Serial ^{1}H MR Spectroscopy in Alzheimers Disease, Frontotemporal Dementia and Dementia with Lewy Bodies

K. Kantarci[1], R. C. Petersen[1], B. F. Boeve[1], D. S. Knopman[1], G. E. Smith[1], R. J. Ivnik[1], E. G. Tangalos[1], C. R. Jack[1]
[1]Mayo Clinic, Rochester, MN, United States

Introduction:

Neurodegenerative dementia is an important clinical group for development of neuroprotective therapies. Non-invasive biological markers are needed to monitor efficacy in these therapeutic trials. In a previous cross-sectional ^{1}H MR spectroscopy (^{1}H MRS) study, we identified that the neuronal marker N-acetylaspartate /Creatine (NAA /Cr) levels are decreased in dementias that are characterized by neuron loss such as Alzheimers disease (AD) and frontotemporal lobar degeneration (FTLD). Myo-inositol (mI) /Cr levels are elevated in dementias that are pathologically characterized by gliosis such as AD and FTLD. Choline (Cho) /Cr levels are elevated in dementias that are characterized by a profound cholinergic deficit such as AD and dementia with Lewy bodies (DLB). The objective of this study was to determine if annual change in metabolite measurements on serial ^{1}H MRS is sensitive to disease progression in common neurodegenerative dementias.

Methods:

We studied 91 cognitively normal elderly, 61 patients with AD, 26 patients with FTLD, and 15 patients with DLB, who underwent a single voxel ^{1}H MRS exam from the posterior cingulate gyri with TR /TE = 2000/30 ms and clinical evaluation twice within an average follow-up period of 15.6 months. We calculated the annualized rate of change in NAA /Cr, mI /Cr and Cho /Cr ratios. We compared the percent annual change in metabolite ratios of patients with different neurodegenerative dementias to cognitively normal elderly using t-tests.

Results:

The percent annual decline in NAA /Cr measurements was greater than normal in patients with AD (p =0.015) and FTLD (p =0.002) but not in patients with DLB. Patients with DLB had a trend of greater rate of Cho /Cr increase than normal (p =0.067). The percent annual change in mI /Cr was not different from normal in any of the dementias.

Table: Mean ± SD % annual change in ^{1}H MRS metabolite ratios in common neurodegenerative dementias.

	Normal	AD	FTLD	DLB
N	91	61	26	15
NAA /Cr	0.65 ± 4.68	-1.68 ± 6.63**	-4.13 ± 11.96*	-0.43 ± 7.71
Cho /Cr	2.60 ± 8.42	1.41 ± 9.73	-0.48 ±11.41	8.38± 12.25***
mI /Cr	1.78 ± 8.18	1.32 ± 7.89	3.34 ± 16.26	-1.84 ± 9.60

*% annual change in metabolite ratios are different normal on t-tests *p=0.002, **p=0.015, ***p=0.067,*

Conclusion:

^{1}H MRS metabolite measurements may be useful markers of disease progression in patients with common neurodegenerative dementias. NAA /Cr ratios may be a useful marker in patients with AD and FTLD, and Cho/Cr ratios may be a useful marker in patients with DLB.

[1] Kantarci K, Petersen RC, Boeve BF,et al. ^{1}H MR Spectroscopy in common dementias. Neurology 2004; 63:1393-1398.

Supported by: AG11378, AG06786, AG16574, Alzheimer's Association.