IN VIVO PROTON MR SPECTROSCOPY IN EVALUATION OF DEMENTIA

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Introduction: Dementia, which involves a gradual loss of intellectual capacities, is the major cause of long-term morbidity and disability in the geriatric population worldwide. It is a syndrome of multi-focal impairment of cognitive or higher mental functions involving progressive decline in memory, intellect and personality, in presence of normal consciousness and attention levels. The expression of the disease may differ at different ages, but the major findings in demented patients of all ages are similar. Main aim of diagnosis is to identify treatable and modifiable causes of dementia. Differential diagnosis depends primarily on careful history and clinical examination, supported by biochemical and radiological investigations. Any method that could identify these changes at an early stage and point towards the underlying pathology, if any, would allow for greater benefit in the management process. ^{1}H MRS offers a sensitive non-invasive technique for in vivo assessment of brain metabolites in dementia, which can aid in the differential diagnosis at an early and possibly reversible stage of the dementing process.

Material and Methods: Single voxel ^{1}H MRS studies on forty one dementia patients (DSM-IV criteria, age group 40-85 years) with impaired cognition (MMSE score 17-24; CDR 0.5-1.5), including 16 patients diagnosed as probable AD (NINCDS-ADRDA), 8 patients with probable Vascular dementia (VaD, NINDS-AIREN), 6 patients each with FTD and AIDS dementia complex (ADC) and 5 patients with dementia secondary to alcohol abuse (Alc. D), were carried out on 1.5T Siemens Magnetom 'Vision' MR system. The MRS studies were performed with a 3.4 cm^3 voxel placed in the hippocampal/temporal and frontal lobes, using TR/TE/Ac (repetition time/time to echo/no. of acquisition) of 1500/20&135/128. Pre- and post-treatment/intervention spectral patterns were also studied in relevant cases. NAA/Cr, Cho/Cr, mI/Cr and mI/NAA ratios in the dementia patients were compared with the metabolite ratios of normal elderly controls, and statistical significance was analyzed using student's t-test. Probability factor ($p<0.05$) was regarded as critical for significance. Twenty healthy cognitively able age matched controls were also subjected to the MRS studies.

Results: Reduction in NAA/Cr was noted in all dementia patients. Increased mI/Cr and decreased NAA/Cr ratios distinguished AD (Fig.1) from normal controls. Increased mI/Cr distinguished AD from other dementias except FTD. Increased mI/NAA was found to be a more sensitive criterion for such distinction in doubtful cases. ^{1}H MRS in common secondary dementing disorders studied showed loss of NAA with decreased NAA/Cr (Fig.2 &3a), which was progressive with increasing severity of the disease process with post-treatment reversal (Fig.3b). Cho/Cr were not different in patients from controls. (Table 1)

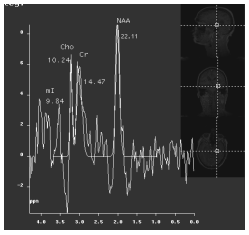


Fig.1 Representative MRS of AD- High mI/Cr & mI/NAA

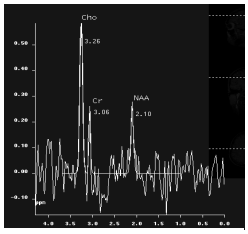
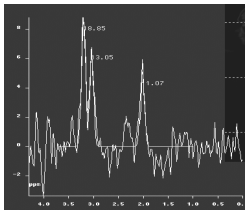


Fig.2 MRS in ADC Low NAA/Cr



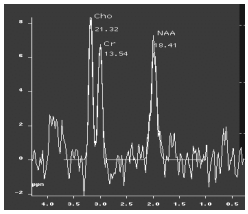


Fig. 3 Alcoholic Dementia
(a) Pre-treatment Low NAA/Cr (b) Post-treatment NAA/Cr normal

Discussion: The proton spectrum in dementias, particularly AD is startlingly different from normal. ^{1}H MRS studies of AD patients reveal decrements in level of NAA reflecting neuronal loss, with a concomitant increase in mI, a glial marker, suggesting abnormalities in the inositol poly-phosphate second messenger system, even at an early stage of the disease. The diffuse NAA decline is independent of regional atrophy and reflects a decrease in neuro-cellular viability. The biochemical changes observed with ^{1}H MRS are sequential and predate structural changes. If excess of mI precedes reduction of NAA, interruption of neural injury might be possible. MR Spectroscopy shows promise for predicting cognitive status and assessing cortical and subcortical neurochemical changes. It has the potential to provide means for establishing diagnosis early, monitoring disease progress and assessing therapeutic/ interventional effects in dementing disorders.

Table 1: ^{1}H MRS metabolite ratios (mean±SD) in controls and patients

	N	NAA/Cr	Cho/Cr	mI/Cr	mI/NAA
Controls	20	1.34± 0.16*	1.09± 0.11	0.58± 0.08	0.43± 0.07
AD	16	1.09± 0.12*	0.99± 0.16	0.66± 0.09*	0.61± 0.06*
FTD	6	1.12± 0.10*	1.04± 0.12	0.68± 0.07*	0.61± 0.08*
VaD	8	1.11± 0.11*	0.98± 0.13	0.55± 0.05	0.49± 0.06
ADC	6	0.98± 0.09*	1.00± 0.14	0.50± 0.04	0.48± 0.08
Alc. D	5	1.18± 0.14*	1.19± 0.11	0.56± 0.07	0.47± 0.04

* *Metabolite ratios statistically significant as compared with controls ($p<0.05 – 0.01$)*

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