High Energy Phosphate Abnormalities Normalize after Antipsychotic Treatment in Schizophrenia: A Longitudinal 31P MRS Study of Basal Ganglia.

J. P. Narayan[1], B. N. Gangadhar[2], G. Venkatasubramanian[2], M. S. Keshavan[3]

[1]Neuroimaging and Interventional Radiology, National Institute of Mental Health & Neurosciences, Bangalore, Karnataka, India, [2]Psychiatry, National Institute of Mental Health & Neurosciences, Bangalore, Karnataka, India, [3]Psychiatry, Western Psychiatric Institute and Clinic, Pittsburgh, PA, United States

Background and Purpose:

Previous cross-sectional study has suggested a major role of neuroleptics in the metabolism of high-energy phosphates. It has been hypothesized that neuroleptics might induce decreased energy demanding processes. Subsequent longitudinal study examining this hypothesis could not confirm this hypothesis probably because of inadequate neuroleptic washout period and shorter follow-up duration. We have reported increased high-energy phosphate metabolism, consistent with disturbed fronto-striatal activity in antipsychotic-naïve schizophrenia. We followed up these patients for one year reassessed them using Magnetic Resonance Spectroscopy (MRS) for the effect of antipsychotic treatment on the abnormalities of high-energy phosphate metabolism of basal ganglia.

Materials & Methods:

14 patients with schizophrenia (diagnosis established by structured clinical interview for DSM-IV; 8 males, mean age 29 years [SD 7]; mean age at onset of psychosis 26 years [SD 9]) and 14 healthy controls (11 males, mean age 29 years [SD 8] underwent ^{31}P MRS was twice over the course of a year on a 1.5 T scanner. No patient was ever previously treated with any psychotropic before the first scan. Psychopathology was assessed using Positive And Negative Symptom Scale. None of the subjects (Patients & HC) had history of recent alcohol use (previous one week) nor scored positive on CAGE questionnaire and none used stimulant or opiate drug. No subject had history of epilepsy or any other neurological or medical disorder. All subjects signed an informed consent. The Institute's ethics committee approved the study. The baseline MRS study was conducted before starting antipsychotics. 2-D Chemical Shift Imaging with Image-Guided In-vivo Spectroscopic [ISIS] localization and volume selective adiabatic high frequency pulses were used. The volume of interest (VOI) was placed on representative slices of the brain in all three orthogonal planes interactively and simultaneously to avoid the ventricles. The VOI was localised to the basal ganglia with a mean size of 25x25x50 mm^3. The magnetic field shimming for homogeneity was done to achieve a line width less than 0.15 ppm. The technical parameters were: Repetition time of 1500 msec, FID sampling rate of 1500 Hz, sampling points of 1024 and 12 measurements. The average FID signal in the spectra was processed using proprietary software by the rater (PNJ) blind to clinical data with Phosphocreatine (PCr) as the reference marker. The spectra were quantified as integral values by an inbuilt program of fitting curves. The integrated area of PCr, inorganic phosphate (Pi), α-, β-, γ- Adenosine Triphosphate (ATP) were measured. PCr/total ATP (PCr/ATP) ratios in right and left basal ganglia were computed. The average of the two sides were used for analysis.

Results:

In patients, PANSS total scores decreased significantly after treatment (Baseline: 56±26; Followup: 80±18, t=3.7; p<0.01). Patients had significantly lower mean PCr/ATP ratio than healthy controls at baseline (PCr/ATP: patients=0.73±0.18, HC=0.92±0.24, t =2.4; p=0.02) but not during the follow-up (PCr/ATP: patients=0.82±0.23, HC=0.93±0.41, t =0.8; p=0.4). Repeated-measures ANOVA showed a significant group effect (df=2,26; F=4.3; $p < 0.05$).

Conclusion:

Findings offer important insights into the mechanism of action of neuroleptics in schizophrenia. The observations support the hypothesis that neuroleptics might invoke reduced energy demanding processes to ameliorate the symptoms of psychosis.