NEURAL SENSITIZATION

Neural sensitization occurs by activation of brain and nerve cell N-methyl-D-aspartate (NMDA), which then increases brain nitric oxide (NO).[1,2,3] Several vicious biochemical cycles are then set in motion. Nitric oxide forms a tissue damaging free radical known as peroxynitrite.[2,4,5,6] Peroxynitrite depletes energy ATP,[7,8] which then further increases the sensitization of NMDA.[9,10]

Chemical exposure can induce sensitization. Pesticides such as organophosphates inhibit acetylcholine, activating muscarinic receptors which increase nitric oxide. Formaldehyde activates NMDA.[1,11] Petrochemicals (VOC's, solvents) disrupt energy production in the mitochondria, increase superoxide which increases peroxynitrite.[12] This can then increase tissue-damaging free radicals in the brain.[13] Mitochondrial disruption occurs in chemically injured patients.[14] Petrochemicals and many other chemicals are irritants[15] that with exposure can cause inflammation. Inflammation of sufficient duration can lead to chronic neurogenic inflammation.[16] Inflammation results in increased cytokines, free radicals and elevated nitric oxide.

Neural sensitization is thus associated with self-perpetuating neuroexcitation and excessive response to further chemical exposure.[11,17] This NMDA activation with increased nitric oxide and peroxynitrite can cause brain cell death and neurogenerative disease.[2,6,10,18,19,20] Peroxynitrite also weakens the blood-brain barrier, allowing chemicals to enter the brain more readily.[21] Nitric oxide also damages the first detoxification step involving the cytochrome p450 system,[22] allowing chemicals (and many drugs) to build up more in the body.

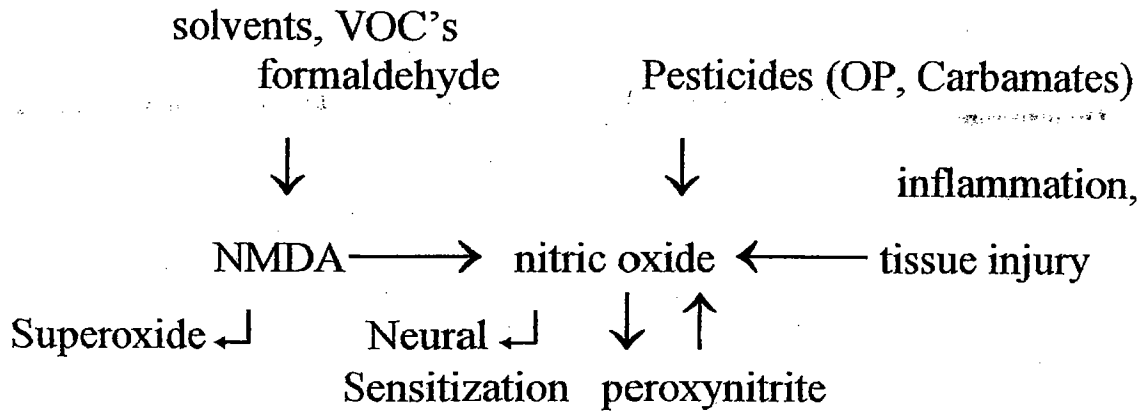
This vicious cycle **MUST** therefore be interrupted to the maximum extent feasible. Because the resulting symptoms of sensitization are warnings that other more silent toxic-induced organ damage of the liver, pancreas, immune system, adrenals, mitochondria and other organs can be also occurring,[16,23,24] masking/blocking symptoms of this cycle is not recommended without healing the disturbed biochemical mechanism. (This would be like turning off a battery warning light without fixing the battery.) Cobalamine (B12) is a nitric oxide scavenger and deficient in the majority of chemically ill patients. The cyano form is not recommended (these patients don't need cyanide and the hydroxy and methyl forms work much better in brain and nerve cells). Superoxide dismutase is deficient in a significant portion of chemically ill patients and its cofactors, copper, zinc, and manganese must be adequate. These are often reduced in chemically injured patients and should be tested and replaced in well absorbed and transported forms, for example, picolinates. Antioxidant function is usually inadequate in chemically ill patients,[23] and increased lipid peroxides and other free radicals are common.

Intervention to help reduce this vicious biochemical cycle includes: methyl or hydroxycobalamine sublingually or I. M. (not oral due to poor absorption), general antioxidants (C, E, selenium), glutathione by nebulizer due to poor oral absorption, and ample alpha lipoic acid to reactivate the glutathione in the many damaged lipid tissues (cell membranes, mitochondria, lymph, brain, etc.). Trimethyl glycine is recommended as a methyl donor to reduce the effects of peroxynitrite. Magnesium should be ample because deficiency is very common with toxic injury and adequate magnesium decreases NMDA activation. Peroxynitrite scavengers such as a mixture of caretenoids are also recommended. Caretenoids tend to be more organ-specific. An inclusion of gingko (brain), silimarin (liver), bilberry (collagen stabilizing, capillary permeability, vision), cranberry (urinary) and other mixed caretenoids is recommended.

Mineral levels should be measured and followed by intracellular (eg. RBC) or lipid functional (eg. lymphocyte mitogenesis, a SpectraCell technology). Functional lymphocyte evaluation and

follow-up of glutathione, lipoic acid, total antioxidant function, C, E and zinc is also recommended. At this time this technology is only available through SpectraCell laboratory.

None of the above is a substitute for exposure controls at home, work and/or school: places where the person spends most of their time. Humans are social beings, and these measures above gradually increase the person's ability to enjoy the company of others and use public places. When society is adequately informed and takes public health reasonable accommodation measures to reduce irritants and toxins in personal products and public places, this further promotes health and reduces sensitization.



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Glutathione

Glutathione is the most important intracellular antioxidant in the body. Improving levels in the mid and lower respiratory tract can help reduce respiratory responses to irritants and help to reduce the severity and duration of the patient's reactions. A nasal form of glutathione may be used for reactions that harm brain function. A glutathione nasal spray has also reduced symptoms in people with chronic rhinitis.[1] There is no blood- brain barrier between the nose and the brain. Scientific studies document that substances being breathed into the nose directly enter the brain. Glutathione can also be absorbed through the lungs (delivered to the lungs as an aerosol) and seems able to cross the blood- brain barrier.[2]

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