Editorial
Oxidative Medicine in Brain Injury

Traumatic brain injury (TBI), a complex injury with a broad spectrum of symptoms and disabilities, not only pertains to adults but also newborns. Nearly one-third of the world population suffers from neurological diseases including Parkinson’s and Alzheimer’s diseases, multiple sclerosis, epilepsy, and spinal cord injury. Sometimes, deficits are seen in childhood and in others, they are delayed, arising in adolescence or young adulthood. Understanding brain injury pathophysiology contributes to identifying new neuroprotective agents. While oxidative stress affects brain tissue and function, the other way round is also true. Oxidative stress and its foregone vicious epigenetic regulation follow traumatic brain injury and hemorrhagic stroke in the vascular neural network. Whether cause or effect, oxidative stress is a double-edged sword. It may help in fighting bacteria, but it may destroy the host too. This latent phase susceptible to an incidental and secondary injury brings about a therapeutic window and sets the grounds for neuroprotection. The aim of this special issue is bringing together the accrued research addressing the role of the reactive oxygen species (ROS) in the pathophysiology of brain injury and possible therapeutic strategies.

This special issue is focused on neuroprotective strategies for the brain, their possible pathways, and pharmacological analogs’ use. The topics include:

- **New insights on oxidative damage and iron associated impairment in Traumatic Brain Injury.** This chapter is focused on the hemorrhage caused by trauma and the ongoing oxidative process generated by biochemical disturbances in brain tissue which increase the level of iron and reactive oxygen species. The relationship between oxidative damage and the traumatic brain injury is well-known, for that reason, diminishing of the factors that potentiate the production of reactive oxygen species has promissory therapeutic uses. Iron chelators scavenge oxidative damage. The authors show an updated overview of the underlying mechanisms of oxidative damage in TBI, introducing the potential use of iron chelators as neuroprotective compounds [1, 2].

- **Copper and neurotoxicity in autism spectrum disorder.** The authors discuss the role of metals, like copper, and the amyloid precursor protein (APP) derivative (s-APP-alpha) as an antioxidant and a possible adjuvant in the treatment of some autistic spectrum disorder symptoms (ASD) [3].

- **Neuroinflammation in demyelinating diseases: oxidative stress as a modulator of glial cross-talk.** A preserved hallmark of this neuroinflammatory scenario is a local increase of oxidative stress, where several cytokines and chemokines are released by glial and other cells generating an environment that determine cell interaction and the outcome of oligodendrocyte maturity and ability to neosynthesize myelin. The authors review the main features of the regulatory aspect of these molecules and propose new putative signal molecules involved in remyelination, focused in the etiology of Multiple Sclerosis [4, 5].

- **Energy-sensing pathways in ischemia: The counterbalance between AMPK and mTORC.** Stroke is an important cause of death and disability, and it is the second leading cause of death worldwide. In humans, middle cerebral artery occlusion (MCAO) is the most common cause of ischemic stroke. This review analyzes to what extent the lack of each of the elements of the system produces damage and which mechanisms are unchained by this deficiency [6, 7].

- **β-amyloid and oxidative stress: perspectives in drug development.** This chapter is focused on the reciprocal regulation of β-amyloid protein (Aβ), that causes oxidative stress, and oxidative stress, that favors Aβ aggregation and toxicity and negatively affects the peptide clearance. Analysis of this strict interaction may offer novel opportunities for therapeutic intervention. Molecules endowed with antioxidant properties deserve attention in this regard [8, 9].

- **Oxidative Stress-Induced Brain Damage Triggered by Voluntary Ethanol Consumption during Adolescence: a Potential Target for Neuroprotection?** The mechanisms involved in alcohol-induced brain damage in developing individuals and the effect of different potential neuroprotectants which prevent alcohol-induced oxidative stress are reviewed. A selective inhibitor of the endocannabinoid anandamide, a flavonol present in different fruits (quercetin), an antibiotic with known neuroprotective properties (minocycline), a SOD/catalase mimetic, a potent antioxidant and anti-inflammatory molecule (resveratrol), the female hormone estradiol known to have antioxidant properties, a powerful scavenger of ROS (melatonin) or an isoquinoline alkaloid (berberine) may be relevant to treating alcoholism [10, 11].

- **Long-term effects of hypoxia-reoxygenation on thioredoxins in rat central nervous system.** Oxidative stress induced by the oxidative pathway dysregulation following ischemia/reperfusion has been proposed as an important cause of neuronal death and brain damage. The proteins of the thioredoxin (Trx) family are crucial mediators of protein function regulating the intracellular hydrogen peroxide levels and redox-sensitive post-translational protein changes. The authors evaluated the long-term effects of common carotid artery ligation-induced ischemia/reperfusion on the protein expression and distribution of fourteen members of the Trx family and related proteins in cerebellum, corpus striatum, and the hippocampus. The thioredoxin proteins displayed a complex, cell-type, and tissue-specific expression pattern following ischemia/reperfusion [12-14].

- **Activation of Melanocortin-4 Receptor by a Synthetic Agonist Inhibits Ethanol-induced Neuroinflammation in Rats.** The activation of melanocortin-4 receptor (MC4R) in the brain decreases the neuroinflammatory response in models of brain damage. The authors discuss whether MC4R activation by a synthetic MC4R-agonist peptide prevents ethanol-induced neuroinflammation, and if alcohol consumption produces changes in MC4R expression in the hippocampus and hypothalamus. The administration of a synthetic MC4R-agonist peptide prevents neuroinflammation induced by excessive alcohol consumption in the hippocampus, hypothalamus and prefrontal cortex. The results could explain the effect of α-MSH and other synthetic MC4R agonists in decreasing alcohol intake, through the reduction of the ethanol-induced inflammatory response in the brain [15, 16].

**AUTHOR CONTRIBUTIONS**

All authors made a substantial, direct and intellectual contribution to the work, and approved it for publication.
CONFLICT OF INTEREST
The authors declare the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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