INTRODUCTION

Schizophrenia is a chronic, debilitating psychotic mental disorder. It affects about 1% of people. A new generation of medications and recent developments in neuropathology, brain imaging and molecular genetics have led to greater understanding of the pathophysiology of schizophrenia and to improve treatment. Nonetheless, it remains an enigmatic illness that places a substantial burden on patients, their families and society. **(Freedman, 2003).**

As in other complex diseases such as multiple sclerosis and systemic lupus, theories have outnumbered facts in schizophrenia. Genetic epidemiologic findings, such as greater concordance with respect to schizophrenia among monozygotic twins than among dizygotic twins and a high incidence of illness among adopted children whose biological mothers have schizophrenia, points out to a significant heritable component that accounts for about 70% of the risk. **(Tsuang, 2000).**

An array of data, such as an increase rate of obstetric complications, minor physical abnormalities, neurologic soft signs, and subtle behavioral abnormalities in children who later developed schizophrenia, support this model for schizophrenia in particular, but most likely also for a range of other neuropsychiatric disorders. **(Weinberger, 1987).**

Schizophrenia has varied and ominous symptoms that generally begin in late adolescence or early adulthood and usually continue throughout life. Most patients have a history of behavioral dysfunction primarily social and learning difficulties. **(Erlenmeyer-Kimling, 2001).**

Diagnostic features of schizophrenia include hallucinations and delusions. In addition to these overt psychotic, or "positive," symptoms, various deficits, or "negative" symptoms, occur, including an inability to pay attention, the loss of a sense of pleasure, the loss of will or drive, disorganization or impoverishment of thoughts and speech, flattening of affect, and social withdrawal. Positive and negative symptoms vary in intensity over time; patients may have predominantly one type at any particular time. Cognitive dysfunction, including a decreased ability to focus attention and deficiencies in short-term verbal and nonverbal memory, is also a core feature of the illness, which predicts vocational and social disabilities for patients. **(Green, 1996).**

Criminal behavior per se is not a concomitant of schizophrenia, but patients may commit violent acts in response to hallucinations or delusions or because of frustration in social interactions. **(Swanson et al., 1991)**

The aetiopathology of schizophrenia remain unknown in spite of century of investigation of the brain. Neuroimaging research has shown involvement of frontal cortex (reduced volumes), temporal

lobe cortex, and sub cortical structures such as hippocampus and amygdala. These brain abnormalities as a group differentiate between patients and matched healthy controls. Moreover such abnormalities are present at the onset and some even before the onset of psychosis, supporting the neurodevelopmental theory of schizophrenia. **(Rajarethinam et al., 2005).**

In vivo neurochemistry can be evaluated using several techniques, including single photon emission computed tomography (SPECT), positron emission tomography (PET), and MR spectroscopy (MRS). MRS uses the same basic principle of MRI, and provides a frequency-signal intensity spectrum that helps measure biochemicals or metabolites. Most commonly used methods include proton (^{1}H) spectroscopy, which provides multiple spectral peaks of glutamate, glutamine, myo-inositol, gamma-amino butyric acid (GABA), and N-acetyl aspartate (NAA) and phosphorous (^{31}P) spectroscopy, which provides assessment of brain membrane phospholipids and high energy metabolism by quantifying phosphomonoesters (PMEs) and phosphodiesters (PDEs). **(Rajarethinam et al., 2005).**

MRS is a non-invasive, non-radioactive procedure that allows quantification of several metabolites in specific regions of the human brain. **(Buckley et al., 1994).**

Schizophrenic patients undergoing proton magnetic resonance spectroscopy show alterations in N-acetyl aspartate levels

in several brain regions, indicating neuronal dysfunction. A decrease in NAA levels has been associated to neuronal death, energetic deficit in the cell body, and axonal injury or lesion. **(Sanches et al., 2004).**

The lower N-acetyl-aspartate levels in the dorsolateral prefrontal cortex of early-onset subjects suggest a reduction in functioning neurons or specifically a reduction in the proliferation of dendrites and synaptic connections, which is not apparent in the adult-onset schizophrenia subjects. **(Stanley et al., 2007).**

Consistent with structural findings, ^{1}H MRS studies suggest that impairments in neuronal integrity are more prominent in chronic as compared with first-episode schizophrenia patients, and can also be found to some degree in unaffected first-degree relatives of patients. **(Rajarethinam et al. 2005).**