2-D 1H MRSI Study of Prefrontal Cortex in the Brain of First-Episode Psychosis Patients

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Introduction: Psychotic disorders (schizophrenia, schizoaffective and bipolar disorders) are a common condition that affects 3-6% of the general population. The specific neural abnormalities that contribute to the development of these disorders are not known[1]. Several recent lines of evidence suggest that patients with psychosis suffer from abnormalities in neuronal mitochondria metabolism, presumably within prefrontal brain networks that modulate emotional and cognitive homeostasis[2]. This work investigates the regional brain metabolism using 2D ^{1}H MRSI in the brain of first-episode psychosis patients (FEP).

Methods: Ten FEP patients were studied prior to initiating treatment and were case-matched to healthy subjects. These patients had diagnoses of Brief Reactive Psychosis (n=2), schizophrenia paranoid type (n=2), schizophreniform disorder (n=1), bipolar disorder depressed with psychosis (n=1), and psychosis not otherwise specified (NOS, n=4). They had a mean psychosis (PANSS) rating of 70 (SD=11). Three of the FEP subject's scans were not useable due to motion artifact. The remaining 7 first-episode psychosis (FEP) patients and 7 healthy subjects were matched for sex (3 women and 4 men in both groups), race (4 white, 3 African-American in both groups) and age (32 v 29 years respectively; p>.5).
All ^{1}H MRSI, MR scout images, and T_1 mapping images for tissue segmentation were acquired with a 4T Varian INOVA system using a volume TEM head coil. Spectra were localized to a 10x80x100 voxel angulated along the anterior-, posterior commissure line using a 3D localized adiabatic LASER sequence with 2D phase encoding. Shimming was optimized by automatic B_0 mapping. Water suppression was provided by an initial broad-band semi-selective excitation pulse and frequency selective DANTE pulse applied to the water resonance. Data were acquired using TE/TR of 62/2000ms, FOV 192x192mm^2 with 24x24 encodes. MRSI data were co-registered with scout images, and tissue segmentation data were analyzed by home-written programs using MATLAB. Spectra were selected in 3 regions – anterior cingulated cortex (ACG), left- (LPFC), and right prefrontal cortex (RPFC) for further analysis (Figure 1). Metabolite data were presented in terms of metabolite ratios after curve fitting (NAA: N-acetyl aspartate; Cr: creatine; Ch: choline). For the correction of tissue dependence of metabolites, gray matter (GM) and white matter (WM) content for each MRI voxel was determined using quantitative T_1-based mapping and algorithm. The tissue type of each MRI voxel was assigned using the quantitative T_1 values. Pixels with T_1 between 600 and 1070 msec, 1071 and 2435 msec, and above 2435 msec were assigned as WM, GM and CSF, respectively.

Results and Discussion: Figure 1 displays patient's spectra and a scout image that is also the slice localization for MRSI. Spectral data from 6 ACG voxels, 4 LPFC and 4 RPFC voxels were selected for statistical analysis, which are summarized in Table 1. Table 1 displays the 3 different metabolite ratios in ACG, RPFC, and LPFC regions. The patients demonstrated significantly lower Cr/Ch ratios in both right (p=.001) and left PFC (p=.05). Patients also exhibited significantly higher Ch/NAA ratios in RPFC (p=.009). The two spectra of the single MRSI voxel in Figure 1 clearly show increased Ch signals in both RPFC and LPFC regions. No significant differences were observed in the ACG. Left PFC Cr/Ch ratios demonstrated medium to large inverse correlations with symptom ratings (PANSS) at baseline (r=-0.58), but not right PFC (r=-0.19). Together, these findings suggest elevated choline levels in FEP at the onset of illness that may be associated with the severity of psychotic symptoms. This finding is in excellent agreement with our hypothesis of mitochondrial dysfunction in patients with psychosis. Increasing choline levels in the brain has been associated with accelerated phospholipid turnover and inhibition of mitochondrial oxidation phosphorylation ultimately caused by mitochondrial dysfunction[3].

Figure 1.

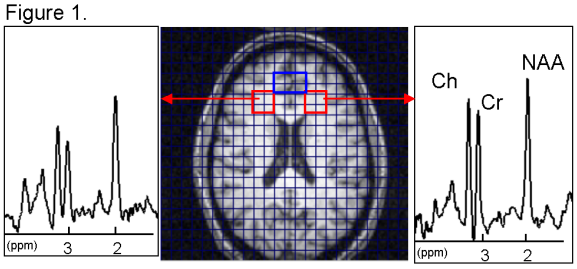

Table 1.

Region	ACG			RPFC			LPFC		
Group/variable	Cr/Ch	Ch/NAA	Cr/NAA	Cr/Ch	Ch/NAA	Cr/NAA	Cr/Ch	Ch/NAA	Cr/NAA
FEP, mean (SD)	1.09 (0.22)	0.70 (0.11)	0.74 (0.06)	0.85* (0.16)	0.70* (0.12)	0.62 (0.07)	0.97* (0.18)	0.63 (0.16)	0.58 (0.12)
Healthy, mean (SD)	1.08 (0.19)	0.65 (0.07)	0.74 (0.05)	1.18 (0.13)	0.52 (0.10)	0.60 (0.07)	1.14 (0.12)	0.53 (0.12)	0.60 (0.11)

* Significantly different from healthy control values.

References:

1. Strakowski SM. Brain Imaging in Affective Disorders. NY: Marcel Dekker, Inc, 2002.
2. Konradi C et al. Arch Gen Psychiatry 2004, 61:300.
3.Farber SA et al. FASEB J 2000; 14: 2198.