Oxidative stress and superoxide dismutase in schizophrenia

NUSRAT S KHAN and INDRAJIT DAS
Academic Department of Psychiatry, Charing Cross & Westminster Medical School, London, W6 8RP.

Oxidative stress are chemical species with an unpaired electron in one of their orbits. Production of oxyradicals occurs throughout the body during cellular metabolism [1]. A complex antioxidant system exists to regulate levels of oxyradicals as excessive production or ineffective removal can result in cellular damage. The antioxidant enzymes present include superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT). SOD dismutates superoxide ($\cdot O_2^-$) to yield hydrogen peroxide ($H_2O_2$) and oxygen ($O_2$):

$$2\cdot O_2^- + 2H^+ \rightarrow H_2O_2 + O_2$$

$H_2O_2$ is removed immediately by either GPx or CAT as it can be converted to $OH^-$ the most toxic radical known. The reactive molecule nitric oxide (NO) has both beneficial and detrimental roles within the central nervous system (CNS); not only is it a messenger involved in neuronal signalling [2], it has also been shown to play a key role in CNS damage. Its damaging effects are mainly due to its reaction with $\cdot O_2^-$ and the subsequent formation of peroxynitrite ($\cdot ONOO^-$) which is a potent source of $OH^-$. Previous studies have found peripheral activities of antioxidant enzymes to be abnormal in schizophrenic subjects [3]. This study was undertaken to measure and compare Cu/Zn-SOD in schizophrenic patients who had never been exposed to neuroleptic treatment to controls and patients treated with neuroleptics.

Blood samples from 20 schizophrenic patients (16 male and 4 female, age range 19-40, mean age 29±1.6 years) meeting DSM III-R criteria for schizophrenia were taken. Twelve of the above schizophrenic patients were treated with sulpiride 500mg/day for 3 months. The main form of schizophrenia was chronic paranoid but other types were also used. 20 healthy volunteers (17 male, 3 female, age range 20-38 years, mean 28±1.7 years) who had not taken any drugs for at least 2 weeks were used as controls. All controls were employees at Charing Cross Hospital or Medical School. Fasting blood samples from patients and controls were drawn into heparinised tubes which were then centrifuged at 1800g for 15 min, the erythrocyte pellet was washed twice with equal volumes of saline and centrifuged at 1800g for 15 min. The washed pellet was stored at -20°C until analysis was carried out. Cu/Zn-SOD activity was measured spectrophotometrically using a method modified from Jewett & Roddin 1994 [4].

Drug naive schizophrenic subjects were found to have significantly raised erythrocyte Cu/Zn SOD activities compared to controls. After neuroleptic treatment enzyme activities were significantly lowered to near normal levels (Fig.1).

Fig. 2 shows that there is a positive correlation between the positive symptoms of schizophrenia (SAPS score) and SOD activities of drug naive patients. This suggests that there increased SOD activity may act as a marker for the positive symptoms in schizophrenia.

We have previously reported raised activities of nitric oxide synthase (NOS) in platelets of drug naive schizophrenic subjects compared to controls and patients on neuroleptic treatment [5]. This increase in NOS activity and catecholamine metabolism may result in the presence of abnormal circulating levels of oxyradicals. Excessive oxyradical production can cause cellular damage. Raised SOD activities reported here may have arisen as a compensatory mechanism to protect against such damage.

Figure 1. Erythrocyte Cu/Zn-SOD activities of healthy control subjects (n=20) compared to drug naive (n=20) and drug treated (n=12) schizophrenic patients. Results are expressed as means ± s.e.m. Statistical analysis was carried out using unpaired Student’s t-test. *p=0.015 comparing drug naive group to control group; + p=0.02 comparing drug naive group to drug treated group.

Figure 2. To show the correlation between SAPS score of drug naive patients (n=7) versus SOD activity.