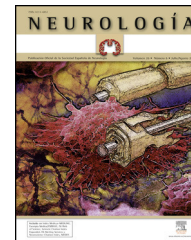




# NEUROLOGÍA

[www.elsevier.es/neurologia](http://www.elsevier.es/neurologia)



## EDITORIAL

### Oxidative stress in neurological diseases: Cause or effect?☆

#### El estrés oxidativo en las enfermedades neurológicas: ¿Causa o consecuencia?

M.L. Díaz-Hung\*, M.E. González Fraguela

*Departamento de Neuroinmunoquímica, Centro Internacional de Restauración Neurológica, La Habana, Cuba*

Oxidative stress is a dynamic and complex situation in which there is an imbalance between the generation of reactive oxygen species (ROS) and the availability and action of antioxidants.<sup>1</sup> The central nervous system (CNS) consumes large amounts of oxygen to carry out physiological processes, and this metabolism process generates abundant free radicals. Certain factors make the CNS susceptible to ROS attacks, such as lack of antioxidant mechanisms, high concentration of polyunsaturated fatty acids, and selectivity of the blood-brain barrier, which limits distribution of some antioxidants including vitamin E.<sup>2</sup>

Oxidative stress has mainly been studied in such neurodegenerative diseases as Alzheimer disease,<sup>3</sup> Parkinson's disease,<sup>4,5</sup> and amyotrophic lateral sclerosis.<sup>6</sup> Oxidative damage has been identified even in early stages of these diseases, indicating that their aetiologies are linked to free radicals.

Reactive oxygen species that elude antioxidant mechanisms and accumulate progressively will trigger lipid peroxidation mechanisms and elicit structural damage to proteins and DNA.<sup>7</sup> These molecular changes are exacerbated in the neuronal populations affected by certain pathological processes. Therefore, pyramidal neurons in the

hippocampus and parietal cortex are specifically affected in Alzheimer disease, whereas the compact substantia nigra, striatal neurons, and motor neurons are affected in Parkinson's disease, Huntington disease, and lateral amyotrophic sclerosis, respectively. Unfortunately, the mechanisms that determine selective neuronal vulnerability are not yet understood.<sup>8</sup>

Different neuronal populations in each region of the brain have their own morphologies and biochemical characteristics. As a result of this diversity, it is very likely that each neuronal population has its own molecular composition that will determine its vulnerability to oxidative stress. These differences have been observed between neuronal populations in the hippocampus, the substantia nigra, and neurons in the cerebral and cerebellar cortices.<sup>9</sup>

New evidence indicates that oxidative stress is present in other CNS disorders. Recent studies in children with autism spectrum disorders have shown that oxidative species/antioxidant imbalance can participate in the pathogenesis of these diseases. These patients showed changes in membrane fluidity, neuronal loss in the cerebellum, and altered oxidative stress markers.<sup>10</sup>

Furthermore, oxidative stress has been associated with neuronal hyperexcitability. Results in this area led to studies on the role of ROS in epilepsy and drug-resistant epilepsy.<sup>11</sup> These studies suggest that epileptic seizures elicit an increase in oxidation of cellular macromolecules before neuronal death takes place. Oxidative stress seems to be the result of excitotoxicity, since seizure-induced neuronal death involves an excess of calcium.<sup>12</sup> Redox state

☆ Please cite this article as: Díaz-Hung ML, González Fraguela ME. El estrés oxidativo en las enfermedades neurológicas: ¿causa o consecuencia?. *Neurología*. 2014;29:451-452.

\* Corresponding author.

E-mail addresses: [mldiaz@neuro.ciren.cu](mailto:mldiaz@neuro.ciren.cu), [meili@infomed.sld.cu](mailto:meili@infomed.sld.cu) (M.L. Díaz-Hung).

improves in patients with drug-resistant epilepsy after surgical resection of the epileptic foci.<sup>13</sup>

Despite evidence indicating that oxidative stress may be a pathogenic factor in neurological diseases, clinical experience with using antioxidants as neuroprotective treatment—mainly such classic antioxidants as vitamins C and E—has obtained poor results overall. However, antioxidant therapy has delivered more encouraging results in animal models of these conditions.<sup>14</sup>

In conclusion, oxidative stress manifests as a pathogenic factor in a variety of neurological diseases, although it may also be associated with their aetiology. Further studies are needed in order to identify mechanisms of selective neuronal vulnerability to ROS in different brain regions, and to determine how effective antioxidant therapy may be for treating these diseases.

## References

1. Du Z, Zhang H, Meng X, Guan Y, Wang H. Role of oxidative stress and intracellular glutathione in the sensitivity to apoptosis induced by proteasome inhibitor in thyroid cancer cells. *BMC Cancer*. 2013;9:56–9.
2. Shucla V, Mishra S, Pant H. Oxidative stress in neurodegeneration. *Adv Pharmacol Sci*. 2011;2011:572634.
3. Lovell M, Markesbery W. Oxidative DNA damage in mild cognitive impairment and late-stage Alzheimer's disease. *Nucleic Acids Res*. 2007;35:7497–504.
4. Nikam S, Nikam P, Ahaley S, Sontakke A. Oxidative stress in Parkinson's disease. *Indian J Clin Biochem*. 2009;24:98–101.
5. Zhou C, Huang Y, Przedborski S. Oxidative stress in Parkinson's disease: a mechanism of pathogenic and therapeutic significance. *Ann N Y Acad Sci*. 2008;1147:104.
6. Chi L, Ke Y, Luo C, Gozal D, Liu R. Depletion of reduced glutathione enhances motor neuron degeneration *in vitro* and *in vivo*. *Neuroscience*. 2007;144:991–1003.
7. Markesbery W, Lovell M. Damage to lipids, proteins, DNA, and RNA in mild cognitive impairment. *Arch Neurol*. 2007;64:954–6.
8. Mattson M, Magnus T. Ageing and neuronal vulnerability. *Nat Rev Neurosci*. 2006;7:278–94.
9. Wang X, Michaelis E. Selective neuronal vulnerability to oxidative stress in the brain. *Front Aging Neurosci*. 2010;12:12.
10. González-Fragueta M, Díaz-Hung M, Vera H, Maragoto C, Noris E, Blanco L, et al. Oxidative stress markers in children with autism spectrum disorders. *Br J Med Med Res*. 2013;3:307–17.
11. Cardenas-Rodriguez N, Huerta-Gertrudis B, Rivera-Espinosa L, Montesinos-Correa H, Bandala C, Carmona-Aparicio L, et al. Role of oxidative stress in refractory epilepsy: evidence in patients and experimental models. *Int J Mol Sci*. 2013;14:1455–76.
12. Waldbaum S, Patel M. Mitochondrial dysfunction and oxidative stress: a contributing link to acquired epilepsy? *J Bioenerg Biomembr*. 2010;42:449–55.
13. López J, González Fragueta ME, Lorigados L, Morales L, Riverón G, Bauza J. Oxidative stress markers in surgically treated patients with refractory epilepsy. *Clin Biochem*. 2007;40:292–8.
14. Kamat C, Gadal S, Mhatre M, Williamson K, Pye Q, Hensley K. Antioxidants in central nervous system diseases: preclinical promise and translational challenges. *J Alzheimers Dis*. 2008;15:473–93.