Oxidative Stress and Neurological Conditions

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Oxidative stress (free radical damage) has been professed to be involved in the pathological process of diseases and conditions ranging from cardiovascular disease, accelerated ageing, mitochondrial dysfunction, inflammatory conditions and neurological conditions. Age-related neurological conditions such as Alzheimer's disease and Parkinson's disease are often associated with oxidative stress however, have we considered the possible impact of oxidative stress in the pathogenesis of conditions such as Autism, ADHD and Schizophrenia? Woody McGinnis is finding that oxidative stress may play a larger role in such conditions than first thought.

Oxidative Stress in Schizophrenia

There is accumulating evidence of altered antioxidant capacity in schizophrenia,[12] which means increased free radical damage. Oxidative stress may contribute to the increased membrane lipid peroxidation. Membrane dysfunction can be secondary to free radical-mediated pathology, and may contribute to specific aspects of schizophrenic symptomatology and complications of its treatment.

Decreased essential fatty acid content has been observed in cell membranes of various tissue types of schizophrenic patients, including neuronal cell membranes. A number of mechanisms may account for these deficits, such as inadequate dietary supply or increased oxidation.[3]

In one study the concentrations of superoxide dismutase (SOD) enzymes were determined in various areas of the brains of patients with schizophrenic disorders. Copper, zinc and manganese SOD levels were significantly increased in the frontal cortex and substantia innominata of schizophrenic brains compared to controls. This supports reports of alterations of antioxidant indices in blood cells of patients with schizophrenia and suggests a specific neuroanatomical distribution pattern of oxidative stress processes possibly related to the pathophysiology of schizophrenia.[4] Decreased red cell glutathione peroxidase[5] and decreased plasma antioxidant capacity[2] has also been found in schizophrenic patients.

Lipid peroxidation may contribute to depressive symptoms

A positive relationship has been found between depressive symptoms and lipid peroxidation in female populations, supporting the hypothesis that lipid peroxidation may affect depressive symptoms.[6] Lowered antioxidant defences against lipid peroxidation have been found to exist in patients with depression. It has therefore been hypothesised that the antioxidant system may be impaired during a mood episode in patients with affective disorders, normalising at the end of the episode. Therapeutic benefit may therefore exist from antioxidant supplementation in patients suffering affective disorders and reports have found this to be true particularly for unstable manic-depressive patients.[7]

Oxidative stress may contribute to Autism

Autism is a condition associated with impaired capacity for methylation and increased oxidative stress.[8] Indirect markers are consistent with increased oxidative stress in autism. In a study, two oxidative stress markers were evaluated in autistic children, 8-hydroxy-2-deoxyguanosine (8-OHdG) and 8-isoprostane-F2alpha (8-iso-PGF2alpha) and compared to control children. The majority of the autistic group showed moderate increase in isoprostane levels, while some showed dramatic increase. The results of this study suggest that lipid peroxidation biomarkers are increased in autistic children.[9] Higher red cell lipid peroxides are also found in autistic patients, indicating higher levels of oxidative stress. Plasma levels of glutathione peroxidase and superoxide dismutase have been found to be significantly lower in autistic children than normal children, indicating a lowered level of

antioxidant activity to deal with the increased oxidative stress.[10]

Toxicity of heavy metals, in particular mercury, is considered a contributing factor to the progression and development of autism. Mercury toxicity exerts some of its toxic effects through increased oxidative stress and free radical damage.

Oxidative stress (and subsequent neurological degeneration) is a risk factor for cognitive impairment

Excessive oxidative stress and free radical damage is a well known risk factor for the development of neurological disorders involving cognitive decline such as Alzheimer's disease, memory loss and dementia.[11]

It is hypothesised that hypoperfusion induced mitochondrial failure plays a key role in the generation of reactive oxygen species, resulting in oxidative damage to brain cellular compartments in the Alzheimer's disease brain.[12]

Brain Antioxidants

The following are some nutrients found to have specific antioxidant actions and work in the brain. Supplementation of antioxidants that work in the brain may be of benefit to combat oxidative stress and subsequent neurodegeneration and neuronal dysfunction.

Acetyl-l-carnitine

Supplemented ALC crosses the blood brain barrier via a specific cation/carnitine transporter[13] and so may be of use in brain protection and nerve regeneration by maintaining the cell/s energy cycle, among other mechanisms. Autistic patients have been found to have a relative deficiency of carnitine,[14] contributing to mitochondrial pathology. Supplementation of this antioxidant and neuroprotective nutrient may therefore assist these patients.

Alpha lipoic acid

Alpha-lipoic acid is taken up and reduced in cells and tissues to dihydrolipoate, which is also exported to the extracellular medium; hence, protection is afforded to both intracellular and extracellular environments. Both alpha-lipoate and especially dihydrolipoate have been shown to be potent antioxidants, to regenerate other antioxidants like vitamin C and vitamin E, and to raise intracellular glutathione levels. Current research reveals protective effects of these compounds in cerebral ischemia-reperfusion, excitotoxic amino acid brain injury, mitochondrial dysfunction and other causes of acute or chronic damage to brain or neural tissue.[15]

Coenzyme Q10

CoQ10 supplementation significantly increases brain mitochondrial energy expenditure. It may also exert neuroprotective effects that may prove useful in the treatment and management of neurodegenerative diseases.

Green Tea

Green tea extract and its main polyphenol constituent (-)-epigallocatechin-3-gallate (EGCG) possesses potent neuroprotective activities. Research has shown that EGCG plays an important role in amyloid precursor protein secretion and protection against toxicity induced by beta-amyloid.[16]

Vitamin E

Vitamin E is a potent lipid-soluble antioxidant that can break the propagation of the free radical chain reaction in the hydrophobic part of the biological membrane. Vitamin E is therefore able to protect neurons by reducing oxidative stress and has been found to protect neurons effectively against the oxidative cell death caused by the Alzheimer's disease-associated amyloid beta protein, hydrogen peroxide and the excitatory amino acid glutamate.[17][18]

A recent study examined the effects of supplementation of essential fatty acids together with antioxidant nutrients in the support of schizophrenia. Schizophrenic patients (N=33) were supplemented with a mixture of EPA/DHA (180:120 mg) and antioxidants (vitamin E/C, 400 IU:500 mg) orally morning and evening (N=33) for 4 months. Levels of fatty acids and lipid peroxides were compared with their levels in normal controls (NC) (N=45). Post-treatment levels of RBC EPUFAs were significantly higher than pre-treatment levels as well as levels in normal controls without any significant increase in plasma peroxides. Concomitantly, there was significant reduction in psychopathology based on reduction in individual total scores for brief psychiatric rating scale (BPRS) and positive and negative syndrome scale (PANSS), general psychopathology-PANSS and increase in Henrich's

Quality of Life (QOL) Scale.[19]

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