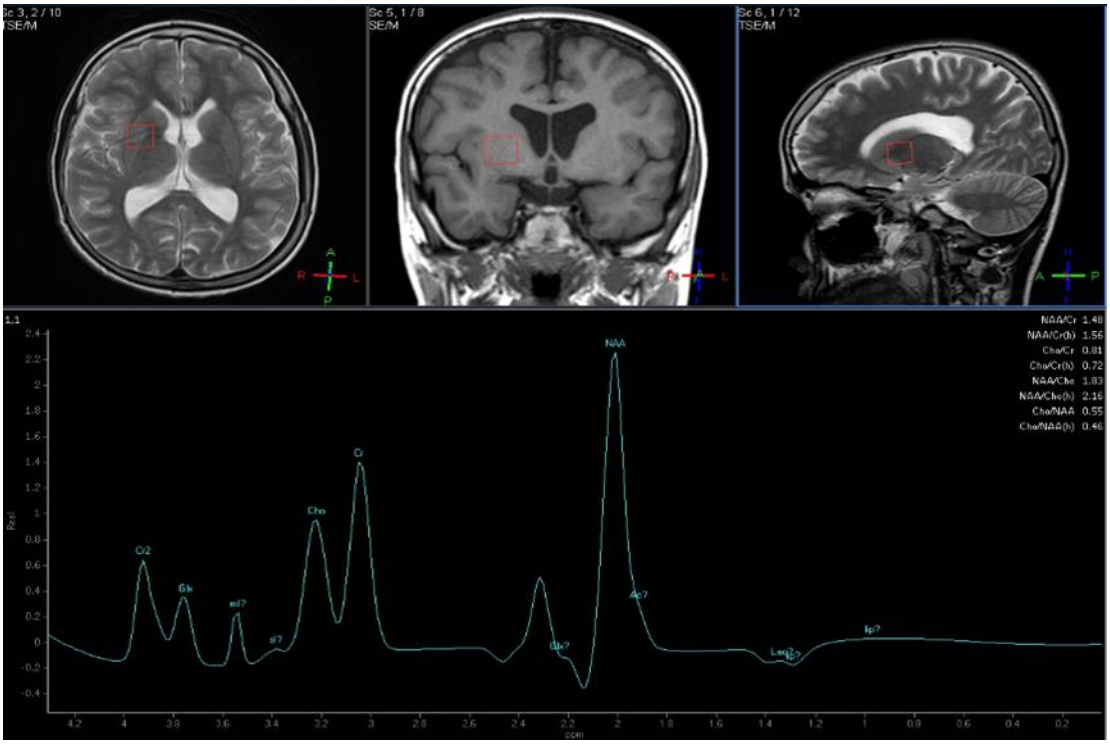

Fig. 9: MRS with intermediate TE (144 ms) performed on the right basal ganglia. NAA/Cr ratio= 1.48, Cho/Cr ratio= 0.81.

Discussion

The notion that diabetes mellitus (DM) impacts brain structure and function is not new. The theory arose for the first time in 1922, and since then the idea has intrigued many investigators, especially in regards to its effect on quality of life in young children and adolescents ***(5)***.

The steady-state concentration of various metabolites can be quantified non-invasively in the human brain using proton magnetic resonance spectroscopy (^{1}H-MRS). Gaining information on pathological alterations of metabolite concentrations is critical for characterizing and understanding the impact of diseases on brain function at the molecular level ***(2).***

Since ***Cr*** is relatively constant throughout the brain tissue and in different pathological conditions, it is often used as a reference resonance for the measurement of the relative changes in NAA or Cho or both. ***NAA*** is the most sensitive central nervous system metabolite. Since, it is a neuro-axonal marker, abnormalities of neural structures, such as reduced neuronal density or viability, lead to reduction of NAA. More recently, reduction of cerebral NAA was shown to be potentially reversible, indicating that NAA levels can also be used as a dynamic marker of neuronal metabolic dysfunction and integrity. ***Cho*** can be viewed as an indirect marker of myelination and cell membrane metabolism. An increase in the Cho peak is associated with conditions such as brain tumors and demyelinating disease. Decreased concentration of Cho maybe due to changes in dynamic behavior of the membrane lipids and/or decreased membrane turnover. ***Lac*** is usually located only under pathological conditions, where energy metabolism is affected severely and it could indicate anaerobic metabolism ***(3)***.

In clinical applications of MR spectroscopy, the ratios of the various metabolites are used more often than absolute metabolite concentrations. Commonly used metabolic ratios include the ratio of N-acetylacetate asparte to creatine (NAA/Cr) and the ratio of choline to creatine (Cho/Cr) ***(6)***.

In this study, most of the diabetic patients selected were poorly controlled having a high HbA_{1c} and/or history of several episodes of DKA or hypoglycemia requiring admission.

The impact of diabetes on the brain neuro-chemical profile was observed in this study.

The major finding observed in the present study is that the NAA/Cr ratio in the white matter of DM patients was significantly lower than in control subjects, which indicates reduced neuronal density and/or neuronal dysfunction. No significant difference was found between both groups regarding the NAA/Cr ratio in the gray matter or basal ganglia. The result is in agreement the previously reported results by *Kreis and Ross* ***(7)*** and *Sarac et al.* ***(3)***. The finding supports the suggestion that white matter integrity alterations may be associated with cognitive impairments in diabetic patients ***(5)***.

Another statistically significant important finding was found regarding the Cho/Cr ratio, which was slightly higher in the gray matter and basal ganglia of diabetic patients when compared with normal subjects. Cho levels are increased with demyelination and other forms of cell membrane breakdown, including gliosis. This finding is consistent with the result reported by *Northam et al.* ***(8)***. However, it is in disagreement with results given by *Kreis and Ross* who reported that Cho was, on average, unchanged ***(7)*** and *Sarac et al.* who found the Cho/Cr ratio to be significantly lower in the pons region, while being normal in other brain regions ***(3)***. The discrepancy in results between our study and these previous studies may be explained by the difference in diabetic populations or due to different ROIs selected in each study.

In the current study, no other significant differences in the metabolite ratios between the diabetic and control groups were noted. However, *Northam et al* reported higher level of mI in brain of type 1 DM compared to non diabetics and suggested that increased levels maybe associated with both gliosis and demyelination or that higher level may represent a homeostatic response of the brain to prolonged hyperglycemia ***(8)***. The study done by *Northam et al.* was performed on children and youth with type 1 DM 12 years after their diagnosis, while in our study the mean duration of DM was 4.5 ±3.3 years. This can explain the normal level of mI in our study.

Our study also revealed significant inverse relation between the duration of diabetes and the NAA/Cr ratio in the white matter of diabetic patients. This finding may support the evidence that neurocognitive deficits become more pronounced with longer duration of type 1 DM ***(9).*** In addition, significant inverse relation was found between the number of DKA episodes and the NAA/Cr ratio in the same region, which suggests that poor glycemic control can have a long term effect on brain structure and function.

Another significant inverse relation was detected between the duration of diabetes and the Cho/Cr ratio in the white matter of diabetic patients. No explanation is given for this finding considering that there was no significant difference regarding this ratio between diabetic and control groups.

Significant lactate peaks were detected in the basal ganglia in 60% of patients examined post recovery from DKA. The presence of lactate peaks suggest anaerobic metabolism during DKA. The basal ganglia are particularly susceptible and this is hypothesized to be related to the high adenosine triphosphate demand of the region. This is consistent with the results of the MRS study done in children with DKA by *Wootton-Gorges. et al*. ***(4)***.

As most of our findings are based upon comparison of diabetic patients with control subjects, statistical comparison was done on the NAA/Cr and Cho/Cr ratios across the different regions of interest in control subjects. Cortical gray matter had a significantly smaller NAA/Cr ratio than the parietal white matter region. The NAA/Cr ratio of the basal ganglia was significantly smaller than that of the white- and gray-matter regions. The Cho/Cr ratio of the white matter was significantly larger than that of the gray matter and basal ganglia regions. The results obtained are similar to the results of the study done by *Safriel et al.*, that was done to define reference values of metabolic ratios in different brain regions (using similar MRS protocol to our study) ***(6)***.

Limitations: Limited number of diabetic patients and control subjects. No clinical neurocognitive tests were done in this study, to determine the corresponding clinical impact and prognostic value of such MRS findings. No follow up was done in this study. Some metabolites such as NAA have been shown to be potentially reversible.

Further MRS studies on larger groups of diabetic patients and control subjects, with follow up and performing clinical neurocognitive tests, is recommended to further evaluate the value of MRS in type 1 DM.

Conclusion

The decrease in NAA indicates reduced neuronal density or neuronal dysfunction as a consequence of long term poorly controlled type 1 DM. The explanation for the increase in Cho may be demyelination/gliosis or increased membrane turnover. The presence of lactate peaks suggest anaerobic metabolism during DKA.

References:

1. McCarthy, A., Lindgren, S., Mengeling, M. and Tsalikian, E. (2000). Effects of diabetes on learning in children. Diabetes Research and Clinical Practice, 50, p.229.
2. Mangia, S., Kumar, A., Moheet, A., Roberts, R., Eberly, L., Seaquist, E. and Tkáč, I. (2013). Neurochemical Profile of Patients with Type 1 Diabetes Measured by 1H-MRS at 4 T. Journal of Cerebral Blood Flow & Metabolism, 33(5), pp.754-759
3. Sarac, K., Akinci, A., Alkan, A., Aslan, M., Baysal, T. and Özcan, C. (2005). Brain metabolite changes on proton magnetic resonance spectroscopy in children with poorly controlled type 1 diabetes mellitus. Neuroradiology, 47(7), pp.562-565.
4. Wootton-Gorges, S. and Glaser, N. (2007). Imaging of the brain in children with type I diabetes mellitus. Pediatric Radiology, 37(9), pp.863-869.
5. Litmanovitch, E. (2015). Short and long term neuro-behavioral alterations in type 1 diabetes mellitus pediatric population. World Journal of Diabetes, 6(2), p.259.
6. Safriel, Y., Pol-Rodriguez, M., Novotny, E., Rothman, D., and Fulbright, R. (2005). Reference Values for Long Echo Time MR Spectroscopy in Healthy Adults. American Journal of Neuroradiology , 26 (6), pp.1439-1445.
7. Kreis, R. and Ross, B. (1992). Cerebral metabolic disturbances in patients with subacute and chronic diabetes mellitus: detection with proton MR spectroscopy. Radiology, 184(1), pp.123-130.
8. Northam, E., Rankins, D., Lin, A., Wellard, R., Pell, G., Finch, S., Werther, G. and Cameron, F. (2009). Central Nervous System Function in Youth With Type 1 Diabetes 12 Years After Disease Onset. Diabetes Care, 32(3), pp.445-450.
9. Desrocher, M. and Rovet, J. (2004). Neurocognitive Correlates of Type 1 Diabetes Mellitus in Childhood. Child Neuropsychology (Neuropsychology, Development and Cognition: Section C), 10(1), pp.36-52.