Short TE Proton MRS in acute and treated Graves' Disease

E. R. Danielsen[1], T. Elberling[2], Å. K. Rasmussen[3], G. Waldemar[2], U. Feldt-Rasmussen[3], C. Thomsen[1]

[1]Dept. of Radiology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, [2]Dept. of Neurology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, [3]Dept. of Endocrinology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark

Introduction:

Graves' disease (GD), an autoimmune disease of the thyroid gland, is the most common cause of thyrotoxicosis (1). Patients often have cognitive and psychiatric symptoms in the acute toxic phase (2,3). Previous studies have shown reduced Cho/Cr (4) and reduced Cho and mI (5). A few studies (6,7) suggest that some patients have long-term neuropsychiatric symptoms despite successful antithyroid treatment. The purpose of our study was to evaluate MRS results in the acute phase of GD and after 1 year in the successfully treated patients to see whether the reported abnormalities are reversible.

Material and Methods:

Subjects: Prospective study including 27 patients with acute GD (1 year follow-up: 24 patients) and 33 sex and age matched healthy volunteers. Sixteen of the patients were included in a previous report (5). GD was diagnosed based on thyroid hormones, TSH, anti-TPO, and scintigraphy of the thyroid gland. Standard T_1 and T_2 weighted MR images were acquired from all participants to exclude cerebral pathology. All subjects underwent a full endocrinological, neurological, and psychiatric evaluation to exclude prior diseases. All subjects had normal serum Na^+, excluding hypo – and hypernatremia effects on MRS. Repositioning of VOIs at the follow-up MRS was based on MRI.

MRS method: The short TE method STEAM (TE/TM/TR/NS 20/30/3000/86, Siemens Vision 1.5 T) was used to acquire spectra from 3 volumes of interest (VOI): an occipito-parietal location primarily containing white matter (WM), a mid occipital location primarily containing grey matter (OGM), and a mid frontal location primarily containing grey matter (FGM). System calibration for quantitation purposes were carried out regularly. Post processing: Metabolite concentrations were calculated from the output of LCModel, using the principle of reciprocity, and corrections as in (8). Statistical analysis: Paired and unpaired student's t-tests.

Results:

Patients acute phase vs. volunteers: OGM: Total Choline (Cho) and myo-Inositol (mI) were 17% and 6% decreased respectively; FGM: Cho was 20% reduced; WM: All i.e. Cho (-16%), mI (-15%), total Creatine (Cr) (-7%), N-acetylaspartate (NAA) (-5%) and Glutamine+glutamate (Glx) (-9%) were significantly reduced. Patients 1year post vs. volunteers: Glx in WM was significantly reduced. Patients acute phase vs. 1 year post: Significant differences corresponding to normalization were found. Details are listed in table 1. The quality of the spectra compared to the quality in (5), see examples of spectra therein.

Discussion/Conclusion:

This study showed that the MRS abnormalities (reduced Cho and mI) reported earlier were reversible after successful anti-thyroid treatment.

Differing from earlier studies of GD in the acute phase, this larger study showed small (-5% to –9%) but significant reductions of NAA, Cr and Glx in WM, adding to the 16% reduced Cho and 15% reduced mI. These abnormalities all were reversible with the exception of Glx that remained 9% reduced ($p< 0.02$ vs. normal).

Further investigations are needed to reveal whether the finding of reduced Glx in WM is associated with the possible neuropsychiatric symptoms in the group of successfully anti-thyroid treated patients. It should be noted however, that previous studies report reduced Glx associated with dementia (9,10) and major depression (11,12), but whether the reduced Glx in the treated GD plays a similar role remains an open question.

References:

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		GD acute mmol/kg	Acute vs. volunteer	GD 1y post mmol/kg	1y post vs acute	1y post vs. volunteer	volunteer mmol/kg
WM	NAA	9.44±0.94	*	9.94±0.81	ns	ns	9.96±0.74
	Cr	5.56±0.73	*	6.06±0.69	*	ns	5.99±0.58
	Cho	1.27±0.20	***	1.59±0.14	******	ns	1.52±0.19
	mI	3.56±0.38	****	4.15±0.47	****	ns	4.20±0.63
	Glx	9.73±1.31	*	9.69±1.17	ns	*	10.67±1.71
OGM	NAA	10.16±0.68	ns	9.89±0.82	*	ns	9.86±0.63
	Cr	7.02±0.67	ns	7.20±0.58	ns	ns	6.97±0.60
	Cho	0.93±0.11	*******	1.15±0.12	*********	ns	1.12±0.11
	mI	4.20±0.46	*	4.73±0.54	**	ns	4.46±0.49
	Glx	14.52±1.50	ns	14.08±1,79	ns	ns	14.92±2.20
FGM	NAA	8.93±1.65	ns	9.75±0.95	*	ns	9.91±1.67
	Cr	6.59±1.42	ns	7.30±0.98	ns	ns	7.12±1.21
	Cho	1.33±0.31	**	1.77±0.31	****	ns	1.67±0.24
	mI	4.34±1.01	ns	5.19±0.72	**	ns	4.97±0.88
	Glx	15.88±4.44	ns	17.60±2.70	ns	ns	17.66±2.19

Table 1: Metabolite concentrations in mmol/kg measured in Graves' disease (GD) and in matched healthy volunteers.
*: $p<0.05$, **: $p<0.01$, ***: $p<0.001$, ****: $p<0.0001$, etc., and ns indicates that $p>0.05$.