

GSH...YOUR BODY'S MOST POWERFUL PROTECTOR

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CHAPTER 20

PSYCHONEUROBIOLOGY

As our understating of the brain has evolved, we have begun to appreciate the intricate interweave of psychiatry, neurology and biochemistry. These fields have overlapped and melded into psychoneurobiology, an integrated medical science that has already yielded important advances in the recognition and treatment of many brain disorders.

Free radicals and oxyradicals have been recognized by psychoneurobiologists as playing an important role in the development and progression of many of these disorders. The brain is particularly susceptible to free radical attack because of it generates more oxidative by-products per gram of tissue than any other organ. The brain's main antioxidant is [glutathione](#)---its importance cannot be overstated. Oxidative stress and glutathione are important factors in such various disorders as brain injury, neurodegenerative disease, schizophrenia, Down syndrome and other pathologies dealt with here and in other chapters. A more complete list is shown in figure 40.....

SCHIZOPHRENIA

The Greek translation of schizophrenia is “split mind,” and may be misleading. The disorder should not be confused with split personality or multiple personality disorder. It is a different illness characterized by psychosis---a severe disturbance of normal thought, perception, speech and behavior. In mood disorders like anxiety and depression, the ability to discern the real from the imagined is relatively intact. A schizophrenic patient on the other hand often suffers from delusions, auditory or visual hallucinations and paranoid thought not based on reality.

Although there is no consensus as to the causes of schizophrenia, most specialists will agree that the symptoms stem from a disturbance of normal brain chemistry. The tendency seems to run in families, but no single schizophrenia gene has been identified.

Psychotherapy by itself is of little value but antipsychotic drugs have been able to reduce relapses by 50% and considerably shorten periods of hospitalization. However, these drugs have significant side effects and long-term complications.

It has long been known that [glutathione](#) levels are lower in schizophrenic patients. Researchers have consistently demonstrated an increase in their oxidative stress and a decrease in their glutathione status. GSH levels even correspond to the severity of the disease. The Russians N.V. and A.V. Govorin further demonstrated that schizophrenics undergoing an acute phase of their disease had higher levels of lipid peroxidation than when in remission. Research scientists such as J.K. Yao and R.D. Reddy of the Veteran's Administration Healthcare System, University of Pittsburgh, suggest that oxidative stress plays an important pathophysiological role in schizophrenia.

A group of neurochemicals called catecholamines are produced normally by the body. They seem to be over-produced in both schizophrenia and Parkinson's disease. The catecholamines break down into ortho-quinones---a group of powerful oxidants. S. Baez's team at the Department of Biochemical Toxicology in Stockholm University examined glutathione's ability to detoxify these metabolites. They concluded that GSH enzymes provided critical protection against the neurodegenerative diseases that are caused or conditioned by these dangerous oxyradicals.

T.D. Buckman and A.S. Kling at UCLA School of Medicine conducted a fascinating study. CT-scans of schizophrenic patients revealed brain atrophy (shrinkage), suggesting damage to nerve tissue. They linked the extent of atrophy to the degree of glutathione peroxidase deficiency. This suggests a unique function of GSH in preserving the brain from tissue damage in schizophrenics. These findings were corroborated by other centers such as Hahnemann University in Philadelphia.

Antipsychotic drugs require long term use and cause a number of side-effects. Haldol, Thorazine and other neuroleptics cause a movement disorder called tardive dyskinesia. This results in involuntary puckering of the lips and writhing of the arms and legs and disfigures a large number of patients. It is possible that lipid peroxidation accounts for neuronal damage in this disorder, and scientists have put this theory to the test.

The Scottish team led by K. Brown and A. Reid measured oxidative breakdown products and antioxidant depletion in diskenetic patients and confirmed the relationship between lipid peroxidation and tardive dyskinesia. Other researchers have shown that lipid peroxidation and GSH depletion are aggravated by the antipsychotic drugs. Y. Sagara at the Salk Institute in La Jolla, California said that treatments resulting in decreased intracellular GSH increase a tendency towards tardive dyskinesia.

Researchers J.L. Cadet and L.A. Kahler from the National Institute of Health in Baltimore, S.P. Mahadik and R.E. Scheffer from the Department of Health Behavior, Medical College of Georgia and others have suggested that antioxidants should be used to prevent side effects in patients taking antipsychotics. The Georgia team also showed that oxidative

injury increases and GSH-peroxidase levels fall even at the earliest stages of psychosis, and that antioxidants may prevent or slow deterioration.

It appears that sustained GSH levels may slow the progress of schizophrenia and decrease the side effects of some of the drugs used against this disease.

Figure 40---Disorders of the brain and nervous system that are linked to oxidative stress may benefit from raised GSH levels

<u>Brain Injury</u>	<u>Neurodegenerative Disease</u>	<u>Others</u>
Brain Injury	Parkinson's disease	Schizophrenia
Trauma	Alzheimer's dementia	Down syndrome
Stroke	Multiple sclerosis (MS)	Tardive dyskinesia
Ischemia	Lou Gehrig's disease (ALS)	Sleep deprivation
Toxicity of lead, Mercury, etc.	Lipofuscinosis (Batten's disease)	Huntington's chorea

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