Regional Brain Metabolite Pattern in Fronto-Temporal Dementia

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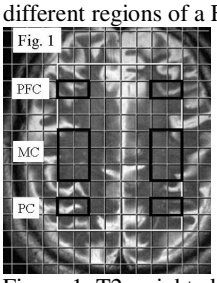
Introduction: Frontal-temporal dementia (FTD) is a neurodegenerative disease of frontal and temporal neocortex. The most striking symptoms of FTD are behavioral and personality changes. Histopathological and neuroimaging examinations have shown atrophy and hypo-function of the frontal and anterior temporal lobes in FTD patients[1]. In the present study, we performed multivoxel magnetic resonance spectroscopic imaging (^{1}H MRSI) to assess metabolic abnormalities in the frontal lobe [prefrontal cortex (PFC) and motor cortex (MC)] of patients with FTD.

Materials and Methods: Fifteen frontal variant FTD patients (mean age= 56.24 years, 8M/7F) and six controls (mean age=57.83, 2M/4 F) were recruited in this study. MR imaging and ^{1}H MRSI was performed on a 3 Tesla scanner equipped with a standard quadrature head coil. Anatomical images were acquired using standard parameters. Two-dimensional multivoxel ^{1}H MRSI was performed using a spin echo sequence. Sequence parameters included: TR/TE = 1700/30ms, NEX = 3 and voxel resolution of 10x9.4x20 mm^3. ^{1}H MRSI data was analyzed from voxels that encompassed PFC, MC and parietal cortex (PC) regions (Fig 1) and exhibited good spectral resolution (FWHM < 20Hz) and signal to noise ratio. Absolute concentration of N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), myo-inositol (mI) was measured using a user-independent spectral fit program [Linear Combination (LC) Model]. A two-tailed heteroscedastic Student t-test was performed to look for any significant difference in metabolic patterns of PC (internal control) and PFC, and PC and MC within the FTD patients. A comparison between controls (n=6) and FTD patients was also performed from the MC to look for difference in metabolite concentration. PFC and PC regions from 3 controls and FTD patients were also compared as only 3 controls had ^{1}H MRSI data from these regions. A p value of less than 0.05 was considered significant.

Results: A significant reduction in NAA and Cr and increase in Cho and mI was observed from the PFC of FTD patients compared to controls. Similarly, significantly lower NAA and higher Cho concentrations were also observed in MC of patients compared to controls. No significant difference was observed for any of the metabolites from PC between controls and patients (Fig 2). Concentration of metabolites from different cortical regions of the brain within FTD patients is shown in Fig 3. Both MC and PFC exhibited significantly lower NAA and higher Cho compared to PC. However, only PFC had significantly lower Cr and significantly higher mI concentrations compared to PC. Representative spectra from different regions of a FTD patient are shown in Fig 4.



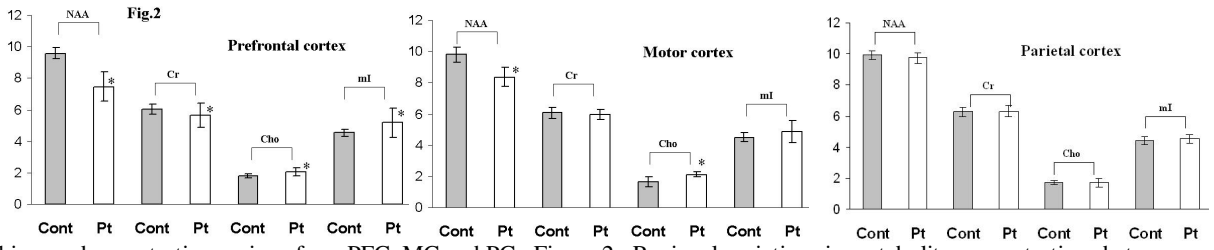
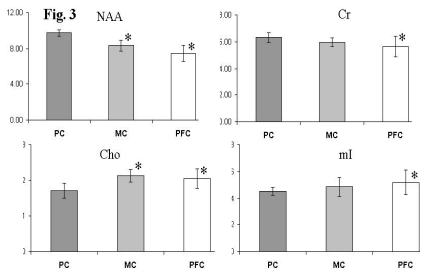


Figure 1. T2 weighted image demonstrating regions from PFC, MC and PC. Figure 2. Regional variations in metabolite concentrations between controls and FTD patients (* indicates significant difference).



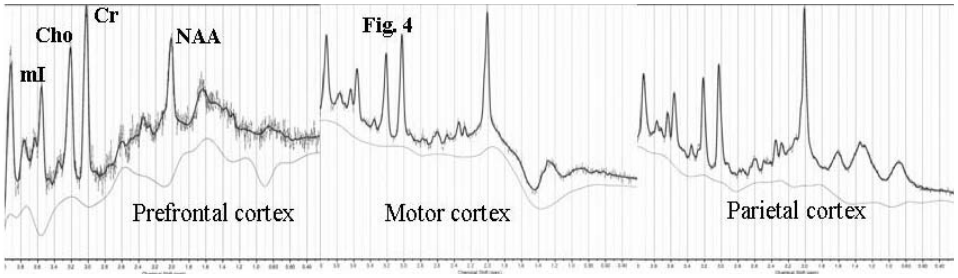


Figure 3. Variation in metabolite concentration of different cortical regions from FTD patients (* indicates significant difference). Figure 4. Representative spectra from different cortical regions of a FTD patient.

Discussion: Reduction of NAA in PFC and MC reflects loss or dysfunction of neurons and axons. Nerve cell death in FTD is induced by the accumulation of structurally deformed tau and ubiquitin proteins[2]. Histologic studies have demonstrated loss of the giant pyramidal Betz cells along with vacuolation and astrogliosis in the cortical layers of the frontal lobe in patients with FTD[3]. Observation of significantly higher mI only in the PFC implies that there exists a variable degree of gliosis in these patients[3]. MC changes in FTD without motor impairment are consistent with observations of EMG abnormalities in patients with clinically asymptomatic motor impairments[4].

Conclusion: Our results demonstrate that PFC is the most severely involved region in patients with frontal variant FTD. ^{1}H MRSI indices may be used to monitor disease progression and therapeutic effects from different locations of the brain involved in FTD.

References:

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