Whole brain voxel-based analyses were performed using cluster-based non-parametric permutation testing on gFA maps. Cerebral levels of GSH were assessed by localized 1H-MRS measurements from a volume of interest in medial prefrontal cortex.

**Results**: As previously described in ASRB, we observed widespread abnormalities of white matter in patients. Interestingly, the degree of white matter alterations (i.e. decreased gFA) patients could be predicted by the levels of blood cytokine, a precursor of GSH, strongly suggesting the important role played by oxidative stress in the pathophysiological mechanism. Also, we found that white matter alterations could be reversed by 6 months of add-on treatment with the antioxidant and GSH precursor N-acetyl-cysteine (NAC). Most importantly, this improvement was positively correlated with an increase in prefrontal GSH levels.

**Discussion**: We propose that developmental redox imbalance inducing oxidative stress may lead to impairments of oligodendrocytes, myelin formation and eventually to the disruption of fibers integrity and conductivity, especially in brain regions having high metabolic demand. In patients, alterations of white matter are inversely correlated with blood levels of GSH precursor cysteine and could be prevented by the early administration of the antioxidant NAC.

**10.4 DIFFUSION WEIGHTED SPECTROSCOPY STUDIES OF CELL-TYPE SPECIFIC ABNORMALITIES IN SCHIZOPHRENIA**

Dost Ongur* 1, Harry Pantazopoulos 1

**Background**: In previous work we used diffusion tensor spectroscopy (DTS) to identify abnormal diffusion of the neuron-specific metabolite NAA in frontal white matter in patients with chronic schizophrenia in the absence of abnormalities in the diffusion of cell-type non-specific metabolites Cr and Cho.

**Methods**: DTS relies on the same principles as DTI, but the diffusion characteristics of metabolites are probed, instead of those of water. Since brain metabolites are concentrated in specific cellular and sub-cellular compartments, their diffusion reflects the local geometry of these compartments. We have implemented a DTS approach at a 4 Tesla Varian MRI scanner (described in Du et al 2013).

**Results**: We have now collected similar data from first episode psychosis patients and matched healthy controls. We find that NAA diffusion is normal in the frontal PFC in first episode patients, but Cr and Cho diffusion is abnormal.

**Discussion**: Taken together, our studies suggest white matter abnormalities in non-neuronal elements in early phases of schizophrenia which are followed by neuronal damage in chronic disease.

**11. AEROBIC EXERCISE TRAINING FOR INDIVIDUALS WITH SCHIZOPHRENIA: THE BROAD BENEFITS ACROSS PHYSICAL HEALTH, COGNITION, AND EVERYDAY FUNCTIONING AND PROMISING MECHANISMS OF ACTION**

Keith Nuechterlein

**University of California, Los Angeles**

**Overall Abstract**: Recently aerobic exercise training has begun to be systematically examined in randomized controlled trials (RCTs) in schizophrenia. This symposium will report and discuss the results of RCTs that examined the impact of aerobic exercise on physical health, cognition, and everyday functioning across first-episode and established illness phases of schizophrenia. In addition, data on neurotrophic and brain structural changes will be examined as promising mechanisms of action.

Dr. Amal Abdel-Baki of the University of Montreal has focused on the physical health benefits of interval training in her RCT with first episode and multi-episode schizophrenia outpatients. She is demonstrating improved waist circumference, diastolic blood pressure, HDL cholesterol, and social functioning in first episode and multi-episode patients. Dr. David Kimhy of Icahn School of Medicine at Mount Sinai in New York has focused on the impact of aerobic exercise training on cardiovascular fitness. Brain-Derived Neurotrophic Factor (BDNF), cognition, and functional outcome in individuals with an established schizophrenic illness. He has demonstrated beneficial effects at each of these levels. Furthermore, relationships between fitness improvements and BDNF increases and the cognitive and functional gains suggest potential mechanisms of action.

Dr. Berend Malechow of Ludwig Maximilian University of