Current Neuropharmacology, 2022, *20,* 1046-1072

REVIEW ARTICLE

Association of Oxidative Stress with Neurological Disorders

Waseem Hassan[1,*], Hamsa Noreen[1], Shakila Rehman[1], Mohammad Amjad Kamal[2,3] and Joao Batista Teixeira da Rocha[4]

[1]*Institute of Chemical Sciences, University of Peshawar, Peshawar 25120, KhyberPakhtunkhwa, Pakistan;* [2]*King Fahd Medical Research Center, King Abdulaziz University, P. O. Box 80216, Jeddah 21589, Saudi Arabia;* [3]*Enzymoics, 7 Peterlee Place, Hebersham, NSW 2770, Australia;* [4]*Departamento de Bioquímica e Biologia Molecular, Programa de Pós-Graduação em Bioquímica, Toxicológica, Universidade Federal de Santa Maria, Santa Maria, RS 97105-900, Brazil*

ARTICLE HISTORY

Received: May 30, 2021
Revised: September 05, 2021
Accepted: October 06, 2021

DOI:
10.2174/1570159X19666211111141246

Abstract: ***Backgorund*:** Oxidative stress is one of the main contributing factors involved in cerebral biochemical impairment. The higher susceptibility of the central nervous system to reactive oxygen species mediated damage could be attributed to several factors. For example, neurons use a greater quantity of oxygen, many parts of the brain have higher concentraton of iron, and neuronal mitochondria produce huge content of hydrogen peroxide. In addition, neuronal membranes have polyunsaturated fatty acids, which are predominantly vulnerable to oxidative stress (OS). OS is the imbalance between reactive oxygen species generation and cellular antioxidant potential. This may lead to various pathological conditions and diseases, especially neurodegenerative diseases such as, Parkinson's, Alzheimer's, and Huntington's diseases.

***Objectives*:** In this study, we explored the involvement of OS in neurodegenerative diseases.

***Methods*:** We used different search terms like "oxidative stress and neurological disorders" "free radicals and neurodegenerative disorders" "oxidative stress, free radicals, and neurological disorders" and "association of oxidative stress with the name of disorders taken from the list of neurological disorders. We tried to summarize the source, biological effects, and physiologic functions of ROS.

***Results*:** Finally, it was noted that more than 190 neurological disorders are associated with oxidative stress.

***Conclusion*:** More elaborated studies in the future will certainly help in understanding the exact mechanism involved in neurological diseases and provide insight into revelation of therapeutic targets.

Keywords: Oxidative stress (OS), neurological disorders, Reactive oxygen species (ROS), brain, free radicals, oxidation.

1. INTRODUCTION

Free radicals are highly reactive molecules having one unpaired electron in the outermost shell. The radicals which involve the oxygen and nitrogen species are known as reactive oxygen species (ROS) and reactive nitrogen species (RNS), respectively [1]. The imbalance between the RONS and antioxidants in the biological system leads to oxidative stress [2]. Precisely, RONS toxicity contributes to mitochondrial dysfunction, glia cell activation, protein misfolding and cellular apoptosis [3]. This review begins with the essential characteristics of ROS, including its generation, regulation, and physiological functions. We also discussed various OS biomarkers *i.e.* lipid peroxidation, protein oxidation, DNA oxidation and glycoxidation.

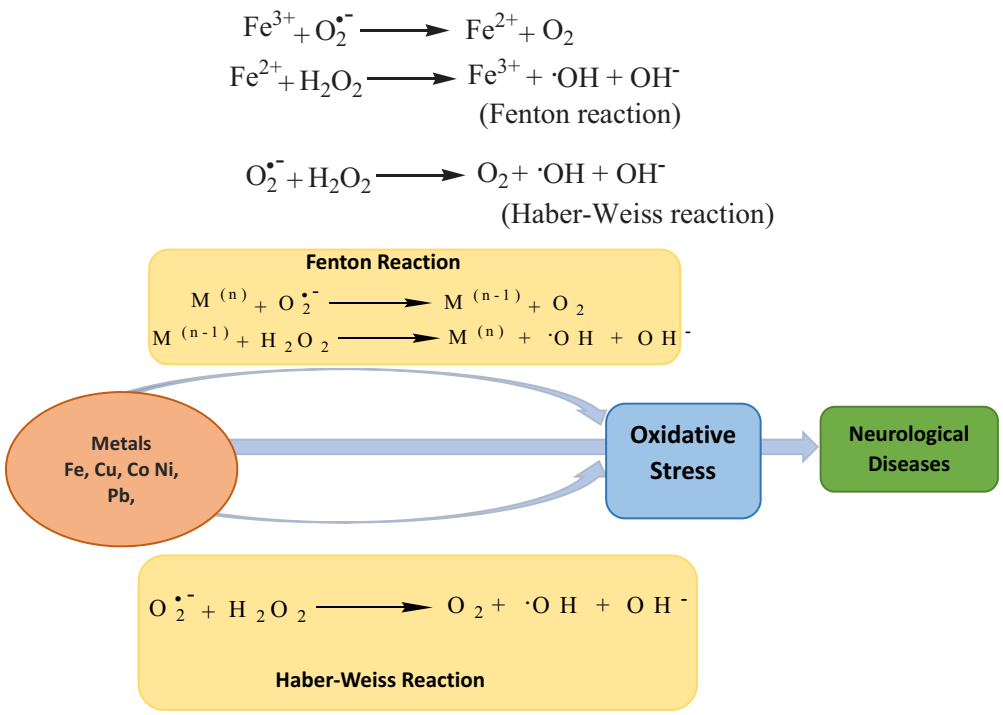
1.1. Reactive Oxygen/Nitrogen Species (RONS)

Reactive oxygen/nitrogen species (RONS) are a group of highly reactive by-products produced in the cells of aerobic organisms. They are generally formed in the peroxisomal fatty acid, mitochondrial electron transport, phagocytic cells and cytochrome P-450 [4, 5]. The important radicals in RONS series are superoxide ($O_2^{\cdot -}$), hydroxyl ($OH^{\cdot}$), nitrogen dioxide ($NO_2^{\cdot}$), nitric oxide ($NO^{\cdot}$), lipid peroxyl ($LOO^{\cdot}$) and peroxyl ($ROO^{\cdot}$), while lipid peroxide (LOOH), ozone (O_3), hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl), singlet oxygen ($^1O_2$), nitrosonium cation (NO^+), peroxynitrite ($ONOO^-$), nitroxyl anion (NO^-), nitrous acid (HNO_2) and dinitrogen trioxide (N_2O_3).

Literature has proposed two pathways for the RONS generation *i.e.* enzymatic and non-enzymatic reactions. Enzymatic sources include xanthine oxidase, 5,10-methylenetetrahydrofolate reductase oxidase, peroxidases, flavin oxidases from peroxisomes phagocytosis, mitochondrial respiratory chain, cytochrome P450 from endoplasmic reticulum (ER), nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (Nox), prostaglandin synthesis, xanthine oxidase (XO), Nox systems and mitochondrial respiratory chain [6, 7]. Non-enzymatically ROS are generated by the reactions of oxygen with organic compounds through oxidative phosphorylation (*i.e.* aerobic respiration) in mitochondria of the cell [8].

*Address correspondence to this author at the Institute of Chemical Sciences, University of Peshawar, Peshawar 25120, Khyber Pakhtunkhwa, Pakistan; E-mail: waseem_anw@yahoo.com

1875-6190/22 $65.00+.00



Scheme 1. Fenton & Haber-Weiss reaction and role of Metal ions and oxidative stress in neurological Diseases.

Moreover, there are two major sources of RONS generation *i.e.* exogenous and endogenous sources. Exogenous sources include cigarette smoke, UV radiations, industrial solvents, water and air pollution, heavy or transition metals (As, Hg, Cd, Fe & Pb *etc.*), alcohol, drugs (tacrolimus, bleomycin, gentamycin & cyclosporine), and cooking (fat, used oil, smoked meat) [9-12]. These exogenous compounds can be metabolized or decomposed into free radicals in the cells. The major endogenous sources are inflammation, immune cell activation, cancer, excessive exercise, mental stress, infection, aging and ischemia [13, 14].

ROS are normally produced in different organelles among which mitochondria is the most important and key structure [13, 14]. Oxidative phosphorylation is the major reaction pathway of mitochondrial RONS formation in the inner mitochondrial membrane. Mitochondrial electron transport chain involves the reduction of oxygen to water through four-electron reduction reaction. Though oxygen reduces to superoxide ($O_2^{\cdot-1}$) by one-electron reduction in mitochondrial electron transport. Mitochondrial manganese superoxide dismutase detoxifies the superoxide anion to form H_2O_2. However, the H_2O_2 can be converted to hydroxyl radical (OH^-) in the presence of reduced transition metals. Furthermore, peroxisomal β-oxidation of fatty acids is another source of RONS generation. Peroxisomes are specifically responsible for the degradation of fatty acids and other molecules. H_2O_2 is formed in this reaction as a by-product [15,16]. Phagocytic cells are also one of the imperative sources of oxidants that protect the central nervous system (CNS) from harmful microorganisms.

Fenton and Haber-Weiss reactions also lead to RONS generation, as displayed in Scheme **1**. In Fenton reaction, Fe^{2+} reacts with H_2O_2, to form the damaging and very reactive hydroxyl radicals. In the Haber-Weiss reaction, superoxide anion reacts with ferric iron, which forms Fe^{2+} and affects the redox cycling [17]. The RONS formation may result in the progressive deterioration of the physiological system.

Oxidative stress is a destructive process that brings changes in cell membranes and other biomolecules *i.e.* lipids, proteins, deoxyribonucleic acid (DNA) and lipoproteins [18, 19]. In addition, the production of ROS in CNS is due to the increase in intracellular free Ca^{2+}, autophagy, the release of excitatory amino acids, apoptosis and accumulation of protein aggregates which leads to critical neurological disorders *i.e.* Parkinson's disease (PD), amyotrophic lateral sclerosis, Alzheimer's disease (AD), Machado–Joseph disease, ageing and Huntington's disease (HD), *etc.* [20]. RONS also affects the heme-containing cytochrome c oxidase I molecule of complex IV of the respiratory chain, and also causes damages to the components of complex I, II, and III [21]. In mitochondria, the overproduction of ROS can cause the oxidative stress in DNA, cell membranes and proteins, which sequentially lead to the mitochondrial damage [22]. Mitochondrial oxidative stress further releases the cytochrome c in cytosol, which ultimately leads to chronic diseases, like cancer, atherosclerosis, rheumatoid arthritis, diabetics, degenerative diseases and apoptosis.

Similarly, a trans-membrane enzyme complex, Nox, is also an important source of $O_2^{\cdot-1}$generation, which catalyzes the transfer of an electron from NADPH to oxygen [23, 24]. Nox is usually present in phagocytes (eosinophils, neutrophils, macrophages, monocytes are known as Phox or NOX2) and in the endothelium of cardiovascular tissue [25]. Previously literature reported seven types of Nox isoforms in mammalian cells *i.e.* Nox1-Nox5 and dual oxidases (Duox1 & Duox2) [24]. Nox isoforms have standardized regulation, function, and cellular localization [26]. In endothelial cells,

Nox4 and Nox2 are present abundantly than Nox1 [27, 28], whereas; in vascular smooth muscle cells Nox1 and Nox4 isoforms are greatly expressed as compared to Nox2 [29]. Nox2 is rich in phagocytes and generates an excess of RONS [24]. Researchers further demonstrated that Nox4 isoforms are commonly present in vascular structures [30, 31]. Besides, Nox4 is basically more active in the cardiovascular systems [32, 33] and generates H_2O_2 rather than O_2^{-1} [34,35].

Xanthine dehydrogenase (XDH) and xanthine oxidases (XO) are commutable types of xanthine oxido-reductase [36]. XO significantly catabolizes the purine to uric acid during the conversion of hypoxanthine into xanthine [37]. XO also produces H_2O_2 and O_2^{-1} by donating electrons to oxygen, which results in the tissue and cell injury [38]. ROS-mediated diseases due to XO are associated with the excess of intracellular calcium, which results in the irreversible conversion of XDH into XO by catalyzing the oxidation of hypoxanthine into xanthine [39].

The endoplasmic reticulum (ER) is the largest intracellular membrane-bounded organelle, specifically associated with the folding of protein and biosynthesis of lipid. Moreover, in ER, two mechanisms are proposed for the generation of ROS [40]. In the first mechanism, endoplasmic reticulum oxidoreduction-1 (ERO-1) and protein disulfide-isomerase (PDI) catalyzes the formations of disulfide bonds and protein folding under optimal conditions to stabilize the membrane in the ER. The transferring of electrons from protein thiol to oxygen in the presence of ERO-1 and PDI generate RONS as a byproduct. In the second mechanism, glutathione (GSH) depletion results in the production of ROS by misfolding the protein. In this case, oxidized thiols interact with PDI ERO-1 *via* glutathione (GSH) [40]. These steps begin the process of disulfide bond formation and breakage in the ER lumen, leading to the creation of more ROS as a byproduct [41]. Consequently, proteins with multiple disulfide bonds are considered more susceptible to ROS formation [40]. As GSH can reduce the imperfectly produced disulfide bonds in oxidizing conditions, but further reduced level of GSH level may result in the higher ROS generation [42].

Peroxisomes are mostly found in eukaryotic cells and are considered very important in multiple metabolic pathways, such as amino acid catabolism, phospholipid biosynthesis, fatty acid oxidation and oxidative pentose phosphate pathway [43]. In the peroxisomes, consumption of oxygen results in H_2O_2 production, but not O_2^-, under optimal conditions. Peroxisomes mainly produce the bulk of H_2O_2 by different oxidases, including D-aspartate oxidase, urate oxidase and acyl-CoA oxidases, which help in the transfer of hydrogen from their respective substrates to the O_2. Besides, other enzyme catalases are also present in peroxisomes, which can degrade the H_2O_2 and sustain the balance between the formation and exclusion of ROS [44]. When peroxisomes are destructed and the catalases level reduces, a higher amount of H_2O_2 discharge into the cytosol causes oxidative stress in the cellular system [44].

1.2. Generation of ROS in Brain

Behavioral and cognitive impairment caused by oxidative stress *via* a series of chain reactions in the central nervous system is an interesting area of discussion and can be studied at multiple levels. Basically, different kinds of neuronal cells are susceptible to oxidative stress at various levels. Among all the neuronal cells amygdala, hippocampus and cerebellar granule cells are most vulnerable to oxidative stress and therefore, first of all, they undergo functional damage [45]. Different preclinical studies reported that three brain regions *i.e.* prefrontal cortex (PFC), hippocampus and amygdala are responsible for cognitive impairments and behavioral disorders [46-49]. Hippocampus undergoes important biochemical changes, which give information about the connections and function of neuronal cells. Moreover, the dentate gyrus–cornu ammonis (CA)3 system in the hippocampus has structural plasticity with remodeling/regenerative power [50, 51]. Further researchers revealed that granule cells of the dentate gyrus (DG) and pyramidal cells of CA3 are oxidative stress-vulnerable sites, but oxidative damage is higher in pyramidal cells of CA1 [52-54].

The elevation of oxidative stress in the cornu ammonis areas (DG, CA1 and CA3) is vital and has shown important functional consequences like DG implicated in memory and learning function and ventral hippocampus is specified for depression and anxiety. In addition, due to chronic oxidative stress, PFC and amygdala show alterations in the dendritic system. Particularly, medial PFC is an important site for dendritic shrinking and amygdalar neurons is responsible for dendritic growth due to the stress [55, 56], which can modify the prefrontal dendritic structural design and connectivity in neuronal networks in the PFC [57]. Interestingly, a higher level of oxidative damage and collapse of antioxidant defense system in the hippocampus and amygdale confirmed that oxidative stress in the brain encompasses biochemical, molecular and structural integrity in amygdala and hippocampus. Therefore, oxidative stress in DG-CA function can damage the remodeling capacity, cell proliferation, neurogenesis and structural plasticity, which can collectively disturb the regular synaptic neurotransmission. Moreover, free radicals oxidize the glutamatergic N-methyl-D-aspartate receptors, as a result, it reduces the synaptic transmission and LTP [58, 59]. Subsequently, these events highlighted the role of oxidative stress in behavioral and cognitive decline.

1.3. Metals and Oxidative Stress in Neurological Disorders

Metals are important for different metabolic processes in organisms [60]. The movement of metal ions across the blood brain barrier in the brain is tightly regulated, and it does not allow the flux of metals from the circulation to the brain [61]. Furthermore, the redox-active metals, because of disruption of metal homeostasis cause the generation of toxic free radicals, consequently, leading to the pathophysiology of neurological disorders. Metals like zinc, copper and iron have a strong interaction with major components of protein linked with degenerative disorders [62]. Redox-active metal ions are strongly involved in the generation of RONS through Fenton chemistry/Haber-Weiss reaction, which leads to oxidative stress in the cellular system [63, 64]. In the Haber-Weiss reaction, metal ions catalyze the formation of dangerous and highly reactive $HO^{\bullet}$ radicals from less reactive $O_2^{\bullet-}$ and H_2O_2 radicals in biological systems [65]. The mechanism of Haber-Weiss reaction can be better understood with the help of Fenton chemistry, in which Fe^{3+} react

with $O_2^{\bullet-}$ forms Fe^{2+} and O_2; Fe^{2+} then reacts with H_2O_2 to produce $HO^{\bullet}$, OH^{-} and restore Fe^{3+} `(Fenton reaction) as given in scheme 1. Other metals, such as Cu^{2+} and Cr^{3+} also generate $HO^{\bullet}$ radicals *via* Fenton reaction/Fenton-like reaction [66-68]. Additionally, vanadium produces $O_2^{\bullet-}$ radical in the oxidation of oxygen by transferring the vanadium (IV) to vanadium (V), whereas in mitochondria, manganese participates in the electron transport chain (ETC) and as a result makes RONS [69, 70]. The reactions involving vanadium, chromium and copper are presented in Scheme **1**.

Different researchers exposed that higher levels of Cu and Fe in the brain may lead to aging, which may cause neurodegenerative disorders [71] like multiple sclerosis, AD, PD, neuroferritinopathies and amyotrophic lateral sclerosis. Similarly, iron plays a role in neuronal fate in the case of AD and PD; the higher concentration of iron pool causes oxidative stress, which affects the signaling cascades and transcriptional activity, leading to neuronal death [72].

The higher metal ions concentration in the brain with increasing age can enhance the redox competition and low-affinity metal-binding site, which normally forms a redox-silent cellular pool. In this way, proteins like Aβ can connect endogenous biometals to promote the liberation of improper redox activity and production of RONS [73].

1.4. Oxidative Stress Biomarkers for Neurological Disorders

In the neuronal microenvironment, oxidative overloading results in the oxidation of proteins [74] DNA [75] and lipids [76], producing alcohols, peroxides, aldehydes, cholesterol oxide and ketones as by-products, which can frequently distress the specific neural system [77]. These major biomarkers of oxidative stress causing neurological disorders are discussed below.

1.4.1. Lipid Peroxidation

Lipid peroxidation is the widely used bioactive marker of oxidative stress. Mechanistically, free radicals attack on the double bond of unsaturated fatty acids and create very reactive lipid peroxy radicals, which initiate the chain reaction and eventually results in the lipid peroxidation. The chain reaction further generates products, such as F2-isoprostanes and 4-hydroxy-2, 3-nonenal (HNE) [78, 79]. Furthermore, HNE can transform proteins and ultimately leads to inhibition of Na^{+}-K^{+}-ATPases, dysregulation of intracellular calcium signaling, inhibition of neuronal glutamate, glucose transporters and activation of kinases. This can finally induce an apoptotic cascade system [80, 81], ultimately leading to the neurodegenerative disorders in the cellular system [82].

1.4.2. Protein Oxidation

Oxidation of protein by ROS forms the hydroxyl groups or protein based carbonyl groups [83]. Carbonyls in proteins can be generated by oxidation of amino acid side-chain hydroxyls groups into derivatives of aldehyde or ketone [84]. Besides, carbonyl groups can directly be formed by oxidizing arginine, lysine, threonine and proline residues, or breaking the peptide bonds *via* α-amidation pathway or oxidizing glutamyl residues [85]. The carbonylation of protein is a superior guesstimate for the measurement of oxidative damage associated with different oxidative stress induced diseases [86-88].

1.4.3. DNA Oxidation

DNA/RNA bases are susceptible to oxidative damage, including nitration, hydroxylation, and carbonylation [89-91]. The oxidation of nucleic acid is highlighted by higher levels of 8-hydroxyguanosine and 8-hydroxy-2-deoxyguanosine [92, 93]. Researchers revealed that oxidative stress damages the DNA strand and generates higher free carbonyls in the nuclei of neuronal cells, causing neurodegenerative diseases [94].

1.4.4. Glycoxidation

Advanced glycation end products (AGEs) are also considered strong neurotoxins and proinflammatory molecules. The non-enzymatic reaction of sugars with protein deposits generates AGEs. A cascade of reactions results subsequently in the creation of AGEs, which are made of irreversibly cross-linked heterogeneous aggregates of protein [95]. The oxidation of glycated proteins ("glycoxidation") causes the accumulation of extracellular AGEs in neurological disorders [96].

1.5. Involvement of Oxidative Stress in Neurological Disorders

Brain is particularly vulnerable to oxidative stress. This could be attributed to various physiological, anatomic, and functional parameters. The average adult human brain weighs in at 1.3 to 1.4 kilograms. It comprises only 2% of the total body weight and yet it consumes 20% of the body's oxygen (O_2) due to its high rate of metabolism. The normal human brain consumes 3.5 ml of oxygen per 100 grams of brain tissue per minute or approximately 49 ml of oxygen per minute. Notably, for energy, the brain depends on the aerobic metabolism of glucose [97]. Similarly, blood flow in the human brain is 800 mL/min, or app. 15% of the total basal cardiac output. The O_2 is consumed to generate adenosine triphosphate (ATP), which occurs mainly via oxidative phosphorylation. ATP is needed for several biochemical processes like action potentials, maintenance of energetic pumps, neurotransmission, and enzymatic reactions. Within the brain, the oxygen utility is region-specific. The gray matter consumes more than twice as much oxygen as white matter. While neurons are reported to consume 75%-80% of energy produced in the brain. The energy is largely utilized in restoration of neuronal membrane potentials following depolarization. Other neuronal functions include but are not limited to vesicle recycling, neurotransmitter synthesis and axoplasmic transport [98-100].

Morphologically, 100 billion neurons are directly or indirectly involved in an incredibly wide range of motor and internal regulatory functions. Neurons differ in size, number and complexity of dendrites, synaptic connections, length of axons, axonal myelination, and other morphological characteristics. Neurons have also been chemically classified on the basis of neurotransmitters such as glutamate, GABA, acetylcholine, dopamine, adenosine, or peptide transmitters and neuromodulators.

Neurons and neuronal functions are extremely sensitive; any disruption of oxygen supply to the brain can cause det-

rimental damage within minutes. Watts *et al.*, discussed in detail the disruption in oxygen metabolism and its involvement in various neurodegenerative disorders, such as alzheimer's, parkinson's and huntington's diseases.

The main feature of neurodegenerative diseases is neuronal death, which is involved in a cascade of hostile events. Infact central nervous system (CNS) is based on the heterogeneity and reciprocal interactions of its neurons, glia, pericytes and extracellular matrix. Neurons play a pivotal role in the neural transmission and neuroplasticity, glial cells (which is 33-66% of the human brain cells) are key components of the synaptic machinery, microglial cells protect against external stressor and maturation of synaptic network, astrocytes are the fundamental regulators of neuronal homeostasis and neuro-glial network function. They also play an active role in neurotransmitter reuptake and ion balance. Neuroinflammation, mitochondrial dysfunction, oxidative stress and excitotoxicity are also involved in Neuronal degeneration. The heterogeneous neuronal response to damaging mechanisms is still datable and extensive work is needed to explore it [101].

This is also another report which highlighted that various neurodegenerative diseases such as Alzheimer's disease AD), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) involve region-specific neurodegeneration. However, exact mechanisms which determine why particular brain regions are selectively vulnerable to neurodegeneration, whilst others remain relatively unaffected remain elusive. However, endogenous factors, such as modest antioxidant defenses, limited regenerative capacity, glypmphatic waste disposal, dependence on excitotoxic and autooxidizable neurotransmitters, polyunsaturated fatty acids prone to peroxidation, calcium load and redox active metal burden render the brain highly vulnerable to oxidative damage [102].

In neurodegenerative conditions, neurons can trigger the appearance of selective neuronal vulnerability (SNV), which is underappreciated or less explored. For example, neurons in the entorhinal cortex, hippocampus CA1 region, frontal cortex, and amygdala are extremely sensitive to the neurodegeneration associated with Alzheimer's disease (AD). In Parkinson's disease (PD), dopaminergic neurons of the substantia nigra are more susceptible to cell death. Or amyotrophic lateral sclerosis (ALS) involves degeneration of spinal motor, cortical and brain stem neurons. The appearance of SNV is not limited to cross-regional differences. For example, in the hippocampal CA1, neurons are much more vulnerable than CA3 neurons in global cerebral ischemia [103-107].

The vulnerability of neurons to OS varies from one brain region to another. Morphologically the hippocampal CA1 and CA3 regions are similar, but they respond to OS very differently. Precisely, the CA1 suffers massive cell death as compared with CA3 region. The cell death is independent of the type of pro-oxidant. For example, the same results were obtained for different agents like Superoxide-producing agents like duroquinone or paraquat or Ferrous sulphate ($FeSO_4$), a hydroxyl radical generator [108-109]. In other studies, the paraquat or xanthine/xanthine oxidase, caused extensive death of neurons in the cerebellar granule cell layer, but not in the cerebral cortex [110]. Furthermore, in midbrain, the substantia nigra pars compacta (A9) and the nearby ventral tegmental area (A10) also show differential vulnerability to OS. Precisely, A9 neurons are more vulnerable to OS as compared with A10 [111]. Semra *et al.*, also reported that neurons in the celiac and superior mesenteric ganglia (CG/SMG) are more sensitive to menadione-induced OS than superior cervical ganglion (SCG) [112].

Wang and Michaelis discussed in details, the mechanism involved in selective vulnerability of neurons to OS [110]. One of the salient features is higher OS in vulnerable neurons. For example, Wang *et al.*, measured superoxide ion concentration in the hippocampus. Interestingly, the vulnerable CA1 neurons showed significantly higher levels of superoxide anion than the resistant CA3. In another study, by H_2DCFDA (2',7'-dichlorodihydrofluorescein-diacetate) method, it was observed that the mitochondria from the CA1 release more ROS than CA3 region [113]. Various transcriptomic studies also showed that neurons from brain regions vulnerable to OS express higher levels of genes related to OS response [114].

ROS and RNS also play a physiological role by enhancing synaptic plasticity, LTP and memory formation. CA1 neurons, but not CA3 neurons, require superoxide for LTP. By using free radical scavengers, the LTP is impaired in CA1 but not in CA3. Mitochondria are not only the powerhouses for ATP but also the major site of free radical generation. Or the mitochondrial toxicants (such as MPTP and rotenone) may lead to ATP decline, dysfunctional mitochondria, and SNV. This may also lead to selective vulnerability of dopaminergic neurons as in PD [115]. In neurodegenerative conditions, the astrocytes and microglia release various cytokines to repair the damaged cells. However, the continuous activation of astrocytes and microglia can also lead to the increased production of ROS/RNS [116]. Some other factors underlying the selective vulnerability of neurons to OS includes deficient DNA damage repair and calcium dysregulation and glutamate hyperactivity [113-116].

Considerable literature is available which describes the role of OS in Neurodegenerative diseases. It is worthy to note that neuronal cells are extremely sensitive to OS because of

(1) their large dependence on oxidative phosphorylation for energy as compared with other cells,

(2) high oxygen concentration (as discussed above),

(3) higher concentration of metal ions (which accumulates in the brain with age),

(4) higher polyunsaturated fatty acids, which are more susceptible to OS and

(5) relatively poor concentrations of antioxidants and related enzymes.

1.5.1. Alzheimer's Disease

Alzheimer's disease is characterized by the deposition of protein aggregates, extracellular amyloid plaques (Aβ), intracellular tau (τ), or neurofibrillary tangles. Various studies have reported a direct relationship between Aβ-induced oxidative imbalance and higher levels of byproducts of lipid

peroxidation (*e.g.*, 4-hydroxynonal, malonidialdehyde), protein oxidation (*e.g.*, carbonyl), and DNA/RNA oxidation (*e.g.*, 8-hydroxylguanosine, 8-hydroxyldeoxyguanosine) [117-119]. The authors also reported decreased levels of various antioxidants, such as uric acid, vitamin C and E and antioxidant enzymes like superoxide dismutase, and catalase in AD patients. Transition metals are also reported to be abnormally distributed in AD, which may catalyze the OS. Increased levels of RNS in astrocytes and neuron is also reported in AD. Precisely, the expression of neuronal (nNOS or NOS-1), cytokine-inducible (iNOS or NOS-2), and endothelial (eNOS or NOS-3) isozymes is reported in gradual modification in astrocytes. There is also a direct association between iNOS and eNOS with Aβ aggregates, which further induce the nitric oxide synthases (NOS) to produce nitric oxide (NO). The higher NO levels are one of the prime causes of the generation of $ONOO^{-}$, which in turn damages the lipids, protein, and DNA/RNA [117-119].

1.5.2. Parkinson's Disease (PD)

Researches highlighted that the loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) leads to motor symptoms and drives symptomatic therapies in PD. There is mounting evidence that substantia nigra of PD patients are found to have elevated levels of oxidized lipids, proteins and DNA, along with reduced levels of glutathione [120-124]. Precisely, increased levels of 4-hydroxyl-2-nonenal (HNE), carbonyl modifications of soluble protein and 8-hydroxy-deoxyguanosine and 8-hydroxy-guanosine are reported in the literature. The link between OS and dopaminergic neuronal degeneration is further supported by the studies, where authors used various toxins to induce OS, for example, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), rotenone, 1,1'-dimethyl-4,4'-bipyridinium dichloride (paraquat), and 6-hydroxydopamine (6-OHDA) [125-129]. NO can also hinder the function of proteins by forming S-nitrosothiols, and mediates lipid peroxidation, thus causing a deteriorating effect in PD brains. The presence of high levels of trace elements (iron, manganese, zinc, selenium, copper, aluminum, *etc.*) is also reported to be involved in neurodegeneration [130, 131]. The production of free radicals in PD is exacerbated by GSH depletion, and high levels of iron or Ca^{2+}. The PD patients show low level of GSH as compared with glutathione disulfide (GSSG) (GSH:GSSG ratio. The ROS production may consequently lead to the loss of dopaminergic neurons [132, 133]. Furthermore, degeneration of the dopamine (DA) neurons of the SNpc suggests that DA itself may be a source of oxidative stress. Similarly, the alterations in catecholamine metabolism and modifications in mitochondrial electron transporter chain (METC) cannot be denied in causing PD. Elevated levels of malondialdehyde, thiobarbituric acid reactive substance and 4-hydroxy-2,3-nonenal are also reported in PD cases.

1.5.3. Huntington's Disease

Oxidative stress has been reported as one of the key players in disease progression for Huntington's disease (HD). Some of the common biomarkers include oxidative modifications to DNA, proteins, and lipids [134, 135]. Infact, 8-hdroxydeoxyguanosine (8-OHdg), an oxidation product of DNA, is a very sensitive biomarker of Huntington's disease. Increased plasma lipid peroxidation byproduct is also reported in HD. Similarly, Iron and Copper have been shown to accumulate in post-mortem brain tissues of HD patients. A recent MRI study showed enhanced accumulation of iron in basal ganglia and cortex of human HD patients. Impairment in the electron transport chain and mitochondrial dysfunction can not be neglected as the major mechanism of OS mediated pathogenesis of HD. Reduced GSH levels, abnormal tryptophan metabolism with enhanced oxidative stress are also reported in the literature [136]. Increased cytoplasmic lipofuscin (a product of unsaturated fatty acid peroxidation) is also reported in HD patients. The oxidation of mitochondrial enzymes also results in decreased catalytic activity of HD patients [137].

1.5.4. Amyotrophic Lateral Sclerosis (ALS)

There is substantial evidence implicating the involvement of OS in ALS patients. The evidence of oxidative damage in ALSO is also apparent from an increase in protein carbonyls [138-141], 8-hydroxy-2-deoxyguanosine (8-OHdG), malondialdehyde-modified proteins, 4-hydroxynonenal (4-HNE) protein conjugates, and nitrotyrosine products in the spinal cord tissue. Moreover, in erythrocytes from sALS patients, a decrease in CAT, GR, and glucose-6-phosphate dehydrogenase activities and a decrease in GSH are also reported [142-147]. Mechanistically, mutation of SOD 1 has been involved in 20% of the Amyotrophic lateral sclerosis (ALS) cases. The major function of SOD1 is the scavenging of excessive superoxide radical ($O_2^{\bullet-}$). The mutant SOD1 may also reduce the expression of glutamate transporter (GLT) 1 and ultimately leads to glutamate toxicity in motor neurons [138-140].

1.5.5. Friedreich Ataxia

Friedreich ataxia is also characterized by a loss of frataxin (an iron transporter protein). This may cause an increase in iron concentration, which promotes the conversion of H_2O_2 to $^{\bullet}OH$ through the Fenton reaction. To prove it further, antioxidant treatment with vitamin E and coenzyme Q10 supplementation has been shown to improve energy generation for some Friedreich ataxia patients [148]. Elevated levels of urine 8-hydroxy-2′-deoxyguanosine [149] and serum malondialdehyde [150] (indicative of DNA damage and lipid peroxidation, respectively) have been reported in patients.

We can conclude that there is extensive data in the literarture, which confirms that oxidative stress is one of the key aspects associated with neurodegenerative diseases and neuronal dysfunction. Oxidative stress can easily impair the brain parts because of its high oxygen utilizing property, reducing the ability of definite neurotransmitters, lipid-rich organization, restrained antioxidant defense mechanisms, and presence of several redox-active metals, which leads to neuropsychiatric and neurodegenerative diseases [151-153].

One of the fundamental sources of DNA damage is ROS, produced from normal metabolic processes. The exogenous sources like UV radiation, x-rays, gamma rays, plant or food toxins, and viruses *etc.* can not be neglected. Brain metabolizes ~ 20% of consumed oxygen, making neurons particularly susceptible to oxidative stress. The cellular process can induce oxidation, alkylation, hydrolysis of bases, bulky adduct formation, or errors in DNA replications. Single-strand

break repair (SSBR) has evolved in vertebrates and plays a pivotal role in the detection and repair of nicks and single-stranded gaps caused by cellular toxins (for example ROS). It is critical for the survival and genetic stability of mammalian cells. Deficiency in SSBR leads to cellular sensitivity to radiation, oxidative stress and base damaging agents [154, 155].

Single strain break (SSB) occurs when one strand of the DNA losses a single nucleotide. Lack of repair represents a severe threat to genetic stability. SSBs are considered the most common damage to DNA (1000 breaks/cell/day) in the cell [156]. It is worthy to note that neurons have low levels of antioxidant enzymes and these cells depend on the single-strand break repair pathway (SSBR). It can be summarized that SSBR proceeds in four stages: break detection, processing of DNA termini, DNA gap filling and ligation. DNA can undergo strand breaks, base damage, helical distortions and strand cross-links *etc.* The damage can be repaired by removing small nucleotides *via* base excision repair (BER) or longer stretches *via* the nucleotide excision repair (NER) pathway. While, for strange break repair, single strand break repair (SSBR) or double strand break repair (DSBR) pathways are discussed in the literature. Any defect in these pathways may lead to human neurological diseases. The deficiency in repair of nuclear and mitochondrial DNA damage has also been linked to several neurodegenerative disorders. There is considerable data that linked the defective DNA repair neurodegenerative syndromes, such as Alzheimer's disease and Parkinson's disease. For example, DNA DSB deficiency has been associated with Ataxia-telangiectasia, Ataxia-telangiectasia-like disorder, Nijmegen breakage syndrome, ATR Seckel syndrome, LIG4 syndrome, Human immunodeficiency with microcephaly and Fanconi anemia. Ataxia telangiectasia was probably the 1st recognized syndromes linked with DNA damage and neurodegeneration. Some of the prominent damages of A-T are immune dysfunction, sterility, extreme radiosensitivity and cancer predisposition [157-158]. It also causes cerebellar dysfunction, which is apparent from muscle hypotonia, truncal swaying while sitting or standing and abnormalities of eye movement [159]. Two other syndromes *i.e.* Ataxia-telangiectasia-like disorder and Nijmegen breakage syndrome, result from mutation of Mre11 and NBS1, respectively [160-162].

Similarly, DNA SSB deficiency also leads to oculomotor apraxia 1 (AOA1) and spinocerebellar ataxia with axonal neuropathy (SCAN1). In the stated syndromes, aprataxin (APTX) and tyrosyl-DNA phosphodiesterase-1 (TDP1) geners are mutated, respectively. It is worthy to note that although rare, AOA1 is the most common recessive ataxia in Japan and second of all autosomal recessive ataxias in Portugal. Mutations in various components of the NER pathway can lead to various human syndromes, for example, xeroderma pigmentosum (XP), Cockayne syndrome (CS), and trichothyrodystrophy (TTD) [163-166]. In the same vein, DNA X-link repair is reported in Fanconi Anemia. Furthermore, Helicase deficiency, Werner Syndrome, Rothmund Thomson syndrome, Bloom Syndrome Ataxia with oculomotor apraxia 2 can also be linked with DNA damage repair [163-166]. However, the interrelationship between DNA repair deficiency and neuropathology is intricate and the full details remain to be elucidated.

Our study reported the association of oxidative stress in 194 neurological disorders in which Alzheimer's disease, Parkinson's disease, epilepsy, dystonia, ALS (Lou Gehrig's disease), Huntington's disease, Machado–Joseph disease and multiple sclerosis afflict millions of humans worldwide and account for tremendous morbidity and mortality. The brief description of these neurological disorders, their characteristics and biomarkers/biochemical parameters are given in Table **1**.

In the present review, we have compiled the detailed information about the association of oxidative stress with neurological disorders. The selected nervous system diseases are recognized and approved by the International Statistical Classification of Diseases and Related Health Problems (ICD), World Health Organization (WHO), the Diagnostic and Statistical Manual of Mental Disorders (DSM). Superoxide dismutase (SOD), cytochrome oxidase activity, cytoplasmic cytochrome *c,* ATP levels, caspase-3 activity, catalase (CAT), total antioxidant status (TAOS), lipid peroxidation mitochondrial DNA (mtDNA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), glutathione peroxidase (GPX) activities gamma glutamyltransferase (Gamma-GT), reactive oxygen species (ROS) levels, malondialdehyde (MDA), protein carbonyls, oxidized nucleic acids, viable retinal ganglion cells (RGC), total radical-trapping antioxidant potential (TRAP), chemiluminescence, carbonyl content, reduced glutathione content, thiobarbituric acid-reactive substances (TBA-RS), sufhydryl content, nitrotyrosine (NT), TUNEL assay, poly(ADP-ribose) (PAR), Reduced/Oxidated Gluthatione, Glyoxalase 1 and glutathione reductase 1, peroxidative damage, thioredoxin (TRx), Akt/p53/p21-mediated pathway, ATM signaling pathway, oxidative stress-induced endothelial cell dysfunction, creatine phosphokinase (CPK), acetylcholinesterase (AchE)) activity, lactate dehydrogenase, mitochondrial function and redox state, mitochondrial membrane potential, transmission electron microscope, oxidative stress, peroxidative damage, hemoglobin-induced cytotoxicity, glutamate excitotoxicity, fluorescent oxidation products (FLOPs) are some of the biomarkers of oxidative stress, which are studied to associate oxidative stress with neurological disorders, as shown in Table **1**.

Whether oxidative stress is the cause or merely a consequence of associated neuronal cell loss is still debatable. Various markers for lipid, protein and DNA damages are reported to be involved in AD, PD, and ALS.

The cell has its own defense mechanism against oxidative burst. But in these conditions, the activities of various antioxidant defense molecules, for example, Superoxide Dismutase (SOD), Catalase, Glutathione Peroxidase (GSHPx) and Glutathione Reductase (GSHRd), are reduced. Reduced concentrations of uric acid (a potential scavenger of ONOO–), and reduced activity of methionine sulfoxide reductase, which reverses oxidation at protein methionine residues, are also noted in various neurodegenerative diseases. PD is specifically characterized by low glutathione (GSH) content. An increase in Iron concentration is also noted in substantia nigra (in PD cases). Infact, this turns out to be one of the basic aspects of the development of metal chelation therapy. Mutation in SOD enzymes is also reported in cases

Table 1. Association of neurological disorders with oxidative stress.

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
1.	Alcoholism	Plasma testosterone, luteinizing hormone and follicle stimulating hormone,Vitamin C, Vitamin E, ß- Carotene, Glutathione and Superoxide Dismutase, Glutathione Reductase, Malondialdehyde	[167]
2.	Alzheimer's disease	Cytochrome oxidase activity, ROS, ATP levels, cytoplasmic cytochrome *c,* caspase-3 activity, mitochondrial DNA (mtDNA)	[168]
3.	Aneurysm	Xanthine oxidase, mitochondrial oxidases and cyclooxygenase inhibition, NADPH oxidases	[169]
4.	Amaurosis fugax	Viable retinal ganglion cells (RGC), TUNEL assay, nitrotyrosine (NT) and poly (ADP-ribose) (PAR)	[170]
5.	Amnesia	Malondialdehyde (MDA), glutathione (GSH) acetylcholinesterase (AchE)) activity	[171]
6.	Amyotrophic lateral sclerosis (ALS)	Disulfide-linked SOD1 multimers, SOD1 proteins	[172]
7.	Arachnoiditis	Tenoxicam, L3 laminectomy	[173]
8.	Arnold-Chiari malformation/chiari malformation	Transmission electron microscope, oxidative stress, peroxidative damage, hemoglobin-induced cytotoxicity, calcium overload, glutamate excitotoxicity, and caspase activation.	[174]
9.	Asperger syndrome	Total antioxidant status (TAOS), non-enzymatic (glutathione and homocysteine) and enzymatic (catalase, superoxide dismutase, and glutathione peroxidase) antioxidants, and lipid peroxidation	[175]
10.	Ataxia/ Friedrichs ataxi	Lipid peroxidation, CoQ10 analog idebenone, C11-BODIPY (581/591) probe	[176]
11.	Ataxia-telangiectasia	Akt/p53/p21-mediated pathway, ATM signaling pathway, oxidative stress-induced endothelial cell dysfunction	[177]
12.	Attention deficit hyperactivity disorder	NOS, XO, GST, PON-1 and ADA activities	[178]
13.	Autism	Lipidperoxidation (malonyldialdehyde), transferrin (iron-binding protein) and ceruloplasmin (copper-binding protein)	[179]
14.	Bipolar disorder	Oxidative damage to proteins and mitochondrial complex I activity.	[180]
15.	Brachial plexus injury	Nitric oxide (NO), nitric oxide synthase (cNOS) and inducible nitric oxide synthase (iNOS) levels, neuronal nitric oxide synthase (nNOS)	[181]
16.	Brain injury	NOX subunit, gp91(phox) (gp91(phox)-/-),4-hydroxy-2-nonenal, malondialdehyde, and 8-hydroxy-2'-deoxyguanosine, NADPH oxidase, copper/zinc-superoxide dismutase (SOD1)	[182]
17.	Brain tumor	(*CAT*, *GPX1*, *NOS3*, *PON1*, *SOD1*, *SOD2*, and *SOD3*)	[183]
18.	Canavan disease	Total radical-trapping antioxidant potential (TRAP), total antioxidant reactivity (TAR), chemiluminescence, thiobarbituric acid-reactive substances (TBA-RS), reduced glutathione content, sufhydryl content and carbonyl content	[184]
19.	Capgras delusion	Retrospective study	[185]
20.	Carpal tunnel syndrome	Nitric oxide synthase (eNOS), nuclear factor (NF)-κβ, and transforming growth factor (TGF)-β	[186]
21.	Causalgia/Complex regional pain syndrome	Lipid peroxidation products (MDA), peroxidase and superoxide dismutase (SOD) activity, uric acid (UA) concentration and total antioxidant status (TAS)	[187]
22.	Central pain syndrome/ Chronic fatigue syndrome/ Chronic pain/ Fibromyalgia	ROS, mitochondrial dysfunction	[188]
23.	Central pontine myelinolysis	Levofloxacin therapy	[189]
24.	Centronuclear myopathy	RYR1-related myopathies, *N*-acetylcysteine, oxidative stress markers	[190]
25.	Cerebral aneurysm	Review	[191]
26.	Cerebral arteriosclerosis	Oxidative stress and mitochondrial markers	[192]
27.	Cerebral atrophy	Homocysteine and markers of oxidative stress (malondialdehyde)	[193]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
28.	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)	Caspase-3 activation, phosphatidylserine exposure and mitochondrial membrane depolarization	[194]
29.	Cerebral palsy	Red cell folate (RCF), magnesium, superoxide dismutase (SOD), glutathione reductase, and peroxidase, serum methylmalonic acid and vitamin C, Plasma hemoglobin, C-reactive protein, α-tocopherol, cholesterol, zinc, protein carbonyls, and total antioxidant capacity	[195]
30.	Cerebral vasculitis (giant cell artiritis), Cranial arthritis/giant cell arthritis/temporal arthritis/cerebral vasculitis	NADPH oxidase	[196]
31.	Charcot-Marie-Tooth disease	Oxidized glutathione	[197]
32.	Chronic inflammatory demyelinating polyneuropathy (CIDP)	NOX2 activity, flow cytometry, enzymatic activity	[198]
33.	Compression neuropathy	(S-) enantiomer and pregabalin, neurofi lament phosphorilated (NFP) protein, (R+)-thioctic acid	[199]
34.	Corticobasal degeneration	Immunocytochemistry, heme oxygenase-1 (HO-1), immunoelectron microscopy, HO-1 immunolabelling	[200]
35.	Cranial arteritis (temporal arteritis)	Malondialdehyde (MDA), liquid chromatography (HPLC)	[201]
36.	Creutzfeldt-Jakob disease	Malondialdehyde (MDA), liquid chromatography (HPLC)	[202]
37.	Cushing's syndrome	Plasma 15-F_{2t} -Isoprostane (15-F_{2t} -IsoP), PA by thromboxaneB_2 levels (TXB_2), and total antioxidant capacity (TAC) and serum vitamin E.	[203]
38.	Cytomegalovirus Infection	Endothelial nitric oxide synthase pathway, asymmetric dimethylarginine (ADMA, the endogenous inhibitor of nitric oxide synthase)	[204]
39.	Dawson disease (Subacute sclerosing panencephalitis (SSPE)	Immunoreactive, 8-hydroxy-2'-deoxyguanosine and 8-hydroxyguanosine, markers of oxidative damage to DNA and ribonucleic acid, products of lipid peroxidation, glutamate	[205]
40.	Dementia	Review	[206]
41.	Dermatomyositis	Mitochondrial/oxidative phosphorylation, type I IFN-regulated transcripts	[207]
42.	Diabetic neuropathy	Nicotinamide adenine dinucleotide phosphate(NADPH)oxidase mitochondrial reactive oxygen species (mtROS), Caspase activity, intracellular ROS, mtROS production, mitochondrial membrane potential (ΔYm) and NADPH oxidase activity	[208]
43.	Diffuse sclerosis	Lipid peroxidation, oxidized proteins and total antioxidant capacity (TAC)	[209]
44.	Down syndrome	Ribonucleic acid and protein expression, (SOD1) and protein levels of copper/zinc superoxide dismutase, glutathione peroxidase (GPx)	[210]
45.	Duchenne muscular dystrophy	Nicotinamide adenine dinucleotide phosphatase (Nox2)-induced oxidative stress, target of rapamycin (mTOR) *via* PI3K/Akt phosphorylation, Inhibition of Nox2 or Src kinase, NADPH oxidase	[211]
46.	Dysautonomia	Angiotensin-II (AngII) into Ang-(1–7), brain NADPH oxidase and SOD activities	[212]
47.	Dyskinesia	Glutathione peroxidase-like activity, thiobarbituric acid-reactive species (TBARS) levels	[213]
48.	Dystonia	Oxidative stress, H2O2 treatment, overexpression of TorsinA	[214]
49.	Encephalitis	Oxidative stress markers, tau protein and cytokines, 8-hydroxy-2'-deoxyguanosine (8-OHdG) and hexanoyl-lysine adduct levels	[215]
50.	Encephalotrigeminal angiomatosis (SWS)	(iTRAQ-8plex)-based liquid chromatography, Proteins, Ingenuity pathway analysis (IPA)	[216]
51.	Epilepsy	Hydroxyl and nitroxyl radicals, melatonin	[217]
52.	Fabry's disease	Plasma Hcy, methionine cycle, molecular analysis, identification of thiobarbituric acid reactive substances, total glutathione and antioxidant enzymes activity, vitamins quantification, glutathione levels and catalase activity	[218]
53.	Fainting (syncope)	qRT-PCR, Ingenuity pathway analysis and gene ontology annotation study	[219]
54.	Familial spastic paralysis/ hereditary Spastic Paraplegia	m-AAA protease and assign proteolytic activity, paraplegin, AFG3L2, Gel filtration analysis, Respiratory chain activity, Luminometric assay of ATP, Mitochondrial protein synthesis analysis	[220]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
55.	Febrile seizures	Total oxidant level and Total anti-oxidant level	[221]
56.	Fisher syndrome	Antioxidant activity (AOA) and malondialdehyde (MDA) levels	[222]
57.	Fetal alcohol syndrome	Intracellular redox state, antioxidant capacity, lipid peroxidation and protein oxidation, endogenous antioxidant glutathione	[223]
58.	Fragile X syndrome	Levels of reactive oxygen species, nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase activation, lipid peroxidation and protein oxidation	[224]
59.	Fragile X-associated tremor/ataxia syndrome (FXTAS)	Electron transport and synthesis of ATP, mitochondrial proteins, oxidative/nitrative stress damage, Citrate synthase activity, Ca^{2+} concentrations, Western blots	[225]
60.	Gaucher's disease	Primary glycosphingolipid abnormalities, lipid peroxidation (malonyldialdehyde levels), an indicator of lipid peroxidation, and the total antioxidant status, glucosylceramide, ceramide, glucosylceramide/ceramide ratio, glucosylsphingosine	[226]
61.	Gerstmann's syndrome	Kinases, phosphorylate, p38 (p-38-P) and SAPK/ JNK (SAPK/JNK-P), mitochondrial abnormalities, multicentric PrP^{res}, Western blots	[227]
62.	Giant cell inclusion disease	Mitochondrial DNA oxidative damage index (mtDNA(ΔCT)) and intima media thickness (IMT)	[228]
63.	Globoid Cell Leukodystrophy/ Krabbe disease	Antioxidant N-acetyl cysteine (NAC), immunohistochemical markers	[229]
64.	Gray matter heterotopia	Immunohistochemical characteristics, cytosine arabinoside (Ara-C)	[230]
65.	Guillain-Barré syndrome	Glutathione peroxidase, levels of myeloperoxidase, levels of lactoferrin, antibody-based enzyme immunoassay	[231]
66.	Generalized anxiety disorder	Sulphydryl group levels, oxidative stress	[232]
67.	Hallervorden-Spatz disease	Histochemistry for iron and immunohistochemistry for Cu/Zn superoxide dismutase (SOD1), Mn superoxide dismutase (SOD2) and ferritin. SOD1-like immunoreactivity (IR), SOD2-IR and ferritin-IR	[233]
68.	Head injury	Review	[234]
69.	Headache	Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), malondialdehyde (MDA) levels	[235]
70.	Holoprosencephaly	Shh expression and activation of protein kinase A (PKA), antagonist of Shh signaling, antioxidants, such as vitamins C or E	[236]
71.	Huntington's disease	Review	[237]
72.	Hydrocephalus	ROS levels, dichlorofluorescein (DCF) fluorescence, and lipid peroxidation, using malondialdehyde (MDA)	[238]
73.	Hypercortisolism	Hypercortisolism and oxidative stress, hypothalamic--pituitary--adrenal axis activity, cortisol (including salivary measures of cortisol awakening response and serum morning levels)	[239]
74.	Hypoxia	Myocyte cell line H9c2, PKCε protein and mRNA, CpG methylation of the SP1-binding sites, HIF-1α, HIF-1α inhibitors (3-(5′-hydroxymethyl-2′-furyl)-1-benzylindazole and 2-methoxy estradiol), ROS scavengers *N*-acetyl-cysteine or tempol	[240]
75.	Inclusion body myositis	Review	[241]
76.	Incontinentia pigmenti	Cerebrospinal fluid levels of cytokines and oxidative stress markers (8-hydroxy-2-deoxyguanosine and the hexanoyl-lysine adduct), Magnetic resonance imaging	[242]
77.	Infantile Refsum disease	Activities of catalase (CAT), glutathione peroxidase (GPx), glucose 6-phosphate dehydrogenase (G6PD), and glutathione S-transferase (GST) along with reduced glutathione (GSH) content	[243]
78.	Infantile spasms/west syndrome	NMDA model Prenatal, betamethasone /postnatal NMDA, Prenatal stress /postnatal, NMDA Down / GBL	[244]
79.	Inflammatory myopathy	Mitochondrial alterations and oxidative stress	[245]
80.	Intracranial hypertension	RyR2 phosphorylation status and TnI degradation, Western blot analysis, phosphorylation status of RyR2 or TnI degradation levels	[246]
81.	Karak syndrome	Pantothenate kinase gene (*PANK2*)	[247]
82.	Kearns-Sayre syndrome	Normal blood cell counts, iron saturation, non-fasting and fasting glucose, glycated haemoglobin (HbA1c), lactate and pyruvate, CSF protein and lactate levels	[248]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
83.	Lafora disease	Mitochondrial alterations, oxidative stress and a deficiency in antioxidant enzymes, proteomic analysis, peroxiredoxin-6	[249]
84.	Learning disabilities	Vitamin E supplemented, levels of SOD and Sir2, fluid percussion injury (FPI)	[250]
85.	Leigh's disease	Review	[251]
86.	Lennox-Gastaut syndrome	DNA oxidative marker (8-hydroxy-2′-deoxyguanosine, 8-OHdG) and markers for lipid peroxidation, including hexanoyl lysine adduct (HEL), in the urine and cerebrospinal fluid (CSF), West syndrome (WS), oxidative products of DNA (8-OHdG) and lipid (4-hydroxynonenal, 4-HNE)	[252]
87.	Lesch-Nyhan syndrome	(Aconitase activity, oxidized glutathione, and lipid peroxides), (superoxide dismutase, protein thiol content, carbonyl protein content, total glutathione, glutathione peroxidase, catalase, and thiobarbituric reducing substances). Immunolocalization of heme-oxygenase 1	[253]
88.	Leukodystrophy	Immunohistochemical markers, mitochondrial manganese-superoxide dismutase, hemoxygenase-1, lipid peroxidation (4-hydroxynonenal and malondialdehyde), nitrotyrosylated proteins	[254]
89.	Lewy body dementia	Superoxide dismutase (SOD), catalase (CAT), glutathione (GLU) and total antioxidant capacity	[255]
90.	Lumbar disc disease	Nitric oxide (NO), superoxide dismutase (SOD), malondialdehyde (MDA), and advanced oxidation protein products (AOPPs)	[256]
91.	Machado-Joseph disease (Spinocerebellar ataxia type 3)	DNA damage by the comet assay	[257]
92.	Menieres disease	Protein oxidation, such as protein carbonyls (PC) and 4-hydroxynonenal (HNE) in lymphocytes, ultraweak luminescence (UCL), heat shock proteins Hsp70 and thioredoxin (Trx) expression and lymphocyte ratio reduced glutathione GSH) vs. oxidized glutathione (GSSG)	[258]
93.	Meningitis	Review	[259]
94.	Menkes disease	Review	[260]
95.	Microcephaly	NBN gene in the central nervous system (CNS), nestin-Cre targeting gene system	[261]
96.	Micropsia	Review	[262]
97.	Migraine	Malondialdehyde (MDA), 4-hydroxy-2-nonenal (HNE), carbonylated proteins, nitric oxide stress, inflammation, lipid- and glucose-metabolism	[263]
98.	Miller Fisher syndrome	Activity of pro- and antioxidant systems, electron paramagnetic resonance (EPR) method, nitric oxide (NO), complexes of NO with nonhemic iron (HbNO), lypo- and superoxide radicals, signals of free Mn^{2+} and Fe^{2+}, blood antioxidant enzymes, ceruloplasmin and katalasa, superoxide dismitase's and glutation reductases	[264]
99.	Mini-stroke (transient ischemic attack)	lipid profile, oxidative stress and antioxidants	[265]
100.	Mitochondrial myopathy	Review	[266]
101.	Motor Neurone Disease - see amyotrophic lateral sclerosis	Review	[267]
102.	Motor skills disorder	Bacterial endotoxin (lipopolysaccharide, LPS) perinatal anoxia (PA), oxidative and inflammatory parameters, TNF-α, IL-1, IL-4, SOD, CAT and DCF, ELISA method	[268]
103.	Mucopolysaccharidoses	Enzyme replacement therapy, malondialdehyde, carbonyl groups in plasma, erythrocyte catalase activity, total antioxidant status, superoxide dismutase enzyme	[269]
104.	Multi-infarct dementia	Morris water maze tests and eight-arm radial maze task, lactic acid and malondialdehyde (MDA), lactate dehydrogenase (LDH), Na^+K^+ATPase, $Ca^{2+}Mg^{2+}$ATPase and superoxide dismutase (SOD), Nicotiflorin protective effect	[270]
105.	Multiple sclerosis	Review	[271]
106.	Multiple system atrophy	Mitochondrial inhibition by 3-nitropropionic acid, striatonigral degeneration and olivopontocerebellar atrophy, astrogliosis and microglial activation	[272]
107.	Muscular dystrophy	Review	[273]
108.	Myalgic encephalomyelitis/ Chronic fatigue syndrome (CFS)	Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale	[274]
109.	Myasthenia gravis	Serum levels of bilirubin and uric acid (UA)	[275]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
110.	Myoclonus	Plasmid-based method of RNA interference (RNAi), Cystatin B knockdown, transfected β-galactosidase-positive neurons, Cystatin B RNAi.	[276]
111.	Myopathy	Expression array analysis, zebrafish and cultured myotubes, oxidant activity, antioxidant N-acetylcysteine	[277]
112.	Neuro-Behçet's disease	Oxidative and antioxidative parameters, total antioxidant capacity (TAC), paraoxonase (PON), arylesterase (ARE), glutathione (GSH) antioxidants and malondialdehyde (MDA) oxidant levels	[278]
113.	Neurofibromatosis	Overexpression of the NF1 gene, mitochondrial respiration, reactive oxygen species (ROS) production, adenylyl cyclase/cyclic AMP (cAMP)/protein kinase A pathway	[279]
114.	Neuroleptic malignant syndrome	CPK activity, muscle rigidity and leukocytosis, ROS production, catalase serum activity	[280]
115.	Neurological manifestations of AIDS	Review	[281]
116.	Neurological sequelae of lupus	Review	[282]
117.	Neuronal ceroid lipofuscinosis	Review	[283]
118.	Neuronal migration disorders	Review	[284]
119.	Neuropathy	Review	[285]
120.	Neurosis	Reactive oxygen metabolites (ROM), anti-oxidant potential	[286]
121.	Niemann-Pick disease	Coenzyme Q10 (CoQ10) and trolox equivalent antioxidant capacity (TEAC), oxidative stress	[287]
122.	Occult Spinal Dysraphism Sequence	Review	[288]
123.	Olivopontocerebellar atrophy	Olivopontocerebellar atrophy (OPCA), lipid peroxidation, immune-histochemically	[289]
124.	Optic neuritis	Reactive oxygen species (ROS), mitochondrial oxidative stress, SOD2 gene	[290]
125.	Orthostatic Hypotension	Urine 17-KS-S (17-ketosteroid sulfate, abbreviated to S), 17-OHCS (17-hydroxycorticosteroids, abb. to OH) and S/OH ratio as endocrinological stress markers	[291]
126.	Otosclerosis	Aldehyde 4-hydroxynonenal (HNE), regular HNE-protein adducts, Ang II, immunoblot-ting	[292]
127.	Overuse syndrome	Morphological and histological changes, biomarkers of oxidative stress, inflammation, and apoptosis.	[293]
128.	Parkinson's disease	Review	[294]
129.	Paraneoplastic diseases	Serum pro-inflammatory cytokines and oxidative stress/antioxidant parametersand, PBMC (Peripheral blood mononuclear cells), TNF-alpha, ROS, GSH and vitamin E	[295]
130.	Paroxysmal attacks	Mutational analysis, Bioinformatic analysis, Northern analysis, Mammalian cell culture and transfection	[296]
131.	Pelizaeus-Merzbacher disease	Innate immune system activation in autopsy, missense mutations in mildly- and severely-affected Plp1-mutant	[297]
132.	Periodic Paralyses	Mitochondrial DNA sequencing and restriction PCR, oxidative phosphorylation functional assays, reactive oxygen species metabolism, and patch-clamp technique	[298]
133.	Peripheral neuropathy	Review	[299]
134.	Pervasive developmental disorders	Oxidative stress status	[300]
135.	Phytanic acid storage disease	Fatty acid induces lipid and protein oxidative damage, thiobarbituric acid-reactive sub-stances, carbonyl formation, glutathione, 2',7'-dichlorofluorescin oxidation (DCFH)	[301]
136.	Pick's disease	2',7'-dichlorofluorescin oxidation (DCFH), corticobasal degeneration, immunocytochemis-try, antisera to heme oxygenase-1 (HO-1)	[302]
137.	Pinched nerve	Antisera to heme oxygenase-1 (HO-1), inflammatory cytokine interleukin (IL)-1β, real-time reverse-transcriptase polymerase chain reaction (RT-PCR), biochemistry, and immu-nofluorescence microscopy	[303]
138.	Pituitary tumors	Ingenuity pathway analysis, protein-mapping data, comparative proteomic data, adenoma nitroproteomic data, and control nitroproteomic data. Fisher's exact test, mitochondrial dysfunction, oxidative stress, cell-cycle dysregulation, and the MAPK-signaling	[304]
139.	Polyneuropathy	Plasma 8-iso-prostaglandin F(2alpha) (8-iso-PGF(2alpha)), superoxide anion (O(2)(.-)) generation, lag phase to peroxidation by peroxynitrite (ONOO(-)), vitamin E-to-lipid ratio, and vitamin C	[305]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Refs.
140.	Polio	DNA constructs and transfections, Immunofluorescence, RNA *in situ* hybridization, Immunoblot analysis of cell lysates	[306]
141.	Polymyositis	Autoimmune inflammatory myopathies, muscle fiber apoptosis, DNA fragmentation or expression of apoptosis-related proteins, inducible and neuronal nitric oxide synthase (NOS)	[307]
142.	Post-Polio syndrome	Review	[308]
143.	Postherpetic Neuralgia (PHN)	Vimang formulations,	[309]
144.	Prader-Willi syndrome	Redox biomarkers profile, total hydroperoxides (TH), non protein-bound iron (NPBI), thiols (SH), advanced oxidation protein products (AOPP) and isoprostanes (IPs), GH therapy, OS biomarkers	[310]
145.	Prion diseases	Review	[311]
146.	Progressive Supranuclear Palsy	Cu/Zn-superoxide dismutase (SOD), glutathione peroxidase (GPx), and 4-hydroxynonenal (HNE)-conjugated GPx, immunosorbent assay	[312]
147.	Pseudotumor cerebri	Elevated pressure, hypoxia, and oxidative stress, bioreduction assays, endocytotic activity	[313]
148.	Quadriplegia	Superoxide dismutase (SOD), glutathione reductase (GR) and catalase (CAT), glutathione peroxidase (GPX) activity	[314]
149.	Rabies	Degeneration of neurites (axons), mock-infected DRG neurons, lipid peroxidation associated with oxidative stress	[315]
150.	Radiculopathy	Antioxidant enzymes superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx), nitric oxide metabolites and lipid hydroperoxides	[316]
151.	Reflex neurovascular dystrophy	8-isoprostane-prostaglandin F2α, cytokines (TNF-α, IL-4, IL-6, IL-7, IL-8, IL-10, IL-17A). Plasma concentrations, radioimmunoassay (RIA), and kinetics of cytokines, antibody-based proximity ligation (PLA)	[317]
152.	REM sleep behavior disorder	Review	[318]
153.	Repetitive stress injury	Isometric torque, range of movement (ROM), delayed-onset muscle soreness (DOMS), creatine kinase (CK), reduced glutathione (GSH), oxidized glutathione (GSSG), thiobarbituric acid-reactive substances (TBARS), protein carbonyls, catalase, uric acid, bilirubin, and total antioxidant capacity (TAC)	[319]
154.	Restless legs syndrome	Total oxidant status (TOS), total antioxidant status (TAS), oxidative stress index (OSI), arylesterase (ARE), paraoxonase (PON), stimulated paraoxonase (stim-PON), lipid hydroperoxides (LOOHs), acetyl cholinesterase (AChE) and butyryl cholinesterase (BuChE)	[320]
155.	Rett syndrome	Plasma NPBI and F2-IsoPs, and intraerythrocyte NPBI	[321]
156.	Reye's syndrome	Serum transaminases (AST, ALT) and plasma ammonia levels, oxidative stress markers, GSH, MDA	[322]
157.	Sandhoff disease	Lucigenin chemiluminescence, cytosolic NADPH oxidase subunits p67phox and p47phox, inflammatory markers (tumor necrosis factor α, monocyte chemotactant protein-1, interleukin 6, and galectin-3), cardiomyocyte-restricted overexpression of ATGL, guanylate cyclase activity, oxidative stress, superoxide dismutase mimetic Mn(III)tetrakis (4-benzoic acid) porphyrin	[323]
158.	Schilder's disease	Mitochondrial energy production, galactose, cyclophilin D protein	[324]
159.	Sensory processing disorder	Sequencing of mutants and transcript analysis, Reporter constructs and transgenic methods, Cell identification, Behavioral assays, Life span measurements, Immunofluorescence staining, Analysis of protein carbonylation by ELISA	[325]
160.	Shingles	Antioxidative substances	[326]
161.	Shy-Drager syndrome	Mitochondrial inhibition by 3-nitropropionic acid, MSA-like pathology, striatonigral degeneration and olivopontocerebellar atrophy, oligodendroglial alpha-SYN overexpression	[327]
162.	Sjögren's syndrome	OS markers, as oxidative DNA damage and propanoyl-lysine	[328]
163.	Sleep apnea	Review	[329]
164.	Sleeping sickness	RNA interference (RNAi), T. brucei trypanothione synthetase (TbTryS) and superoxide dismutase B (TbSODB)	[330]
165.	Spasticity	Enzyme-linked immunosorbent assay, coronary spastic angina (CSA), inactive stage of CSA (iCSA), stable effort angina (SEA)	[331]

(Table 1) contd….

S. No.	Neurological Disorder	Biochemical Parameters or Immunocytochemistry or Electron Microscopy or Other Technique	Ref #
166.	Spina bifida	Selenium, vitamin B12, serum folates, plasma thiol compounds and amino acids. Homocysteine transsulfuration, total cysteine/total homocysteine ratio (tCys/tHcy),	[332]
167.	Spinal cord injury	Review	[333]
168.	Spinal cord tumors	Free radicals – tissue necrosis, inflammation, infection, apoptosis	[334]
169.	Spinal muscular atrophy	Fibroblast cell lines, Reactive oxygen species content, antioxidant effect of curcumin, real-time PCR array	[335]
170.	Spinal and bulbar muscular atrophy	Urinary 8-OHdG	[336]
171.	Spinocerebellar ataxia	Review	[337]
172.	Split-brain	Creatine kinase, free radicals, oxidative phosphorylation parameters, spin-trapping electron paramagnetic resonance spectroscopy (EPR)	[338]
173.	Stroke	Review	[339]
174.	Sturge-Weber syndrome	Isobaric tags for relative and absolute quantification (iTRAQ-8plex)-based liquid chromatography interfaced with tandem mass spectrometry (LC-MS/MS), Ingenuity pathway analysis (IPA)	[340]
175.	Subacute sclerosing panencephalitis	*In situ* nick end-labeling and immunohistochemistry, 8-hydroxy-2'-deoxyguanosine and 8-hydroxyguanosine, 4-hydroxy-2-nonenal-modified proteins, lipid peroxidation	[341]
176.	Subcortical arteriosclerotic encephalopathy	Superoxide, hydrogen peroxide, glutathione (GSH) and thiobarbiturate-reactive substances (TBARS)	[342]
177.	Tarsal tunnel syndrome	Metallothionein, lipid peroxidation (malondialdehyde, MDA), and poly(ADP-ribose) polymerase-1 (PARP-1)	[343]
178.	Tardive dyskinesia	Review	[344]
179.	Tay-Sachs disease	Special Issue	[345]
180.	Temporal arteritis	Immunohistochemical Analysis, Tyrosine Nitration, lipid peroxidation, density of Factor $VIII^{+}$ vessels	[346]
181.	Tetanus	Sphingolipid Determination by 14C-labeling and Thin Layer Chromatography, Sphingomyelinase Activity Analysis, Immunocytochemistry, Western-blot Analysis	[347]
182.	Tic Douloureux	Lipid peroxidation (malondialdehyde (MDA)), pro-nociceptive action of ROS, hydrogen peroxide	[348]
183.	Tourette syndrome	Ferritin, hemoglobin, zinc, non-ceruloplasmin copper, immunological markers, immunoglobulins	[349]
184.	Transient ischemic attack	Lipid profile(serum cholesterol, triglycerides, serum HDL and serum LDL cholesterol), markers of lipid peroxidation (MDA), oxidative stress and antioxidants (Erythrocyte SOD and serum Vitamin E)	[350]
185.	Transmissible spongiform encephalopathies	Review	[351]
186.	Traumatic brain injury	Review	[352]
187.	Tremor	Nutritional antioxidants	[353]
188.	Trypanosomiasis	NRF2/HO-1, HO-1 activity, macrophage parasitism, antioxidants, including NRF2 activators	[354]
189.	Tuberous sclerosis	Tsc2 gene, Immunohistochemical analysis	[355]
190.	Von Hippel-Lindau disease (VHL)	P1465 hydroxylation, phosphorylation, and nondegradative ubiquitylation. Egln-9-type prolyl hydroxylases, PHD1 and PHD2, coimmunoprecipitated, Ser5 phosphorylation of Rbp1	[356]
191.	West syndrome	Oxidative stress	[357]
192.	Wilson's disease	Glutathione (GSH), total antioxidant capacity (TAC) and malonodialdehyde (MDA), cytokines, and glutamate	[358]
193.	X-Linked Spinal and Bulbar Muscular Atrophy	Antioxidant cocktail, axonal degeneration	[359]
194.	Zellweger syndrome	PEX13 brain mutants, reactive oxygen species and mitochondrial superoxide dismutase-2 (MnSOD)	[360]

of ALS, which seems to be associated with a toxic gain of function in SOD1 rather than a loss in its activity. This evidence indicates that reduced antioxidant potential might contribute to the increased oxidative stress that is associated with these disorders. Similarly, in another study, the authors indicated that mitochondrial dysfunction and especially the OS occurs early in all major neurodegenerative diseases. The authors briefly discussed the role of mitochondria in AD, PD, ALS and HD [153].

CONCLUSION

In this review, we tried to cover the genetic, pharmacological, biochemical, and preclinical therapeutic studies, case reports, and clinical trials to explore the molecular aspects of neurological or neurodegenerative disorders, which might be associated with oxidative stress. The data obtained after deep insight into the literature show that out of more than 350 neurological disorders, only 194 are associated with the oxidative stress. Various facts proposed that ROS can be produced by different mechanisms and they play multifaceted parts in promoting the chronic diseases. Predominantly, ROS react with numerous cellular macromolecules like nucleic acids, proteins, carbohydrates and lipids, which completely modify their functions. When it is over the threshold, a late-onset infection arises. Owing to the higher oxygen use of neurons, in the brain, more ROS can accumulate in contrast to other organs, thus leading to neurodegenerative disease. Despite the fact that oxidative stress is detected in the extensively studied neurodegenerative disorders, but the specific pathogenesis and pathways are still unclear. More elaborated studies in the future will certainly help in understanding the exact mechanism involved in neurological diseases and provide insight into revelation of therapeutic targets.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Aiken, C.T.; Kaake, R.M.; Wang, X.; Huang, L. Oxidative stress-mediated regulation of proteasome complexes. *Mol. Cell. Proteomics,* **2011**, *10*(5), 006924. http://dx.doi.org/10.1074/mcp.M110.006924 PMID: 21543789

[2] Ienco, E.C.; LoGerfo, A.; Carlesi, C.; Orsucci, D.; Ricci, G.; Mancuso, M.; Siciliano, G. Oxidative stress treatment for clinical trials in neurodegenerative diseases. *J. Alzheimers Dis.,* **2011**, *24*(Suppl. 2), 111-126. http://dx.doi.org/10.3233/JAD-2011-110164 PMID: 21422516

[3] Fulda, S.; Gorman, A.M.; Hori, O.; Samali, A. Cellular stress responses: cell survival and cell death. *Int. J. Cell Biol.,* **2010**, *2010*, 214074. http://dx.doi.org/10.1155/2010/214074 PMID: 20182529

[4] Martin, L.J. Mitochondrial and cell death mechanisms in neurodegenerative diseases. *Pharmaceuticals (Basel),* **2010**, *3*(4), 839-915. http://dx.doi.org/10.3390/ph3040839 PMID: 21258649

[5] Hathazi, D.; Scurtu, F.; Bischin, C.; Mot, A.; Attia, A.A.A.; Kongsted, J.; Silaghi-Dumitrescu, R. The reaction of oxy hemoglobin with nitrite: Mechanism, antioxidant-modulated effect, and implications for blood substitute evaluation. *Molecules,* **2018**, *23*(2), 350. http://dx.doi.org/10.3390/molecules23020350 PMID: 29414908

[6] Song, P.; Zou, M.H. Roles of reactive oxygen species in physiology and pathology. *Atherosclerosis: risks, mechanisms, and therapies*; Wang, H.; Patterson, C., Eds.; John Wiley & Sons Inc: Hoboken, NJ, **2015**, pp. 379-392.

[7] Mani, S. Production of reactive oxygen species and its implication in human diseases. *Free radicals in human health and disease*; Rani, V.; Yadav, U.C., Eds.; Springer: New Delhi, **2015**, pp. 3-15. http://dx.doi.org/10.1007/978-81-322-2035-0_1

[8] Sies, H.; Jones, D.P. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nat. Rev. Mol. Cell Biol.,* **2020**, *21*(7), 363-383. http://dx.doi.org/10.1038/s41580-020-0230-3 PMID: 32231263

[9] Rosca, A.E.; Iesanu, M.I.; Zahiu, C.D.M.; Voiculescu, S.E.; Paslaru, A.C.; Zagrean, A.M. Capsaicin and gut microbiota in health and disease. *Molecules,* **2020**, *25*(23), 5681. http://dx.doi.org/10.3390/molecules25235681 PMID: 33276488

[10] Valko, M.; Rhodes, C.J.; Moncol, J.; Izakovic, M.; Mazur, M. Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chem. Biol. Interact.,* **2006**, *160*(1), 1-40. http://dx.doi.org/10.1016/j.cbi.2005.12.009 PMID: 16430879

[11] Valko, M.; Morris, H.; Cronin, M.T. Metals, toxicity and oxidative stress. *Curr. Med. Chem.,* **2005**, *12*(10), 1161-1208. http://dx.doi.org/10.2174/0929867053764635 PMID: 15892631

[12] Malekmohammad, K.; Sewell, R.D.E.; Rafieian-Kopaei, M. Antioxidants and atherosclerosis: Mechanistic aspects. *Biomolecules,* **2019**, *9*(8), 301. http://dx.doi.org/10.3390/biom9080301 PMID: 31349600

[13] Balaban, R.S.; Nemoto, S.; Finkel, T. Mitochondria, oxidants, and aging. *Cell,* **2005**, *120*(4), 483-495. http://dx.doi.org/10.1016/j.cell.2005.02.001 PMID: 15734681

[14] Liguori, I.; Russo, G.; Curcio, F.; Bulli, G.; Aran, L.; Della-Morte, D.; Gargiulo, G.; Testa, G.; Cacciatore, F.; Bonaduce, D.; Abete, P. Oxidative stress, aging, and diseases. *Clin. Interv. Aging,* **2018**, *13*, 757-772. http://dx.doi.org/10.2147/CIA.S158513 PMID: 29731617

[15] Singh, A.; Kukreti, R.; Saso, L.; Kukreti, S. Oxidative stress: A key modulator in neurodegenerative diseases. *Molecules,* **2019**, *24*(8), 1583. http://dx.doi.org/10.3390/molecules24081583 PMID: 31013638

[16] Islam, M.T. Oxidative stress and mitochondrial dysfunction-linked neurodegenerative disorders. *Neurol. Res.,* **2017**, *39*(1), 73-82. http://dx.doi.org/10.1080/01616412.2016.1251711 PMID: 27809706

[17] Bjørklund, G.; Dadar, M.; Chirumbolo, S.; Aaseth, J.; Peana, M. Metals, autoimmunity, and neuroendocrinology: Is there a connection? *Environ. Res.,* **2020**, *187*, 109541. http://dx.doi.org/10.1016/j.envres.2020.109541 PMID: 32445945

[18] Engedal, N.; Žerovnik, E.; Rudov, A.; Galli, F.; Olivieri, F.; Procopio, A.D.; Rippo, M.R.; Monsurrò, V.; Betti, M.; Albertini, M.C. From oxidative stress damage to pathways, networks, and autophagy *via* microRNAs. *Oxid. Med. Cell. Longev.,* **2018**, *2018*, 4968321. http://dx.doi.org/10.1155/2018/4968321 PMID: 29849898

[19] Grimm, A.; Eckert, A. Brain aging and neurodegeneration: from a mitochondrial point of view. *J. Neurochem.,* **2017**, *143*(4), 418-431. http://dx.doi.org/10.1111/jnc.14037 PMID: 28397282

[20] Patten, D.A.; Germain, M.; Kelly, M.A.; Slack, R.S. Reactive oxygen species: stuck in the middle of neurodegeneration. *J. Alzheimers Dis.,* **2010**, *20*(2)(Suppl. 2), S357-S367. http://dx.doi.org/10.3233/JAD-2010-100498 PMID: 20421690

[21] Lassmann, H. Mechanisms of neurodegeneration shared between multiple sclerosis and Alzheimer's disease. *J. Neural Transm. (Vienna),* **2011**, *118*(5), 747-752. http://dx.doi.org/10.1007/s00702-011-0607-8 PMID: 21373761

[22] Higgins, G.C.; Beart, P.M.; Shin, Y.S.; Chen, M.J.; Cheung, N.S.; Nagley, P. Oxidative stress: emerging mitochondrial and cellular themes and variations in neuronal injury. *J. Alzheimers Dis.,* **2010**, *20*(2)(Suppl. 2), S453-S473. http://dx.doi.org/10.3233/JAD-2010-100321 PMID: 20463398

[23] Ma, M.W.; Wang, J.; Dhandapani, K.M.; Wang, R.; Brann, D.W. NADPH oxidases in traumatic brain injury - Promising therapeutic targets? *Redox Biol.,* **2018**, *16*, 285-293. http://dx.doi.org/10.1016/j.redox.2018.03.005 PMID: 29571125

[24] Babior, B.M. NADPH oxidase. *Curr. Opin. Immunol.,* **2004**, *16*(1), 42-47. http://dx.doi.org/10.1016/j.coi.2003.12.001 PMID: 14734109

[25] Buvelot, H.; Jaquet, V.; Krause, K.H. Mammalian NADPH Oxidases. *Methods Mol. Biol.,* **2019**, *1982*, 17-36. http://dx.doi.org/10.1007/978-1-4939-9424-3_2 PMID: 31172464

[26] Song, P.; Zou, M.H. Regulation of NAD(P)H oxidases by AMPK in cardiovascular systems. *Free Radic. Biol. Med.,* **2012**, *52*(9), 1607-1619. http://dx.doi.org/10.1016/j.freeradbiomed.2012.01.025 PMID: 22357101

[27] Burtenshaw, D.; Hakimjavadi, R.; Redmond, E.M.; Cahill, P.A. Nox, reactive oxygen species and regulation of vascular cell fate. *Antioxidants,* **2017**, *6*(4), 90. http://dx.doi.org/10.3390/antiox6040090 PMID: 29135921

[28] Hiramoto, K.; Yamate, Y.; Sato, E.F. Gp91phox NADPH oxidase modulates litter size by regulating mucin1 in the uterus of mice. *Syst. Biol. Reprod. Med.,* **2017**, *63*(2), 130-139. http://dx.doi.org/10.1080/19396368.2017.1282063 PMID: 28301257

[29] Altenhöfer, S.; Radermacher, K.A.; Kleikers, P.W.; Wingler, K.; Schmidt, H.H. Evolution of NADPH oxidase inhibitors: Selectivity and mechanisms for target engagement. *Antioxid. Redox Signal.,* **2015**, *23*(5), 406-427. http://dx.doi.org/10.1089/ars.2013.5814 PMID: 24383718

[30] Roy, K.; Wu, Y.; Meitzler, J.L.; Juhasz, A.; Liu, H.; Jiang, G.; Lu, J.; Antony, S.; Doroshow, J.H. NADPH oxidases and cancer. *Clin. Sci. (Lond.),* **2015**, *128*(12), 863-875. http://dx.doi.org/10.1042/CS20140542 PMID: 25818486

[31] Muñoz, M.; López-Oliva, M.E.; Rodríguez, C.; Martínez, M.P.; Sáenz-Medina, J.; Sánchez, A.; Climent, B.; Benedito, S.; García-Sacristán, A.; Rivera, L.; Hernández, M.; Prieto, D. Differential contribution of Nox1, Nox2 and Nox4 to kidney vascular oxidative stress and endothelial dysfunction in obesity. *Redox Biol.,* **2020**, *28*, 101330. http://dx.doi.org/10.1016/j.redox.2019.101330 PMID: 31563085

[32] Kim, Y.M.; Kim, S.J.; Tatsunami, R.; Yamamura, H.; Fukai, T.; Ushio-Fukai, M. ROS-induced ROS release orchestrated by Nox4, Nox2, and mitochondria in VEGF signaling and angiogenesis. *Am. J. Physiol. Cell Physiol.,* **2017**, *312*(6), C749-C764. http://dx.doi.org/10.1152/ajpcell.00346.2016 PMID: 28424170

[33] Morel, F.; Rousset, F.; Vu Chuong Nguyen, M.; Trocme, C.; Grange, L.; Lardy, B. NADPH oxidase Nox4, a putative therapeutic target in osteoarthritis. *Bull. Acad Natl. Med.,* **2015**, *199*(4-5), 673-686. http://dx.doi.org/10.1016/S0001-4079(19)30941-0 PMID: 27509686

[34] Montezano, A.C.; Touyz, R.M. Reactive oxygen species and endothelial function--role of nitric oxide synthase uncoupling and Nox family nicotinamide adenine dinucleotide phosphate oxidases. *Basic Clin. Pharmacol. Toxicol.,* **2012**, *110*(1), 87-94. http://dx.doi.org/10.1111/j.1742-7843.2011.00785.x PMID: 21883939

[35] Reyes-Martinez, C.; Nguyen, Q.M.; Kassan, M.; Gonzalez, A.A. (Pro)renin receptor-dependent induction of profibrotic factors is mediated by COX-2/EP4/NOX-4/Smad pathway in collecting duct cells. *Front. Pharmacol.,* **2019**, *10*, 803. http://dx.doi.org/10.3389/fphar.2019.00803 PMID: 31396082

[36] Jiang, J.; Huang, K.; Xu, S.; Garcia, J.G.N.; Wang, C.; Cai, H. Targeting NOX4 alleviates sepsis-induced acute lung injury *via* attenuation of redox-sensitive activation of CaMKII/ERK1/2/MLCK and endothelial cell barrier dysfunction. *Redox Biol.,* **2020**, *36*, 101638. http://dx.doi.org/10.1016/j.redox.2020.101638 PMID: 32863203

[37] Dasuri, K.; Zhang, L.; Keller, J.N. Oxidative stress, neurodegeneration, and the balance of protein degradation and protein synthesis. *Free Radic. Biol. Med.,* **2013**, *62*, 170-185. http://dx.doi.org/10.1016/j.freeradbiomed.2012.09.016 PMID: 23000246

[38] Furuhashi, M. New insights into purine metabolism in metabolic diseases: role of xanthine oxidoreductase activity. *Am. J. Physiol. Endocrinol. Metab.,* **2020**, *319*(5), E827-E834. http://dx.doi.org/10.1152/ajpendo.00378.2020 PMID: 32893671

[39] Battelli, M.G.; Polito, L.; Bortolotti, M.; Bolognesi, A. Xanthine oxidoreductase-derived reactive species: physiological and pathological effects. *Oxid. Med. Cell. Longev.,* **2016**, *2016*, 3527579. http://dx.doi.org/10.1155/2016/3527579 PMID: 26823950

[40] Bhandary, B.; Marahatta, A.; Kim, H.R.; Chae, H.J. An involvement of oxidative stress in endoplasmic reticulum stress and its associated diseases. *Int. J. Mol. Sci.,* **2012**, *14*(1), 434-456. http://dx.doi.org/10.3390/ijms14010434 PMID: 23263672

[41] Higa, A.; Chevet, E. Redox signaling loops in the unfolded protein response. *Cell. Signal.,* **2012**, *24*(8), 1548-1555. http://dx.doi.org/10.1016/j.cellsig.2012.03.011 PMID: 22481091

[42] Dandekar, A.; Mendez, R.; Zhang, K. Cross talk between ER stress, oxidative stress, and inflammation in health and disease. *Methods Mol. Biol.,* **2015**, *1292*, 205-214. http://dx.doi.org/10.1007/978-1-4939-2522-3_15 PMID: 25804758

[43] Vallée, A.; Lecarpentier, Y. Crosstalk between peroxisome proliferator-activated receptor gamma and the canonical WNT/β-catenin pathway in chronic inflammation and oxidative stress during carcinogenesis. *Front. Immunol.,* **2018**, *9*, 745. http://dx.doi.org/10.3389/fimmu.2018.00745 PMID: 29706964

[44] Valko, M.; Leibfritz, D.; Moncol, J.; Cronin, M.T.; Mazur, M.; Telser, J. Free radicals and antioxidants in normal physiological functions and human disease. *Int. J. Biochem. Cell Biol.,* **2007**, *39*(1), 44-84. http://dx.doi.org/10.1016/j.biocel.2006.07.001 PMID: 16978905

[45] Wang, X.; Michaelis, E.K. Selective neuronal vulnerability to oxidative stress in the brain. *Front. Aging Neurosci.,* **2010**, *2*, 12. http://dx.doi.org/10.3389/fnagi.2010.00012 PMID: 20552050

[46] Masood, A.; Nadeem, A.; Mustafa, S.J.; O'Donnell, J.M. Reversal of oxidative stress-induced anxiety by inhibition of phosphodiesterase-2 in mice. *J. Pharmacol. Exp. Ther.,* **2008**, *326*(2), 369-379. http://dx.doi.org/10.1124/jpet.108.137208 PMID: 18456873

[47] Salim, S.; Asghar, M.; Taneja, M.; Hovatta, I.; Chugh, G.; Vollert, C.; Vu, A. Potential contribution of oxidative stress and inflammation to anxiety and hypertension. *Brain Res.,* **2011**, *1404*, 63-71. http://dx.doi.org/10.1016/j.brainres.2011.06.024 PMID: 21704983

[48] Patki, G.; Allam, F.H.; Atrooz, F.; Dao, A.T.; Solanki, N.; Chugh, G.; Asghar, M.; Jafri, F.; Bohat, R.; Alkadhi, K.A.; Salim, S. Grape powder intake prevents ovariectomy-induced anxiety-like behavior, memory impairment and high blood pressure in female Wistar rats. *PLoS One,* **2013**, *8*(9), e74522. http://dx.doi.org/10.1371/journal.pone.0074522 PMID: 24040270

[49] Solanki, N.; Alkadhi, I.; Atrooz, F.; Patki, G.; Salim, S. Grape powder prevents cognitive, behavioral, and biochemical impairments in a rat model of posttraumatic stress disorder. *Nutr. Res.,* **2015**, *35*(1), 65-75. http://dx.doi.org/10.1016/j.nutres.2014.11.008 PMID: 25533441

[50] Sousa, N.; Lukoyanov, N.V.; Madeira, M.D.; Almeida, O.F.; Paula-Barbosa, M.M. Reorganization of the morphology of hippocampal neurites and synapses after stress-induced damage correlates with behavioral improvement. *Neuroscience,* **2000**, *97*(2), 253-266. http://dx.doi.org/10.1016/S0306-4522(00)00050-6 PMID: 10799757

[51] McEwen, B.S. Understanding the potency of stressful early life experiences on brain and body function. *Metabolism,* **2008**, *57*(2)(Suppl. 2), S11-S15.

http://dx.doi.org/10.1016/j.metabol.2008.07.006 PMID: 18803958

[52] Chang, B.J.; Jang, B.J.; Son, T.G.; Cho, I.H.; Quan, F.S.; Choe, N.H.; Nahm, S.S.; Lee, J.H. Ascorbic acid ameliorates oxidative damage induced by maternal low-level lead exposure in the hippocampus of rat pups during gestation and lactation. *Food Chem. Toxicol.,* **2012**, *50*(2), 104-108. http://dx.doi.org/10.1016/j.fct.2011.09.043 PMID: 22056337

[53] Huang, T.T.; Zou, Y.; Corniola, R. Oxidative stress and adult neurogenesis--effects of radiation and superoxide dismutase deficiency. *Semin. Cell Dev. Biol.,* **2012**, *23*(7), 738-744. http://dx.doi.org/10.1016/j.semcdb.2012.04.003 PMID: 22521481

[54] Huang, Y.; Coupland, N.J.; Lebel, R.M.; Carter, R.; Seres, P.; Wilman, A.H.; Malykhin, N.V. Structural changes in hippocampal subfields in major depressive disorder: A high-field magnetic resonance imaging study. *Biol. Psychiatry,* **2013**, *74*(1), 62-68. http://dx.doi.org/10.1016/j.biopsych.2013.01.005 PMID: 23419546

[55] Ng, L.H.L.; Huang, Y.; Han, L.; Chang, R.C.; Chan, Y.S.; Lai, C.S.W. Ketamine and selective activation of parvalbumin interneurons inhibit stress-induced dendritic spine elimination. *Transl. Psychiatry,* **2018**, *8*(1), 272. http://dx.doi.org/10.1038/s41398-018-0321-5 PMID: 30531859

[56] Leuner, B.; Shors, T.J. Stress, anxiety, and dendritic spines: what are the connections? *Neuroscience,* **2013**, *251*, 108-119. http://dx.doi.org/10.1016/j.neuroscience.2012.04.021 PMID: 22522470

[57] Liston, C.; McEwen, B.S.; Casey, B.J. Psychosocial stress reversibly disrupts prefrontal processing and attentional control. *Proc. Natl. Acad. Sci. USA,* **2009**, *106*(3), 912-917. http://dx.doi.org/10.1073/pnas.0807041106 PMID: 19139412

[58] Haxaire, C.; Turpin, F.R.; Potier, B.; Kervern, M.; Sinet, P.M.; Barbanel, G.; Mothet, J.P.; Dutar, P.; Billard, J.M. Reversal of age-related oxidative stress prevents hippocampal synaptic plasticity deficits by protecting D-serine-dependent NMDA receptor activation. *Aging Cell,* **2012**, *11*(2), 336-344. http://dx.doi.org/10.1111/j.1474-9726.2012.00792.x PMID: 22230264

[59] Rai, S.; Kamat, P.K.; Nath, C.; Shukla, R. A study on neuroinflammation and NMDA receptor function in STZ (ICV) induced memory impaired rats. *J. Neuroimmunol.,* **2013**, *254*(1-2), 1-9. http://dx.doi.org/10.1016/j.jneuroim.2012.08.008 PMID: 23021418

[60] Bertini, I.; Cavallaro, G. Metals in the "omics" world: copper homeostasis and cytochrome c oxidase assembly in a new light. *J. Biol. Inorg. Chem.,* **2008**, *13*(1), 3-14. http://dx.doi.org/10.1007/s00775-007-0316-9 PMID: 17987327

[61] Mills, E.; Dong, X.P.; Wang, F.; Xu, H. Mechanisms of brain iron transport: insight into neurodegeneration and CNS disorders. *Future Med. Chem.,* **2010**, *2*(1), 51-64. http://dx.doi.org/10.4155/fmc.09.140 PMID: 20161623

[62] Barnham, K.J.; Bush, A.I. Metals in Alzheimer's and Parkinson's diseases. *Curr. Opin. Chem. Biol.,* **2008**, *12*(2), 222-228. http://dx.doi.org/10.1016/j.cbpa.2008.02.019 PMID: 18342639

[63] Halliwell, B. The wanderings of a free radical. *Free Radic. Biol. Med.,* **2009**, *46*(5), 531-542. http://dx.doi.org/10.1016/j.freeradbiomed.2008.11.008 PMID: 19111608

[64] Halliwell, B. Role of free radicals in the neurodegenerative diseases: therapeutic implications for antioxidant treatment. *Drugs Aging,* **2001**, *18*(9), 685-716. http://dx.doi.org/10.2165/00002512-200118090-00004 PMID: 11599635

[65] Hassan, W.; Noreen, H.; Rehman, S.; Gul, S.; Kamal, M.A.; Kamdem, J.P.; Zaman, B.; da Rocha, J.B.T. J, B.T.da.Rocha. Oxidative stress and antioxidant potential of one hundred medicinal plants. *Curr. Top. Med. Chem.,* **2017**, *17*(12), 1336-1370. http://dx.doi.org/10.2174/1568026617666170102125648 PMID: 28049396

[66] Bokare, A.D.; Choi, W. Review of iron-free Fenton-like systems for activating H_2O_2 in advanced oxidation processes. *J. Hazard. Mater.,* **2014**, *275*, 121-135. http://dx.doi.org/10.1016/j.jhazmat.2014.04.054 PMID: 24857896

[67] Patel, M. Targeting oxidative stress in central nervous system disorders. *Trends Pharmacol. Sci.,* **2016**, *37*(9), 768-778. http://dx.doi.org/10.1016/j.tips.2016.06.007 PMID: 27491897

[68] Kurutas, E.B. The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: *current state. Nutr. J.,* **2016**, *15*(1), 71. http://dx.doi.org/10.1186/s12937-016-0186-5 PMID: 27456681

[69] Ścibior, A. Vanadium (V) and magnesium (Mg) - In vivo interactions: A review. *Chem. Biol. Interact.,* **2016**, *258*, 214-233. http://dx.doi.org/10.1016/j.cbi.2016.09.007 PMID: 27620816

[70] Neal, A.P.; Guilarte, T.R. Mechanisms of lead and manganese neurotoxicity. *Toxicol. Res. (Camb.),* **2013**, *2*(2), 99-114. http://dx.doi.org/10.1039/c2tx20064c PMID: 25722848

[71] Ke, Y.; Qian, Z.M. Brain iron metabolism: neurobiology and neurochemistry. *Prog. Neurobiol.,* **2007**, *83*(3), 149-173. http://dx.doi.org/10.1016/j.pneurobio.2007.07.009 PMID: 17870230

[72] Belaidi, A.A.; Bush, A.I. Iron neurochemistry in Alzheimer's disease and Parkinson's disease: targets for therapeutics. *J. Neurochem.,* **2016**, *139*(1)(Suppl. 1), 179-197. http://dx.doi.org/10.1111/jnc.13425 PMID: 26545340

[73] Salvador, G.A.; Uranga, R.M.; Giusto, N.M. Iron and mechanisms of neurotoxicity. *Int. J. Alzheimers Dis.,* **2010**, *2011*, 720658. PMID: 21234369

[74] Bochkov, V.N.; Oskolkova, O.V.; Birukov, K.G.; Levonen, A.L.; Binder, C.J.; Stöckl, J. Generation and biological activities of oxidized phospholipids. *Antioxid. Redox Signal.,* **2010**, *12*(8), 1009-1059. http://dx.doi.org/10.1089/ars.2009.2597 PMID: 19686040

[75] Sedelnikova, O.A.; Redon, C.E.; Dickey, J.S.; Nakamura, A.J.; Georgakilas, A.G.; Bonner, W.M. Role of oxidatively induced DNA lesions in human pathogenesis. *Mutat. Res.,* **2010**, *704*(1-3), 152-159. http://dx.doi.org/10.1016/j.mrrev.2009.12.005 PMID: 20060490

[76] Adibhatla, R.M.; Hatcher, J.F. Lipid oxidation and peroxidation in CNS health and disease: from molecular mechanisms to therapeutic opportunities. *Antioxid. Redox Signal.,* **2010**, *12*(1), 125-169. http://dx.doi.org/10.1089/ars.2009.2668 PMID: 19624272

[77] Kura, B.; Szeiffova Bacova, B.; Kalocayova, B.; Sykora, M.; Slezak, J. Oxidative Stress-Responsive MicroRNAs in Heart Injury. *Int. J. Mol. Sci.,* **2020**, *21*(1), 358. http://dx.doi.org/10.3390/ijms21010358 PMID: 31948131

[78] Peña-Bautista, C.; Vento, M.; Baquero, M.; Cháfer-Pericás, C. Lipid peroxidation in neurodegeneration. *Clin. Chim. Acta,* **2019**, *497*, 178-188. http://dx.doi.org/10.1016/j.cca.2019.07.037 PMID: 31377127

[79] Ma, F.; Wu, T.; Zhao, J.; Ji, L.; Song, A.; Zhang, M.; Huang, G. Plasma homocysteine and serum folate and vitamin b_{12} levels in mild cognitive impairment and Alzheimer's disease: A case-control study. *Nutrients,* **2017**, *9*(7), 725. http://dx.doi.org/10.3390/nu9070725 PMID: 28698453

[80] Tong, B.C.; Wu, A.J.; Li, M.; Cheung, K.H. Calcium signaling in Alzheimer's disease & therapies. *Biochim. Biophys. Acta Mol. Cell Res.,* **2018**, *1865*(11 Pt B), 1745-1760. http://dx.doi.org/10.1016/j.bbamcr.2018.07.018 PMID: 30059692

[81] Abarikwu, S.O.; Pant, A.B.; Farombi, E.O. 4-Hydroxynonenal induces mitochondrial-mediated apoptosis and oxidative stress in SH-SY5Y human neuronal cells. *Basic Clin. Pharmacol. Toxicol.,* **2012**, *110*(5), 441-448. http://dx.doi.org/10.1111/j.1742-7843.2011.00834.x PMID: 22118713

[82] Bruce-Keller, A.J.; Li, Y.J.; Lovell, M.A.; Kraemer, P.J.; Gary, D.S.; Brown, R.R.; Markesbery, W.R.; Mattson, M.P. 4-Hydroxynonenal, a product of lipid peroxidation, damages cholinergic neurons and impairs visuospatial memory in rats. *J. Neuropathol. Exp. Neurol.,* **1998**, *57*(3), 257-267. http://dx.doi.org/10.1097/00005072-199803000-00007 PMID: 9600218

[83] Hawkins, C.L.; Davies, M.J. Detection, identification, and quantification of oxidative protein modifications. *J. Biol. Chem.,* **2019**, *294*(51), 19683-19708. http://dx.doi.org/10.1074/jbc.REV119.006217 PMID: 31672919

[84] Reeg, S.; Grune, T. Protein oxidation in aging: Does it play a role in aging progression? *Antioxid. Redox Signal.,* **2015**, *23*(3), 239-255.
http://dx.doi.org/10.1089/ars.2014.6062 PMID: 25178482

[85] Hauck, A.K.; Huang, Y.; Hertzel, A.V.; Bernlohr, D.A. Adipose oxidative stress and protein carbonylation. *J. Biol. Chem.,* **2019**, *294*(4), 1083-1088.
http://dx.doi.org/10.1074/jbc.R118.003214 PMID: 30563836

[86] Levine, R.L.; Williams, J.A.; Stadtman, E.R.; Shacter, E. Carbonyl assays for determination of oxidatively modified proteins. *Methods Enzymol.,* **1994**, *233*, 346-357.
http://dx.doi.org/10.1016/S0076-6879(94)33040-9 PMID: 8015469

[87] Smith, M.A.; Sayre, L.M.; Anderson, V.E.; Harris, P.L.; Beal, M.F.; Kowall, N.; Perry, G. Cytochemical demonstration of oxidative damage in Alzheimer disease by immunochemical enhancement of the carbonyl reaction with 2,4-dinitrophenylhydrazine. *J. Histochem. Cytochem.,* **1998**, *46*(6), 731-735.
http://dx.doi.org/10.1177/002215549804600605 PMID: 9603784

[88] Korolainen, M.A.; Nyman, T.A.; Nyyssönen, P.; Hartikainen, E.S.; Pirttilä, T. Multiplexed proteomic analysis of oxidation and concentrations of cerebrospinal fluid proteins in Alzheimer disease. *Clin. Chem.,* **2007**, *53*(4), 657-665.
http://dx.doi.org/10.1373/clinchem.2006.078014 PMID: 17289803

[89] Lovell, M.A.; Markesbery, W.R. Oxidative DNA damage in mild cognitive impairment and late-stage Alzheimer's disease. *Nucleic Acids Res.,* **2007**, *35*(22), 7497-7504.
http://dx.doi.org/10.1093/nar/gkm821 PMID: 17947327

[90] Kieroń, M.; Żekanowski, C.; Falk, A.; Wężyk, M. Oxidative DNA damage signalling in neural stem cells in Alzheimer's disease. *Oxid. Med. Cell. Longev.,* **2019**, *2019*, 2149812.
http://dx.doi.org/10.1155/2019/2149812 PMID: 31814869

[91] Peña-Bautista, C.; Tirle, T.; López-Nogueroles, M.; Vento, M.; Baquero, M.; Cháfer-Pericás, C. Oxidative damage of DNA as early marker of Alzheimer's disease. *Int. J. Mol. Sci.,* **2019**, *20*(24), 6136.
http://dx.doi.org/10.3390/ijms20246136 PMID: 31817451

[92] Ke, S.; Yang, Z.; Yang, F.; Wang, X.; Tan, J.; Liao, B. Long noncoding RNA NEAT1 aggravates Aβ-induced neuronal damage by targeting miR-107 in Alzheimer's disease. *Med. J.,* **2019**, *60*(7), 640-650.
http://dx.doi.org/10.3349/ymj.2019.60.7.640 PMID: 31250578

[93] Chen, Z.; Zhong, C. Oxidative stress in Alzheimer's disease. *Neurosci. Bull.,* **2014**, *30*(2), 271-281.
http://dx.doi.org/10.1007/s12264-013-1423-y PMID: 24664866

[94] Ahmad, W.; Ijaz, B.; Shabbiri, K.; Ahmed, F.; Rehman, S. Oxidative toxicity in diabetes and Alzheimer's disease: mechanisms behind ROS/ RNS generation. *J. Biomed. Sci.,* **2017**, *24*(1), 76.
http://dx.doi.org/10.1186/s12929-017-0379-z PMID: 28927401

[95] Smith, M.A.; Perry, G.; Richey, P.L.; Sayre, L.M.; Anderson, V.E.; Beal, M.F.; Kowall, N. Oxidative damage in Alzheimer's. *Nature,* **1996**, *382*(6587), 120-121.
http://dx.doi.org/10.1038/382120b0 PMID: 8700201

[96] Srikanth, V.; Maczurek, A.; Phan, T.; Steele, M.; Westcott, B.; Juskiw, D.; Münch, G. Advanced glycation endproducts and their receptor RAGE in Alzheimer's disease. *Neurobiol. Aging,* **2011**, *32*(5), 763-777.
http://dx.doi.org/10.1016/j.neurobiolaging.2009.04.016 PMID: 19464758

[97] Greene, A.E.; Todorova, M.T.; Seyfried, T.N. Perspectives on the metabolic management of epilepsy through dietary reduction of glucose and elevation of ketone bodies. *J. Neurochem.,* **2003**, *86*(3), 529-537.
http://dx.doi.org/10.1046/j.1471-4159.2003.01862.x PMID: 12859666

[98] Hyder, F.; Rothman, D.L.; Bennett, M.R. Cortical energy demands of signaling and nonsignaling components in brain are conserved across mammalian species and activity levels. *Proc. Natl. Acad. Sci. USA,* **2013**, *110*(9), 3549-3554.
http://dx.doi.org/10.1073/pnas.1214912110 PMID: 23319606

[99] Harris, J.J.; Jolivet, R.; Attwell, D. Synaptic energy use and supply. *Neuron,* **2012**, *75*(5), 762-777.
http://dx.doi.org/10.1016/j.neuron.2012.08.019 PMID: 22958818

[100] Attwell, D.; Laughlin, S.B. An energy budget for signaling in the grey matter of the brain. *J. Cereb. Blood Flow Metab.,* **2001**, *21*(10), 1133-1145.
http://dx.doi.org/10.1097/00004647-200110000-00001 PMID: 11598490

[101] Salim, S. Oxidative stress and the central nervous system. *J. Pharmacol. Exp. Ther.,* **2017**, *20*(7), 550-561.

[102] Cragnolini, A.B.; Lampitella, G.; Virtuoso, A.; Viscovo, I.; Panetsos, F.; Papa, M.; Cirillo, G. Regional brain susceptibility to neurodegeneration: what is the role of glial cells? *Neural Regen. Res.,* **2020**, *15*(5), 838-842.
http://dx.doi.org/10.4103/1673-5374.268897 PMID: 31719244

[103] Terry, R.D.; Masliah, E.; Salmon, D.P.; Butters, N.; DeTeresa, R.; Hill, R.; Hansen, L.A.; Katzman, R. Physical basis of cognitive alterations in Alzheimer's disease: synapse loss is the major correlate of cognitive impairment. *Ann. Neurol.,* **1991**, *30*(4), 572-580.
http://dx.doi.org/10.1002/ana.410300410 PMID: 1789684

[104] Dauer, W.; Przedborski, S. Parkinson's disease: mechanisms and models. *Neuron,* **2003**, *39*(6), 889-909.
http://dx.doi.org/10.1016/S0896-6273(03)00568-3 PMID: 12971891

[105] Rowland, L.P.; Shneider, N.A. Amyotrophic lateral sclerosis. *N. Engl. J. Med.,* **2001**, *344*(22), 1688-1700.
http://dx.doi.org/10.1056/NEJM200105313442207 PMID: 11386269

[106] Mueller, S.G.; Stables, L.; Du, A.T.; Schuff, N.; Truran, D.; Cashdollar, N.; Weiner, M.W. Measurement of hippocampal subfields and age-related changes with high resolution MRI at 4T. *Neurobiol. Aging,* **2007**, *28*(5), 719-726.
http://dx.doi.org/10.1016/j.neurobiolaging.2006.03.007 PMID: 16713659

[107] Bura, V.; Caglic, I.; Snoj, Z.; Sushentsev, N.; Berghe, A.S.; Priest, A.N.; Barrett, T. MRI features of the normal prostatic peripheral zone: the relationship between age and signal heterogeneity on T2WI, DWI, and DCE sequences. *Eur. Radiol.,* **2021**, *31*(7), 4908-4917.
http://dx.doi.org/10.1007/s00330-020-07545-7 PMID: 33398421

[108] Vornov, J.J.; Park, J.; Thomas, A.G. Regional vulnerability to endogenous and exogenous oxidative stress in organotypic hippocampal culture. *Exp. Neurol.,* **1998**, *149*(1), 109-122.
http://dx.doi.org/10.1006/exnr.1997.6673 PMID: 9454620

[109] Wang, X.; Pal, R.; Chen, X.W.; Limpeanchob, N.; Kumar, K.N.; Michaelis, E.K. High intrinsic oxidative stress may underlie selective vulnerability of the hippocampal CA1 region. *Brain Res. Mol. Brain Res.,* **2005**, *140*(1-2), 120-126.
http://dx.doi.org/10.1016/j.molbrainres.2005.07.018 PMID: 16137784

[110] Wang, X.; Zaidi, A.; Pal, R.; Garrett, A.S.; Braceras, R.; Chen, X.W.; Michaelis, M.L.; Michaelis, E.K. Genomic and biochemical approaches in the discovery of mechanisms for selective neuronal vulnerability to oxidative stress. *BMC Neurosci.,* **2009**, *10*, 12.
http://dx.doi.org/10.1186/1471-2202-10-12 PMID: 19228403

[111] McCormack, A.L.; Atienza, J.G.; Langston, J.W.; Di Monte, D.A. Decreased susceptibility to oxidative stress underlies the resistance of specific dopaminergic cell populations to paraquat-induced degeneration. *Neuroscience,* **2006**, *141*(2), 929-937.
http://dx.doi.org/10.1016/j.neuroscience.2006.03.069 PMID: 16677770

[112] Semra, Y.K.; Wang, M.; Peat, N.J.; Smith, N.C.; Shotton, H.R.; Lincoln, J. Selective susceptibility of different populations of sympathetic neurons to diabetic neuropathy *in vivo* is reflected by increased vulnerability to oxidative stress *in vitro*. *Neurosci. Lett.,* **2006**, *407*(3), 199-204.
http://dx.doi.org/10.1016/j.neulet.2006.08.045 PMID: 16973273

[113] Mattiasson, G.; Friberg, H.; Hansson, M.; Elmér, E.; Wieloch, T. Flow cytometric analysis of mitochondria from CA1 and CA3 regions of rat hippocampus reveals differences in permeability transition pore activation. *J. Neurochem.,* **2003**, *87*(2), 532-544.
http://dx.doi.org/10.1046/j.1471-4159.2003.02026.x PMID: 14511130

[114] Morel, Y.; Barouki, R. Repression of gene expression by oxidative stress. *Biochem. J.,* **1999**, *342*(Pt 3), 481-496.

http://dx.doi.org/10.1042/bj3420481 PMID: 10477257

[115] Betarbet, R.; Sherer, T.B.; MacKenzie, G.; Garcia-Osuna, M.; Panov, A.V.; Greenamyre, J.T. Chronic systemic pesticide exposure reproduces features of Parkinson's disease. *Nat. Neurosci.,* **2000**, *3*(12), 1301-1306.
http://dx.doi.org/10.1038/81834 PMID: 11100151

[116] Streit, W.J. Microglia as neuroprotective, immunocompetent cells of the CNS. *Glia,* **2002**, *40*(2), 133-139.
http://dx.doi.org/10.1002/glia.10154 PMID: 12379901

[117] Praticò, D. Oxidative stress hypothesis in Alzheimer's disease: A reappraisal. *Trends Pharmacol. Sci.,* **2008**, *29*(12), 609-615.
http://dx.doi.org/10.1016/j.tips.2008.09.001 PMID: 18838179

[118] Zhao, Y.; Zhao, B. Oxidative stress and the pathogenesis of Alzheimer's disease. *Oxid. Med. Cell. Longev.,* **2013**, *2013*, 316523.
http://dx.doi.org/10.1155/2013/316523 PMID: 23983897

[119] Wang, X.; Wang, W.; Li, L.; Perry, G.; Lee, H.G.; Zhu, X. Oxidative stress and mitochondrial dysfunction in Alzheimer's disease. *Biochim. Biophys. Acta,* **2014**, *1842*(8), 1240-1247.
http://dx.doi.org/10.1016/j.bbadis.2013.10.015 PMID: 24189435

[120] Bosco, D.A.; Fowler, D.M.; Zhang, Q.; Nieva, J.; Powers, E.T.; Wentworth, P., Jr; Lerner, R.A.; Kelly, J.W. Elevated levels of oxidized cholesterol metabolites in Lewy body disease brains accelerate alpha-synuclein fibrilization. *Nat. Chem. Biol.,* **2006**, *2*(5), 249-253.
http://dx.doi.org/10.1038/nchembio782 PMID: 16565714

[121] Trist, B.G.; Hare, D.J.; Double, K.L. Oxidative stress in the aging substantia nigra and the etiology of Parkinson's disease. *Aging Cell,* **2019**, *18*(6), e13031.
http://dx.doi.org/10.1111/acel.13031 PMID: 31432604

[122] Smeyne, M.; Smeyne, R.J. Glutathione metabolism and Parkinson's disease. *J. Free Radic. Biol. Med.,* **2013**, *62*, 13-25.
http://dx.doi.org/10.1016/j.freeradbiomed.2013.05.001 PMID: 23665395

[123] Puspita, L.; Chung, S.Y.; Shim, J.W. Oxidative stress and cellular pathologies in Parkinson's disease. *Mol. Brain,* **2017**, *10*(1), 53.
http://dx.doi.org/10.1186/s13041-017-0340-9 PMID: 29183391

[124] Hemmerle, A.M.; Herman, J.P.; Seroogy, K.B. Stress, depression and Parkinson's disease. *Exp. Neurol.,* **2012**, *233*(1), 79-86.
http://dx.doi.org/10.1016/j.expneurol.2011.09.035 PMID: 22001159

[125] Richardson, J.R.; Quan, Y.; Sherer, T.B.; Greenamyre, J.T.; Miller, G.W. Paraquat neurotoxicity is distinct from that of MPTP and rotenone. *Toxicol. Sci.,* **2005**, *88*(1), 193-201.
http://dx.doi.org/10.1093/toxsci/kfi304 PMID: 16141438

[126] Callio, J.; Oury, T.D.; Chu, C.T. Manganese superoxide dismutase protects against 6-hydroxydopamine injury in mouse brains. *J. Biol. Chem.,* **2005**, *280*(18), 18536-18542.
http://dx.doi.org/10.1074/jbc.M413224200 PMID: 15755737

[127] Vila, M.; Przedborski, S. Targeting programmed cell death in neurodegenerative diseases. *Nat. Rev. Neurosci.,* **2003**, *4*(5), 365-375.
http://dx.doi.org/10.1038/nrn1100 PMID: 12728264

[128] Perier, C.; Bové, J.; Vila, M.; Przedborski, S. The rotenone model of Parkinson's disease. *Trends Neurosci.,* **2003**, *26*(7), 345-346.
http://dx.doi.org/10.1016/S0166-2236(03)00144-9 PMID: 12850429

[129] Fukushima, T.; Gao, T.; Tawara, T.; Hojo, N.; Isobe, A.; Yamane, Y. Inhibitory effect of nicotinamide to paraquat toxicity and the reaction site on complex I. *Arch. Toxicol.,* **1997**, *71*(10), 633-637.
http://dx.doi.org/10.1007/s002040050437 PMID: 9332700

[130] Zatta, P.; Lucchini, R.; van Rensburg, S.J.; Taylor, A. The role of metals in neurodegenerative processes: Aluminum, manganese, and zinc. *Brain Res. Bull.,* **2003**, *62*(1), 15-28.
http://dx.doi.org/10.1016/S0361-9230(03)00182-5 PMID: 14596888

[131] Torres-Vega, A.; Pliego-Rivero, B.F.; Otero-Ojeda, G.A.; Gómez-Oliván, L.M.; Vieyra-Reyes, P. Limbic system pathologies associated with deficiencies and excesses of the trace elements iron, zinc, copper, and selenium. *Nutr. Rev.,* **2012**, *70*(12), 679-692.
http://dx.doi.org/10.1111/j.1753-4887.2012.00521.x PMID: 23206282

[132] Brown, D.R. Metals in neurodegenerative disease. *Metallomics,* **2011**, *3*(3), 226-228.
http://dx.doi.org/10.1039/c1mt90005f PMID: 21327191

[133] Rivera-Mancía, S.; Pérez-Neri, I.; Ríos, C.; Tristán-López, L.; Rivera-Espinosa, L.; Montes, S. The transition metals copper and iron in neurodegenerative diseases. *Chem Biol Interact,* **2010**, *186*(2), 184.
http://dx.doi.org/10.1016/j.cbi.2010.04.010

[134] Hands, S.L.; Mason, R.; Sajjad, M.U.; Giorgini, F.; Wyttenbach, A. Metallothioneins and copper metabolism are candidate therapeutic targets in Huntington's disease. *Biochem. Soc. Trans.,* **2010**, *38*(2), 552-558.
http://dx.doi.org/10.1042/BST0380552 PMID: 20298220

[135] Squadrone, S.; Brizio, P.; Abete, M.C.; Brusco, A. Trace elements profile in the blood of Huntington' disease patients. *J. Trace Elem. Med. Biol.,* **2020**, *57*, 18-20.
http://dx.doi.org/10.1016/j.jtemb.2019.09.006 PMID: 31546208

[136] Duran, R.; Barrero, F.J.; Morales, B.; Luna, J.D.; Ramirez, M.; Vives, F. Oxidative stress and plasma aminopeptidase activity in Huntington's disease. *J. Neural Transm. (Vienna),* **2010**, *117*(3), 325-332.
http://dx.doi.org/10.1007/s00702-009-0364-0 PMID: 20094738

[137] Essa, M.M.; Moghadas, M.; Ba-Omar, T.; Walid Qoronfleh, M.; Guillemin, G.J.; Manivasagam, T.; Justin-Thenmozhi, A.; Ray, B.; Bhat, A.; Chidambaram, S.B.; Fernandes, A.J.; Song, B.J.; Akbar, M. Protective effects of antioxidants in Huntington's disease: An extensive review. *Neurotox. Res.,* **2019**, *35*(3), 739-774.
http://dx.doi.org/10.1007/s12640-018-9989-9 PMID: 30632085

[138] Cunha-Oliveira, T.; Montezinho, L.; Mendes, C.; Firuzi, O.; Saso, L.; Oliveira, P.J.; Silva, F.S.G. Oxidative stress in amyotrophic lateral sclerosis: Pathophysiology and opportunities for pharmacological intervention. *Oxid. Med. Cell. Longev.,* **2020**, *2020*, 5021694.
http://dx.doi.org/10.1155/2020/5021694 PMID: 33274002

[139] Riancho, J.; Gonzalo, I.; Ruiz-Soto, M.; Berciano, J. Why do motor neurons degenerate? Actualization in the pathogenesis of amyotrophic lateral sclerosis. *Berciano J. Neurologia,* **2019**, *34*(1), 27-37.
http://dx.doi.org/10.1016/j.nrleng.2015.12.019 PMID: 26853842

[140] Walker, A.K.; Atkin, J.D. Stress signaling from the endoplasmic reticulum: A central player in the pathogenesis of amyotrophic lateral sclerosis. *IUBMB Life,* **2011**, *63*(9), 754-763.
http://dx.doi.org/10.1002/iub.520 PMID: 21834058

[141] Niebrój-Dobosz, I.; Dziewulska, D.; Kwieciński, H. Oxidative damage to proteins in the spinal cord in amyotrophic lateral sclerosis (ALS). *Folia Neuropathol.,* **2004**, *42*(3), 151-156.
PMID: 15535033

[142] Mitsumoto, H.; Garofalo, D.C.; Santella, R.M.; Sorenson, E.J.; Oskarsson, B.; Fernandes, J.A.M., Jr; Andrews, H.; Hupf, J.; Gilmore, M.; Heitzman, D.; Bedlack, R.S.; Katz, J.S.; Barohn, R.J.; Kasarskis, E.J.; Lomen-Hoerth, C.; Mozaffar, T.; Nations, S.P.; Swenson, A.J.; Factor-Litvak, P. Plasma creatinine and oxidative stress biomarkers in amyotrophic lateral sclerosis. *Amyotroph. Lateral Scler. Frontotemporal Degener.,* **2020**, *21*(3-4), 263-272.
http://dx.doi.org/10.1080/21678421.2020.1746810 PMID: 32276554

[143] Chico, L.; Ienco, E.C.; Bisordi, C.; Lo Gerfo, A.; Petrozzi, L.; Petrucci, A.; Mancuso, M.; Siciliano, G. Amyotrophic lateral sclerosis and oxidative stress: A double-blind therapeutic trial after curcumin supplementation. *CNS Neurol. Disord. Drug Targets,* **2018**, *17*(10), 767-779.
http://dx.doi.org/10.2174/1871527317666180720162029 PMID: 30033879

[144] D'Amico, E.; Factor-Litvak, P.; Santella, R.M.; Mitsumoto, H. Clinical perspective on oxidative stress in sporadic amyotrophic lateral sclerosis. *Free Radic. Biol. Med.,* **2013**, *65*, 509-527.
http://dx.doi.org/10.1016/j.freeradbiomed.2013.06.029 PMID: 23797033

[145] Yeo, W.S.; Kim, Y.J.; Kabir, M.H.; Kang, J.W.; Ahsan-Ul-Bari, M.; Kim, K.P. Mass spectrometric analysis of protein tyrosine nitration in aging and neurodegenerative diseases. *Mass Spectrom. Rev.,* **2015**, *34*(2), 166-183.
http://dx.doi.org/10.1002/mas.21429 PMID: 24889964

[146] Abe, K.; Pan, L.H.; Watanabe, M.; Kato, T.; Itoyama, Y. Induction of nitrotyrosine-like immunoreactivity in the lower motor neuron of

amyotrophic lateral sclerosis. *Neurosci. Lett.,* **1995**, *199*(2), 152-154.
http://dx.doi.org/10.1016/0304-3940(95)12039-7 PMID: 8584246

[147] Babu, G.N.; Kumar, A.; Chandra, R.; Puri, S.K.; Singh, R.L.; Kalita, J.; Misra, U.K. Oxidant-antioxidant imbalance in the erythrocytes of sporadic amyotrophic lateral sclerosis patients correlates with the progression of disease. *Neurochem. Int.,* **2008**, *52*(6), 1284-1289.
http://dx.doi.org/10.1016/j.neuint.2008.01.009 PMID: 18308427

[148] Kim, G.H.; Kim, J.E.; Rhie, S.J.; Yoon, S. The role of oxidative stress in neurodegenerative diseases. *Exp. Neurobiol.,* **2015**, *24*(4), 325-340.
http://dx.doi.org/10.5607/en.2015.24.4.325 PMID: 26713080

[149] Schulz, J.B.; Dehmer, T.; Schöls, L.; Mende, H.; Hardt, C.; Vorgerd, M.; Bürk, K.; Matson, W.; Dichgans, J.; Beal, M.F.; Bogdanov, M.B. Oxidative stress in patients with Friedreich ataxia. *Neurology,* **2000**, *55*(11), 1719-1721.
http://dx.doi.org/10.1212/WNL.55.11.1719 PMID: 11113228

[150] Emond, M.; Lepage, G.; Vanasse, M.; Pandolfo, M. Increased levels of plasma malondialdehyde in Friedreich ataxia. *Neurology,* **2000**, *55*(11), 1752-1753.
http://dx.doi.org/10.1212/WNL.55.11.1752 PMID: 11113241

[151] Halliwell, B. Oxidative stress and neurodegeneration: where are we now? *J. Neurochem.,* **2006**, *97*(6), 1634-1658.
http://dx.doi.org/10.1111/j.1471-4159.2006.03907.x PMID: 16805774

[152] Khatri, N.; Thakur, M.; Pareek, V.; Kumar, S.; Sharma, S.; Datusalia, A.K. Oxidative stress: major threat in traumatic brain injury. *CNS Neurol. Disord. Drug Targets,* **2018**, *17*(9), 689-695.
http://dx.doi.org/10.2174/1871527317666180627120501 PMID: 29952272

[153] Lin, M.T.; Beal, M.F. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. *Nature,* **2006**, *443*(7113), 787-795.
http://dx.doi.org/10.1038/nature05292 PMID: 17051205

[154] Jeggo, P.A.; Tesmer, J.; Chen, D.J. Genetic analysis of ionising radiation sensitive mutants of cultured mammalian cell lines. *Mutat. Res.,* **1991**, *254*(2), 125-133.
http://dx.doi.org/10.1016/0921-8777(91)90003-8 PMID: 2002809

[155] Cantoni, O.; Murray, D.; Meyn, R.E. Induction and repair of DNA single-strand breaks in EM9 mutant CHO cells treated with hydrogen peroxide. *Chem. Biol. Interact.,* **1987**, *63*(1), 29-38.
http://dx.doi.org/10.1016/0009-2797(87)90102-5 PMID: 3115605

[156] Narciso, L.; Parlanti, E.; Racaniello, M.; Simonelli, V.; Cardinale, A.; Merlo, D.; Dogliotti, E. The response to oxidative DNA damage in neurons: mechanisms and disease. *Neural Plast.,* **2016**, *2016*, 3619274.
http://dx.doi.org/10.1155/2016/3619274 PMID: 26942017

[157] Frappart, P.O.; McKinnon, P.J. Ataxia-telangiectasia and related diseases. *Neuromol. Med.,* **2006**, *8*(4), 495-511.
http://dx.doi.org/10.1385/NMM:8:4:495 PMID: 17028372

[158] Perlman, S.; Becker-Catania, S.; Gatti, R.A. Ataxia-telangiectasia: diagnosis and treatment. *Semin. Pediatr. Neurol.,* **2003**, *10*(3), 173-182.
http://dx.doi.org/10.1016/S1071-9091(03)00026-3 PMID: 14653405

[159] Sedgwick, R.P.; Boder, E. *Handbook of Clinical Neurology*; Vinken, P.; Bruyn, G.; Klawans, H., Eds.; Elsevier: New York, **1991**, pp. 347-423.

[160] Carney, J.P.; Maser, R.S.; Olivares, H.; Davis, E.M.; Le Beau, M.; Yates, J.R., III; Hays, L.; Morgan, W.F.; Petrini, J.H. The hMre11/hRad50 protein complex and Nijmegen breakage syndrome: linkage of double-strand break repair to the cellular DNA damage response. *Cell,* **1998**, *93*(3), 477-486.
http://dx.doi.org/10.1016/S0092-8674(00)81175-7 PMID: 9590181

[161] Stewart, G.S.; Maser, R.S.; Stankovic, T.; Bressan, D.A.; Kaplan, M.I.; Jaspers, N.G.; Raams, A.; Byrd, P.J.; Petrini, J.H.; Taylor, A.M. The DNA double-strand break repair gene hMRE11 is mutated in individuals with an ataxia-telangiectasia-like disorder. *Cell,* **1999**, *99*(6), 577-587.
http://dx.doi.org/10.1016/S0092-8674(00)81547-0 PMID: 10612394

[162] Taylor, A.M.; Groom, A.; Byrd, P.J. Ataxia-telangiectasia-like disorder (ATLD)-its clinical presentation and molecular basis. *DNA Repair (Amst.),* **2004**, *3*(8-9), 1219-1225.
http://dx.doi.org/10.1016/j.dnarep.2004.04.009 PMID: 15279810

[163] Cleaver, J.E. Cancer in xeroderma pigmentosum and related disorders of DNA repair. *Nat. Rev. Cancer,* **2005**, *5*(7), 564-573.
http://dx.doi.org/10.1038/nrc1652 PMID: 16069818

[164] Nouspikel, T. Nucleotide excision repair and neurological diseases. *DNA Repair (Amst.),* **2008**, *7*(7), 1155-1167.
http://dx.doi.org/10.1016/j.dnarep.2008.03.015 PMID: 18456575

[165] Compe, E.; Malerba, M.; Soler, L.; Marescaux, J.; Borrelli, E.; Egly, J.M. Neurological defects in trichothiodystrophy reveal a coactivator function of TFIIH. *Nat. Neurosci.,* **2007**, *10*(11), 1414-1422.
http://dx.doi.org/10.1038/nn1990 PMID: 17952069

[166] Kraemer, K.H.; Patronas, N.J.; Schiffmann, R.; Brooks, B.P.; Tamura, D.; DiGiovanna, J.J. Xeroderma pigmentosum, trichothiodystrophy and Cockayne syndrome: A complex genotype-phenotype relationship. *Neuroscience,* **2007**, *145*(4), 1388-1396.
http://dx.doi.org/10.1016/j.neuroscience.2006.12.020 PMID: 17276014

[167] Kulkarni, S.R.; Ravindra, K.P.; Rataboli, P. Levels of plasma testosterone, antioxidants and oxidative stress in alcoholic patients attending de-addiction centre. *Biol. Med. (Aligarh),* **2009**, *1*(4), 11-20.

[168] Cardoso, S.M.; Santana, I.; Swerdlow, R.H.; Oliveira, C.R. Mitochondria dysfunction of Alzheimer's disease cybrids enhances Abeta toxicity. *J. Neurochem.,* **2004**, *89*(6), 1417-1426.
http://dx.doi.org/10.1111/j.1471-4159.2004.02438.x PMID: 15189344

[169] Guzik, B.; Sagan, A.; Ludew, D.; Mrowiecki, W.; Chwała, M.; Bujak-Gizycka, B.; Filip, G.; Grudzien, G.; Kapelak, B.; Zmudka, K.; Mrowiecki, T.; Sadowski, J.; Korbut, R.; Guzik, T.J. Mechanisms of oxidative stress in human aortic aneurysms--association with clinical risk factors for atherosclerosis and disease severity. *Int. J. Cardiol.,* **2013**, *168*(3), 2389-2396.
http://dx.doi.org/10.1016/j.ijcard.2013.01.278 PMID: 23506637

[170] Suk-Yee, Li.; Zhong-Jie, Fu.; Huan, Ma.; Wai-Chi, Jang. Effect of lutein on retinal neurons and oxidative stress in a model of acute retinal ischemia/reperfusion. *Invest. Ophthalmol. Vis. Sci.,* **2009**, *50*, 2.

[171] Golechha, M.; Bhatia, J.; Arya, D.S. Studies on effects of Emblica officinalis (Amla) on oxidative stress and cholinergic function in scopolamine induced amnesia in mice. *J. Environ. Biol.,* **2012**, *33*(1), 95-100.
PMID: 23033650

[172] Furukawa, Y.; Fu, R.; Deng, H.X.; Siddique, T.; O'Halloran, T.V. Disulfide cross-linked protein represents a significant fraction of ALS-associated Cu, Zn-superoxide dismutase aggregates in spinal cords of model mice. *Proc. Natl. Acad. Sci. USA,* **2006**, *103*(18), 7148-7153.
http://dx.doi.org/10.1073/pnas.0602048103 PMID: 16636274

[173] Cemil, B.; Kurt, G.; Aydın, C.; Akyurek, N.; Erdogan, B.; Ceviker, N. Evaluation of tenoxicam on prevention of arachnoiditis in rat laminectomy model. *Eur. Spine J.,* **2011**, *20*(8), 1255-1258.
http://dx.doi.org/10.1007/s00586-011-1706-9 PMID: 21327813

[174] Castejón, O.J.; Arismendi, G.J. Nerve cell nuclear and nucleolar abnormalities in the human oedematous cerebral cortex. An electron microscopic study using cortical biopsies. *J. Submicrosc. Cytol. Pathol.,* **2004**, *36*(3-4), 273-283.
PMID: 15906602

[175] Parellada, M.; Moreno, C.; Mac-Dowell, K.; Leza, J.C.; Giraldez, M.; Bailón, C.; Castro, C.; Miranda-Azpiazu, P.; Fraguas, D.; Arango, C. Plasma antioxidant capacity is reduced in Asperger syndrome. *J. Psychiatr. Res.,* **2012**, *46*(3), 394-401.
http://dx.doi.org/10.1016/j.jpsychires.2011.10.004 PMID: 22225920

[176] Cotticelli, M.G.; Crabbe, A.M.; Wilson, R.B.; Shchepinov, M.S. Insights into the role of oxidative stress in the pathology of Friedreich ataxia using peroxidation resistant polyunsaturated fatty acids. *Redox Biol.,* **2013**, *1*(1), 398-404.
http://dx.doi.org/10.1016/j.redox.2013.06.004 PMID: 25499576

[177] Zhan, H.; Suzuki, T.; Aizawa, K.; Miyagawa, K.; Nagai, R. Ataxia telangiectasia mutated (ATM)-mediated DNA damage response in oxidative stress-induced vascular endothelial cell senescence. *J. Biol. Chem.,* **2010**, *285*(38), 29662-29670. http://dx.doi.org/10.1074/jbc.M110.125138 PMID: 20639198

[178] Ceylan, M.F.; Sener, S.; Bayraktar, A.C.; Kavutcu, M. Changes in oxidative stress and cellular immunity serum markers in attention-deficit/hyperactivity disorder. *Psychiatry Clin. Neurosci.,* **2012**, *66*(3), 220-226. http://dx.doi.org/10.1111/j.1440-1819.2012.02330.x PMID: 22443244

[179] Chauhan, A.; Chauhan, V.; Brown, W.T.; Cohen, I. Oxidative stress in autism: increased lipid peroxidation and reduced serum levels of ceruloplasmin and transferrin-the antioxidant proteins. *Life Sci.,* **2004**, *75*(21), 2539-2549. http://dx.doi.org/10.1016/j.lfs.2004.04.038 PMID: 15363659

[180] Andreazza, A.C.; Shao, L.; Wang, J.F.; Young, L.T. Mitochondrial complex I activity and oxidative damage to mitochondrial proteins in the prefrontal cortex of patients with bipolar disorder. *Arch. Gen. Psychiatry,* **2010**, *67*(4), 360-368. http://dx.doi.org/10.1001/archgenpsychiatry.2010.22 PMID: 20368511

[181] Cheng, X.; Liu, F.L.; Zhang, J.; Wang, L.L.; Li, F.L.; Liu, S.; Zhou, L.H. EGb761 protects motoneurons against avulsion-induced oxidative stress in rats. *J. Brachial Plex. Peripher. Nerve Inj.,* **2010**, *5*, 12. PMID: 20497551

[182] Chen, H.; Song, Y.S.; Chan, P.H. Inhibition of NADPH oxidase is neuroprotective after ischemia-reperfusion. *J. Cereb. Blood Flow Metab.,* **2009**, *29*(7), 1262-1272. http://dx.doi.org/10.1038/jcbfm.2009.47 PMID: 19417757

[183] Rajaraman, P.; Hutchinson, A.; Rothman, N.; Black, P.M.; Fine, H.A.; Loeffler, J.S.; Selker, R.G.; Shapiro, W.R.; Linet, M.S.; Inskip, P.D. Oxidative response gene polymorphisms and risk of adult brain tumors. *Neuro-oncol.,* **2008**, *10*(5), 709-715. http://dx.doi.org/10.1215/15228517-2008-037 PMID: 18682580

[184] Pederzolli, C.D.; Mescka, C.P.; Scapin, F.; Rockenbach, F.J.; Sgaravatti, A.M.; Sgarbi, M.B. N-acetylaspartic acid promotes oxidative stress in cerebral cortex of rats. *Int. J. Dev. Neurosci.,* **2007**, *25*(5), 317-324.

[185] Capgras, M.S.T. Syndrome and its relationship to neurodegenerative disease. *Arch. Neurol.,* **2007**, *64*(12), 1762-1766. PMID: 18071040

[186] Kim, J.K.; Koh, Y.D.; Kim, J.S.; Hann, H.J.; Kim, M.J.J. Oxidative stress in subsynovial connective tissue of idiopathic carpal tunnel syndrome. *Orthop. Res.,* **2010**, *28*(11), 1463-1468. http://dx.doi.org/10.1002/jor.21163 PMID: 20872582

[187] Eisenberg, E.; Shtahl, S.; Geller, R.; Reznick, A.Z.; Sharf, O.; Ravbinovich, M.; Erenreich, A.; Nagler, R.M. Serum and salivary oxidative analysis in complex regional pain syndrome. *Pain,* **2008**, *138*(1), 226-232. http://dx.doi.org/10.1016/j.pain.2008.04.019 PMID: 18539395

[188] Meeus, M.; Nijs, J.; Hermans, L.; Goubert, D.; Calders, P. The role of mitochondrial dysfunctions due to oxidative and nitrosative stress in the chronic pain or chronic fatigue syndromes and fibromyalgia patients: peripheral and central mechanisms as therapeutic targets? *Expert Opin. Ther. Targets,* **2013**, *17*(9), 1081-1089. http://dx.doi.org/10.1517/14728222.2013.818657 PMID: 23834645

[189] Vallurupalli, S.; Huesmann, G.; Gregory, J.; Jakoby, M.G., IV Levofloxacin-associated hypoglycaemia complicated by pontine myelinolysis and quadriplegia. *Diabet. Med.,* **2008**, *25*(7), 856-859. http://dx.doi.org/10.1111/j.1464-5491.2008.02465.x PMID: 18644072

[190] Witherspoon, J.W.; Meilleur, K.G. Review of RyR1 pathway and associated pathomechanisms. *Acta Neuropathol Commun.,* **2016**, *4*(1), 121.

[191] Starke, R.M.; Chalouhi, N.; Ali, M.S.; Jabbour, P.M.; Tjoumakaris, S.I.; Gonzalez, L.F.; Rosenwasser, R.H.; Koch, W.J.; Dumont, A.S. The role of oxidative stress in cerebral aneurysm formation and rupture. *Curr. Neurovasc. Res.,* **2013**, *10*(3), 247-255. http://dx.doi.org/10.2174/15672026113109990003 PMID: 23713738

[192] Aliev, J.L.; Puchowicz, M.; Siedlak, S.L.; Obrenovich, M.E.; Shenk, J.C.; Smith, M.A. Does the oxidative stress and cerebral atherosclerosis initiate brain hypoperfusion and the development of alzheimer disease? *Atheroscler. Suppl.,* **2008**, *9*(1), 154. http://dx.doi.org/10.1016/S1567-5688(08)70622-6

[193] Bleich, S.; Spilker, K.; Kurth, C.; Degner, D.; Quintela-Schneider, M.; Javaheripour, K.; Rüther, E.; Kornhuber, J.; Wiltfang, J. Oxidative stress and an altered methionine metabolism in alcoholism. *Neurosci. Lett.,* **2000**, *293*(3), 171-174. http://dx.doi.org/10.1016/S0304-3940(00)01505-6 PMID: 11036188

[194] Formichi, P.; Radi, E.; Battisti, C.; Di Maio, G.; Tarquini, E.; Leonini, A.; Di Stefano, A.; Dotti, M.T.; Federico, A. Apoptosis in CADASIL: An *in vitro* study of lymphocytes and fibroblasts from a cohort of Italian patients. *J. Cell. Physiol.,* **2009**, *219*(2), 494-502. http://dx.doi.org/10.1002/jcp.21695 PMID: 19180562

[195] Schoendorfer, N.C.; Vitetta, L.; Sharp, N.; DiGeronimo, M.; Wilson, G.; Coombes, J.S.; Boyd, R.; Davies, P.S. Micronutrient, antioxidant, and oxidative stress status in children with severe cerebral palsy. *JPEN J. Parenter. Enteral Nutr.,* **2013**, *37*(1), 97-101. http://dx.doi.org/10.1177/0148607112447200 PMID: 22610980

[196] Quinn, M.T.; Schepetkin, I.A. Role of NADPH oxidase in formation and function of multinucleated giant cells. *J. Innate Immun.,* **2009**, *1*(6), 509-526. http://dx.doi.org/10.1159/000228158 PMID: 20375608

[197] Niemann, A.; Huber, N.; Wagner, K.M.; Somandin, C.; Horn, M.; Lebrun-Julien, F.; Angst, B.; Pereira, J.A.; Halfter, H.; Welzl, H.; Feltri, M.L.; Wrabetz, L.; Young, P.; Wessig, C.; Toyka, K.V.; Suter, U. The Gdap1 knockout mouse mechanistically links redox control to Charcot-Marie-Tooth disease. *Brain,* **2014**, *137*(Pt 3), 668-682. http://dx.doi.org/10.1093/brain/awt371 PMID: 24480485

[198] Andrea, C.; Giuseppe, M.; Paolina, S.; Federico, C.; Paolo, C.; Cristina, C.; Antonio, A. NADPH oxidases (NOX) enzymes induced oxidative stress in CIDP patients (P1.070). *Neurology,* **2014**, *82*(10), P1.070.

[199] Nwankow, E.I.; Francesco, A.; Lorenzo, D.C.M.; Alessandra, P.; Laura, B.; Carla, G.; Seyed, K.T. thioctic acid enantiomers prevent central nervous system changes occurring in a model of compressive neuropathy. *Ital. J. Anat. Embryol.,* **2011**, *116*(1), 4.

[200] Vázquez, M.C.; Balboa, E.; Alvarez, A.R.; Zanlungo, S. Oxidative stress: A pathogenic mechanism for Niemann-Pick type C disease. *Oxid. Med. Cell. Longev.,* **2012**, *2012*, 205713.

[201] Borkowski, A.; Younge, B.R.; Szweda, L.; Mock, B.; Björnsson, J.; Moeller, K.; Goronzy, J.J.; Weyand, C.M. Reactive nitrogen intermediates in giant cell arteritis: selective nitration of neocapillaries. *Am. J. Pathol.,* **2002**, *161*(1), 115-123. http://dx.doi.org/10.1016/S0002-9440(10)64163-6 PMID: 12107096

[202] Bleich, S.; Kropp, S.; Degner, D.; Zerr, I.; Pilz, J.; Gleiter, C.H.; Otto, M.; Rüther, E.; Kretzschmar, H.A.; Wiltfang, J.; Kornhuber, J.; Poser, S. Creutzfeldt-Jakob disease and oxidative stress. *Acta Neurol. Scand.,* **2000**, *101*(5), 332-334. http://dx.doi.org/10.1034/j.1600-0404.2000.9s290a.x PMID: 10987323

[203] Karamouzis, I.; Berardelli, R.; D'Angelo, V.; Fussotto, B.; Zichi, C.; Giordano, R.; Settanni, F.; Maccario, M.; Ghigo, E.; Arvat, E. Enhanced oxidative stress and platelet activation in patients with Cushing's syndrome. *Clin. Endocrinol. (Oxf.),* **2015**, *82*(4), 517-524. http://dx.doi.org/10.1111/cen.12524 PMID: 24923553

[204] Weis, M.; Kledal, T.N.; Lin, K.Y.; Panchal, S.N.; Gao, S.Z.; Valantine, H.A.; Mocarski, E.S.; Cooke, J.P. Cytomegalovirus infection impairs the nitric oxide synthase pathway: role of asymmetric dimethylarginine in transplant arteriosclerosis. *Circulation,* **2004**, *109*(4), 500-505. http://dx.doi.org/10.1161/01.CIR.0000109692.16004.AF PMID: 14732750

[205] Caksen, H.; Ozkan, M.; Cemek, M.; Cemek, F. Oxidant and antioxidant status in children with subacute sclerosing panencephalitis. *Child Neurol.,* **2014**, *29*(11), 1448-1452. http://dx.doi.org/10.1177/0883073813494475 PMID: 23872915

[206] Mao, P. Oxidative stress and its clinical applications in dementia. *J. Neurodegener. Dis.,* **2013**, *2013*, 319898. http://dx.doi.org/10.1155/2013/319898 PMID: 26316986

[207] Baechler, E.C.; Bauer, J.W.; Slattery, C.A.; Ortmann, W.A.; Espe, K.J.; Novitzke, J.; Ytterberg, S.R.; Gregersen, P.K.; Behrens, T.W.; Reed, A.M. An interferon signature in the peripheral blood of dermatomyositis patients is associated with disease activity. *Mol. Med.,* **2007**, *13*(1-2), 59-68. http://dx.doi.org/10.2119/2006-00085.Baechler PMID: 17515957

[208] Mohit, C.; Kirti, K.; Joanna, T.; Ruhul, C.; Eva, M.K.; Rakesh, C. Oxidative stress in diabetic neuropathy: source of reactive oxygen species. *Endocrinol. stud.,* **2012**, *2*(2), 6.

[209] Cruz-Dominguez, M.D.P.; Olga, M.C.; Daniel, M. Plasma oxidative stress in patients with diffuse systemic sclerosis *versus* control group. *Arthritis Rheum.,* **2009**, *60*(10), 1715.

[210] Amparo, G.; José, L.G-G.; Laura, A.; Nuria, T.; Pilar, A.; Francisco, D.; Federico, V.P. Decreased cell proliferation and higher oxidative stress in fibroblasts from down syndrome fetuses. Preliminary study. *Biochim. Biophys. Acta (BBA) Mol. Basis Dis.,* **2014**, *1842*(1), 116-125. http://dx.doi.org/10.1016/j.bbadis.2013.10.014

[211] Pal, R.; Palmieri, M.; Loehr, J.A.; Li, S.; Abo-Zahrah, R.; Monroe, T.O.; Thakur, P.B.; Sardiello, M.; Rodney, G.G. Src-dependent impairment of autophagy by oxidative stress in a mouse model of Duchenne muscular dystrophy. *Nat. Commun.,* **2014**, *5*, 4425. http://dx.doi.org/10.1038/ncomms5425 PMID: 25028121

[212] Xia, H.; Suda, S.; Bindom, S.; Feng, Y.; Gurley, S.B.; Seth, D.; Navar, L.G.; Lazartigues, E. ACE2-mediated reduction of oxidative stress in the central nervous system is associated with improvement of autonomic function. *PLoS One,* **2011**, *6*(7), e22682. http://dx.doi.org/10.1371/journal.pone.0022682 PMID: 21818366

[213] Burger, M.E.; Alves, A.; Callegari, L.; Athayde, F.R.; Nogueira, C.W.; Zeni, G.; Rocha, J.B. Ebselen attenuates reserpine-induced orofacial dyskinesia and oxidative stress in rat striatum. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2003**, *27*(1), 135-140. http://dx.doi.org/10.1016/S0278-5846(02)00344-5 PMID: 12551736

[214] Kuner, R.; Teismann, P.; Trutzel, A.; Naim, J.; Richter, A.; Schmidt, N.; von Ahsen, O.; Bach, A.; Ferger, B.; Schneider, A. TorsinA protects against oxidative stress in COS-1 and PC12 cells. *Neurosci. Lett.,* **2003**, *350*(3), 153-156. http://dx.doi.org/10.1016/S0304-3940(03)00904-2 PMID: 14550917

[215] Miyata, R.; Tanuma, N.; Hayashi, M.; Imamura, T.; Takanashi, J.; Nagata, R.; Okumura, A.; Kashii, H.; Tomita, S.; Kumada, S.; Kubota, M. Oxidative stress in patients with clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS). *Brain Dev.,* **2012**, *34*(2), 124-127. http://dx.doi.org/10.1016/j.braindev.2011.04.004 PMID: 21576007

[216] Sudarsanam, A.; Ardern-Holmes, S.L. Sturge-Weber syndrome: from the past to the present. *Eur. J. Paediatr. Neurol.,* **2014**, *18*(3), 257-266. http://dx.doi.org/10.1016/j.ejpn.2013.10.003 PMID: 24275166

[217] Mareš, J.; Stopka, P.; Nohejlová, K.; Rokyta, R. Oxidative stress induced by epileptic seizure and its attenuation by melatonin. *Physiol. Res.,* **2013**, *62*(1)(Suppl. 1), S67-S74. http://dx.doi.org/10.33549/physiolres.932576 PMID: 24329705

[218] Müller, K.B.; Galdieri, L.C.; Pereira, V.G.; Martins, A.M.; D'Almeida, V. Evaluation of oxidative stress markers and cardiovascular risk factors in fabry disease patients. *Genet. Mol. Biol.,* **2012**, *35*(2), 418-423. http://dx.doi.org/10.1590/S1415-47572012005000031 PMID: 22888289

[219] Huang, Y.J.; Zhou, Z.W.; Xu, M.; Ma, Q.W.; Yan, J.B.; Wang, J.Y.; Zhang, Q.Q.; Huang, M.; Bao, L. Alteration of gene expression profiling including GPR174 and GNG2 is associated with vasovagal syncope. *Pediatr. Cardiol.,* **2015**, *36*(3), 475-480. http://dx.doi.org/10.1007/s00246-014-1036-x PMID: 25367286

[220] Atorino, L.; Silvestri, L.; Koppen, M.; Cassina, L.; Ballabio, A.; Marconi, R.; Langer, T.; Casari, G. Loss of m-AAA protease in mitochondria causes complex I deficiency and increased sensitivity to oxidative stress in hereditary spastic paraplegia. *J. Cell Biol.,* **2003**, *163*(4), 777-787. http://dx.doi.org/10.1083/jcb.200304112 PMID: 14623864

[221] Abuhandan, M.; Calik, M.; Taskin, A.; Yetkin, I.; Selek, S.; Iscan, A. The oxidative and antioxidative status of simple febrile seizure patients. *J. Pak. Med. Assoc.,* **2013**, *63*(5), 594-597. PMID: 23757987

[222] Ghabaee, M.; Jabedari, B.; Al-E-Eshagh, N.; Ghaffarpour, M.; Asadi, F. Serum and cerebrospinal fluid antioxidant activity and lipid peroxidation in Guillain-Barre syndrome and multiple sclerosis patients. *Int. J. Neurosci.,* **2010**, *120*(4), 301-304. http://dx.doi.org/10.3109/00207451003695690 PMID: 20374079

[223] Brocardo, P.S.; Boehme, F.; Patten, A.; Cox, A.; Gil-Mohapel, J.; Christie, B.R. Anxiety- and depression-like behaviors are accompanied by an increase in oxidative stress in a rat model of fetal alcohol spectrum disorders: Protective effects of voluntary physical exercise. *Neuropharmacology,* **2012**, *62*(4), 1607-1618. http://dx.doi.org/10.1016/j.neuropharm.2011.10.006 PMID: 22019722

[224] el Bekay, R.; Romero-Zerbo, Y.; Decara, J.; Sanchez-Salido, L.; Del Arco-Herrera, I.; Rodríguez-de Fonseca, F.; de Diego-Otero, Y. Enhanced markers of oxidative stress, altered antioxidants and NADPH-oxidase activation in brains from Fragile X mental retardation 1-deficient mice, a pathological model for Fragile X syndrome. *Eur. J. Neurosci.,* **2007**, *26*(11), 3169-3180. http://dx.doi.org/10.1111/j.1460-9568.2007.05939.x PMID: 18005058

[225] Ross-Inta, C.; Omanska-Klusek, A.; Wong, S.; Barrow, C.; Garcia-Arocena, D.; Iwahashi, C.; Berry-Kravis, E.; Hagerman, R.J.; Hagerman, P.J.; Giulivi, C. Evidence of mitochondrial dysfunction in fragile X-associated tremor/ataxia syndrome. *Biochem. J.,* **2010**, *429*(3), 545-552. http://dx.doi.org/10.1042/BJ20091960 PMID: 20513237

[226] Moraitou, M.; Dimitriou, E.; Dekker, N.; Monopolis, I.; Aerts, J.; Michelakakis, H. Gaucher disease: plasmalogen levels in relation to primary lipid abnormalities and oxidative stress. *Blood Cells Mol. Dis.,* **2014**, *53*(1-2), 30-33. http://dx.doi.org/10.1016/j.bcmd.2014.01.005 PMID: 24521822

[227] Isidro, F.; Margarita, C.; Rosa, B.; Maria, J.R. Recio, R.M. San Segundo. Gerstmann-Straüssler-Scheinker PRNP P102L-129V mutation. *Transl. Neurosci.,* **2011**, *2*(1), 23-32.

[228] Lee, Y.L.; Liu, C.E.; Cho, W.L.; Kuo, C.L.; Cheng, W.L.; Huang, C.S.; Liu, C.S. Presence of cytomegalovirus DNA in leucocytes is associated with increased oxidative stress and subclinical atherosclerosis in healthy adults. *Biomarkers,* **2014**, *19*(2), 109-113. http://dx.doi.org/10.3109/1354750X.2013.877967 PMID: 24446591

[229] Hawkins-Salsbury, J.A.; Qin, E.Y.; Reddy, A.S.; Vogler, C.A.; Sands, M.S. Oxidative stress as a therapeutic target in globoid cell leukodystrophy. *Exp. Neurol.,* **2012**, *237*(2), 444-452. http://dx.doi.org/10.1016/j.expneurol.2012.07.013 PMID: 22849820

[230] Takano, T.; Akahori, S.; Takeuchi, Y.; Ohno, M. Neuronal apoptosis and gray matter heterotopia in microcephaly produced by cytosine arabinoside in mice. *Brain Res.,* **2006**, *1089*(1), 55-66. http://dx.doi.org/10.1016/j.brainres.2006.03.047 PMID: 16638609

[231] Sakai, T.; Inoue, A.; Koh, C.S.; Ikeda, S. [A study of free radical defense and oxidative stress in the sera of patients with neuroimmunological disorders]. *Arerugi,* **2000**, *49*(1), 12-18. PMID: 10707474

[232] Kaya, M.C.; Bez, Y.; Karababa, I.F.; Emhan, A.; Aksoy, N.; Bulut, M.; Guneş, M.; Atli, A.; Selek, S. Decreased serum sulphydryl levels as a sign of increased oxidative stress in generalized anxiety disorder. *Psychiatry Investig.,* **2013**, *10*(3), 281-285. http://dx.doi.org/10.4306/pi.2013.10.3.281 PMID: 24302952

[233] Nishiyama, K.; Murayama, S.; Nishimura, Y.; Asayama, K.; Kanazawa, I. Superoxide dismutase-like immunoreactivity in spheroids in Hallervorden-Spatz disease. *Acta Neuropathol.,* **1997**, *93*(1), 19-23. http://dx.doi.org/10.1007/s004010050578 PMID: 9006653

[234] Shohami, E.; Beit-Yannai, E.; Horowitz, M.; Kohen, R. Oxidative stress in closed-head injury: brain antioxidant capacity as an indica-

tor of functional outcome. *J. Cereb. Blood Flow Metab.,* **1997**, *17*(10), 1007-1019.
http://dx.doi.org/10.1097/00004647-199710000-00002 PMID: 9346425

[235] Vurucu, S.; Karaoglu, A.; Paksu, M.S.; Yesilyurt, O.; Oz, O.; Unay, B.; Akin, R. Relationship between oxidative stress and chronic daily headache in children. *Hum. Exp. Toxicol.,* **2013**, *32*(2), 113-119.
http://dx.doi.org/10.1177/0960327112459204 PMID: 23315275

[236] Aoto, K.; Shikata, Y.; Higashiyama, D.; Shiota, K.; Motoyama, J. Fetal ethanol exposure activates protein kinase A and impairs Shh expression in prechordal mesendoderm cells in the pathogenesis of holoprosencephaly. *Birth Defects Res. A Clin. Mol. Teratol.,* **2008**, *82*(4), 224-231.
http://dx.doi.org/10.1002/bdra.20447 PMID: 18338389

[237] Chen, C.M. Mitochondrial dysfunction, metabolic deficits, and increased oxidative stress in Huntington's disease. *Chang Gung Med. J.,* **2011**, *34*(2), 135-152.
PMID: 21539755

[238] Socci, D.J.; Bjugstad, K.B.; Jones, H.C.; Pattisapu, J.V.; Arendash, G.W. Evidence that oxidative stress is associated with the pathophysiology of inherited hydrocephalus in the H-Tx rat model. *Exp. Neurol.,* **1999**, *155*(1), 109-117.
http://dx.doi.org/10.1006/exnr.1998.6969 PMID: 9918710

[239] Tomiyama, A.J.; Epel, E.S.; McClatchey, T.M.; Poelke, G.; Kemeny, M.E.; McCoy, S.K.; Daubenmier, J. Associations of weight stigma with cortisol and oxidative stress independent of adiposity. *Health Psychol.,* **2014**, *33*(8), 862-867.
http://dx.doi.org/10.1037/hea0000107 PMID: 25068456

[240] Patterson, A.J.; Xiao, D.; Xiong, F.; Dixon, B.; Zhang, L. Hypoxia-derived oxidative stress mediates epigenetic repression of PKCε gene in foetal rat hearts. *Cardiovasc. Res.,* **2012**, *93*(2), 302-310.
http://dx.doi.org/10.1093/cvr/cvr322 PMID: 22139554

[241] Askanas, V.; Engel, W.K. Inclusion-body myositis: A myodegenerative conformational disorder associated with Abeta, protein misfolding, and proteasome inhibition. *Neurology,* **2006**, *66*(2), S39-S48.
http://dx.doi.org/10.1212/01.wnl.0000192128.13875.1e PMID: 16432144

[242] Ohkawa, N.; Okumura, A.; Miyata, R.; Tanuma, N.; Hayashi, M.; Sato, H.; Shimizu, T. Cerebrospinal fluid oxidative stress marker levels and cytokine concentrations in a neonate with incontinentia pigmenti. *Pediatr. Neurol.,* **2014**, *51*(5), 737-740.
http://dx.doi.org/10.1016/j.pediatrneurol.2014.07.023 PMID: 25238668

[243] Dalazen, G.R.; Terra, M.; Jacques, C.E.; Coelho, J.G.; Freitas, R.; Mazzola, P.N.; Dutra-Filho, C.S. Pipecolic acid induces oxidative stress *in vitro* in cerebral cortex of young rats and the protective role of lipoic acid. *Metab. Brain Dis.,* **2014**, *29*(1), 175-183.
http://dx.doi.org/10.1007/s11011-013-9466-3 PMID: 24338030

[244] Galanopoulou, A.S.; Moshé, S.L. Pathogenesis and new candidate treatments for infantile spasms and early life epileptic encephalopathies: A view from preclinical studies. *Neurobiol. Dis.,* **2015**, *79*, 135-149.
http://dx.doi.org/10.1016/j.nbd.2015.04.015 PMID: 25968935

[245] Renjini, R.N.; Narayanappa, G.; Sudha, M.; Balaraju, S.; Rajeswarababu, M. Mitochondrial alterations and oxidative stress in an acute transient mouse model of muscle degeneration: Implications for muscular dystrophy and related muscle pathologies. *J. Biochem., 289*(1), 485-509.

[246] Hall, S.R.; Wang, L.; Milne, B.; Hong, M. Left ventricular dysfunction after acute intracranial hypertension is associated with increased hydroxyl free radical production, cardiac ryanodine hyperphosphorylation, and troponin I degradation. *J. Heart Lung Transplant.,* **2005**, *24*(10), 1639-1649.
http://dx.doi.org/10.1016/j.healun.2004.11.004 PMID: 16210142

[247] Mubaidin, A.; Roberts, E.; Hampshire, D.; Dehyyat, M.; Shurbaji, A.; Mubaidien, M.; Jamil, A.; Al-Din, A.; Kurdi, A.; Woods, C.G. Karak syndrome: A novel degenerative disorder of the basal ganglia and cerebellum. *J. Med. Genet.,* **2003**, *40*(7), 543-546.
http://dx.doi.org/10.1136/jmg.40.7.543 PMID: 12843330

[248] Holloman, C.M.; Wolfe, L.A.; Gahl, W.A.; Boerkoel, C.F. Kearns-Sayre syndrome presenting as isolated growth failure. *BMJ Case Rep.,* **2013**, *2013*, 7272.
http://dx.doi.org/10.1136/bcr-2012-007272 PMID: 23420719

[249] Romá-Mateo, C.; Aguado, C.; García-Giménez, J.L.; Ibáñez-Cabellos, J.S.; Seco-Cervera, M.; Pallardó, F.V.; Knecht, E.; Sanz, P. Increased oxidative stress and impaired antioxidant response in Lafora disease. *Mol. Neurobiol.,* **2015**, *51*(3), 932-946.
http://dx.doi.org/10.1007/s12035-014-8747-0 PMID: 24838580

[250] Aiguo Wu, ; Zhe Ying, ; Gomez-Pinilla, F. Vitamin E protects against oxidative damage and learning disability after mild traumatic brain injury in rats. *Neurorehabil. Neural Repair,* **2010**, *24*(3), 290-298.
http://dx.doi.org/10.1177/1545968309348318 PMID: 19841436

[251] Baertling, F.; Rodenburg, R.J.; Schaper, J.; Smeitink, J.A.; Koopman, W.J.; Mayatepek, E.; Morava, E.; Distelmaier, F. A guide to diagnosis and treatment of Leigh syndrome. *J. Neurol. Neurosurg. Psychiatry,* **2014**, *85*(3), 257-265.
http://dx.doi.org/10.1136/jnnp-2012-304426 PMID: 23772060

[252] Masaharu, H.; Naoyuki, T.; Rie, M. The Involvement of Oxidative Stress in Epilepsy. *Department of Clinical Neuropathology*; pp. 305-318.

[253] Visser, J.E.; Smith, D.W.; Moy, S.S.; Breese, G.R.; Friedmann, T.; Rothstein, J.D.; Jinnah, H.A. Oxidative stress and dopamine deficiency in a genetic mouse model of Lesch-Nyhan disease. *Brain Res. Dev. Brain Res.,* **2002**, *133*(2), 127-139.
http://dx.doi.org/10.1016/S0165-3806(02)00280-8 PMID: 11882343

[254] Powers, J.M.; Pei, Z.; Heinzer, A.K.; Deering, R.; Moser, A.B.; Moser, H.W.; Watkins, P.A.; Smith, K.D. Adreno-leukodystrophy: oxidative stress of mice and men. *J. Neuropathol. Exp. Neurol.,* **2005**, *64*(12), 1067-1079.
http://dx.doi.org/10.1097/01.jnen.0000190064.28559.a4 PMID: 16319717

[255] Tabet, N.; Walker, Z.; Mantle, D.; Costa, D.; Orrell, M. *In vivo* dopamine pre-synaptic receptors and antioxidant activities in patients with Alzheimer's disease, dementia with Lewy bodies and in controls. A preliminary report. *Dement. Geriatr. Cogn. Disord.,* **2003**, *16*(1), 46-51.
http://dx.doi.org/10.1159/000069993 PMID: 12714800

[256] Hou, G.; Lu, H.; Chen, M.; Yao, H.; Zhao, H. Oxidative stress participates in age-related changes in rat lumbar intervertebral discs. *Arch. Gerontol. Geriatr.,* **2014**, *59*(3), 665-669.
http://dx.doi.org/10.1016/j.archger.2014.07.002 PMID: 25081833

[257] Pacheco, L.S.; da Silveira, A.F.; Trott, A.; Houenou, L.J.; Algarve, T.D.; Belló, C.; Lenz, A.F.; Mânica-Cattani, M.F.; da Cruz, I.B. Association between Machado-Joseph disease and oxidative stress biomarkers. *Mutat. Res. Genet. Toxicol. Environ. Mutagen.,* **2013**, *757*(2), 99-103.
http://dx.doi.org/10.1016/j.mrgentox.2013.06.023 PMID: 23994570

[258] Calabrese, V.; Cornelius, C.; Maiolino, L.; Luca, M.; Chiaramonte, R.; Toscano, M.A.; Serra, A. Oxidative stress, redox homeostasis and cellular stress response in Ménière's disease: role of vitagenes. *Neurochem. Res.,* **2010**, *35*(12), 2208-2217.
http://dx.doi.org/10.1007/s11064-010-0304-2 PMID: 21042850

[259] Barichello, T.; Generoso, J.S.; Simões, L.R.; Elias, S.G.; Quevedo, J. Role of oxidative stress in the pathophysiology of pneumococcal meningitis. *Oxid. Med. Cell. Longev.,* **2013**, *2013*, 371465.
http://dx.doi.org/10.1155/2013/371465 PMID: 23766853

[260] Rotilio, G.; Carrì, M.T.; Rossi, L.; Ciriolo, M.R. Copper-dependent oxidative stress and neurodegeneration. *IUBMB Life,* **2000**, *50*(4-5), 309-314.
http://dx.doi.org/10.1080/15216540051081074 PMID: 11327325

[261] Liu, B.; Chen, X.; Wang, Z.Q.; Tong, W.M. DNA damage and oxidative injury are associated with hypomyelination in the corpus callosum of newborn Nbn(CNS-del) mice. *J. Neurosci. Res.,* **2014**, *92*(2), 254-266.
http://dx.doi.org/10.1002/jnr.23313 PMID: 24272991

[262] Marilita, M.M.; Eirini, N.; Irini, P.C.; Constantinos, A.D. Age-related macular degeneration: Pathogenesis, geneticbackground, and the role of nutritional supplements. *J. Chem.,* **2014**, *2014*, 9.

[263] Bernecker, C.; Ragginer, C.; Fauler, G.; Horejsi, R.; Möller, R.; Zelzer, S.; Lechner, A.; Wallner-Blazek, M.; Weiss, S.; Fazekas, F.; Bahadori, B.; Truschnig-Wilders, M.; Gruber, H.J. Oxidative stress is associated with migraine and migraine-related metabolic risk in females. *Eur. J. Neurol.,* **2011**, *18*(10), 1233-1239. http://dx.doi.org/10.1111/j.1468-1331.2011.03414.x PMID: 21518147

[264] Dogonadze, S.I.; Ninua, N.G.; Gordeziani, M.G.; Kavlashvili, M.S.; Sanikidze, T.V. The role of oxidative stress in pathogenesis of GBS. *Georgian Med. News,* **2006**, *140*(140), 43-47. PMID: 17179587

[265] Jaspreet, K.; Sarika, A.; Bhawna, S.; Thakur, L.C.; Gambhir, J. Role of oxidative stress in pathophysiology of transient ischemic attack and stroke. *Int. J. Biol. Med. Res.,* **2011**, *2*(3), 611-615.

[266] Tritschler, H.J.; Packer, L.; Medori, R. Oxidative stress and mitochondrial dysfunction in neurodegeneration. *Biochem. Mol. Biol. Int.,* **1994**, *34*(1), 169-181. PMID: 7849618

[267] Cookson, M.R.; Shaw, P.J. Oxidative stress and motor neurone disease. *Brain Pathol.,* **1999**, *9*(1), 165-186. http://dx.doi.org/10.1111/j.1750-3639.1999.tb00217.x PMID: 9989458

[268] Stigger, F.; Lovatel, G.; Marques, M.; Bertoldi, K.; Moysés, F.; Elsner, V.; Siqueira, I.R.; Achaval, M.; Marcuzzo, S. Inflammatory response and oxidative stress in developing rat brain and its consequences on motor behavior following maternal administration of LPS and perinatal anoxia. *Int. J. Dev. Neurosci.,* **2013**, *31*(8), 820-827. http://dx.doi.org/10.1016/j.ijdevneu.2013.10.003 PMID: 24140242

[269] Filippon, L.; Vanzin, C.S.; Biancini, G.B.; Pereira, I.N.; Manfredini, V.; Sitta, A.; Peralba, Mdo, C.; Schwartz, I.V.; Giugliani, R.; Vargas, C.R. Oxidative stress in patients with mucopolysaccharidosis type II before and during enzyme replacement therapy. *Mol. Genet. Metab.,* **2011**, *103*(2), 121-127. http://dx.doi.org/10.1016/j.ymgme.2011.02.016 PMID: 21420339

[270] Huang, J.L.; Fu, S.T.; Jiang, Y.Y.; Cao, Y.B.; Guo, M.L.; Wang, Y.; Xu, Z. Protective effects of Nicotiflorin on reducing memory dysfunction, energy metabolism failure and oxidative stress in multi-infarct dementia model rats. *Pharmacol. Biochem. Behav.,* **2007**, *86*(4), 741-748. http://dx.doi.org/10.1016/j.pbb.2007.03.003 PMID: 17448528

[271] Jonathan, W.; Alastair, W.; Neil, S.; Kevin, K. Mechanisms of oxidative damage in multiple sclerosis and a cell therapy approach to treatment, review article. *Autoimmune Dis.,* **2011**, *2011*, 11.

[272] Stefanova, N.; Reindl, M.; Neumann, M.; Haass, C.; Poewe, W.; Kahle, P.J.; Wenning, G.K. Oxidative stress in transgenic mice with oligodendroglial α-synuclein overexpression replicates the characteristic neuropathology of multiple system atrophy. *Am. J. Pathol.,* **2005**, *166*(3), 869-876. http://dx.doi.org/10.1016/S0002-9440(10)62307-3 PMID: 15743798

[273] Terrill, J.R.; Radley-Crabb, H.G.; Iwasaki, T.; Lemckert, F.A.; Arthur, P.G.; Grounds, M.D. Oxidative stress and pathology in muscular dystrophies: focus on protein thiol oxidation and dysferlinopathies. *FEBS J.,* **2013**, *280*(17), 4149-4164. http://dx.doi.org/10.1111/febs.12142 PMID: 23332128

[274] Maes, M.; Kubera, M.; Uytterhoeven, M.; Vrydags, N.; Bosmans, E. Increased plasma peroxides as a marker of oxidative stress in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Med. Sci. Monit.,* **2011**, *17*(4), SC11-SC15. http://dx.doi.org/10.12659/MSM.881699 PMID: 21455120

[275] Fuhua, P.; Xuhui, D.; Zhiyang, Z.; Ying, J.; Yu, Y.; Feng, T.; Jia, L.; Lijia, G.; Xueqiang, H. Antioxidant status of bilirubin and uric acid in patients with *Myasthenia gravis*. *Neuroimmunomodulation,* **2012**, *19*(1), 43-49. http://dx.doi.org/10.1159/000327727 PMID: 22067621

[276] Lehtinen, M.K.; Tegelberg, S.; Schipper, H.; Su, H.; Zukor, H.; Manninen, O.; Kopra, O.; Joensuu, T.; Hakala, P.; Bonni, A.; Lehesjoki, A.E. Cystatin B deficiency sensitizes neurons to oxidative stress in progressive myoclonus epilepsy, EPM1. *J. Neurosci.,* **2009**, *29*(18), 5910-5915. http://dx.doi.org/10.1523/JNEUROSCI.0682-09.2009 PMID: 19420257

[277] Dowling, J.J.; Arbogast, S.; Hur, J.; Nelson, D.D.; McEvoy, A.; Waugh, T.; Marty, I.; Lunardi, J.; Brooks, S.V.; Kuwada, J.Y.; Ferreiro, A. Oxidative stress and successful antioxidant treatment in models of RYR1-related myopathy. *Brain,* **2012**, *135*(Pt 4), 1115-1127. http://dx.doi.org/10.1093/brain/aws036 PMID: 22418739

[278] Isil, G.G.; Birgul, E.C.; Tongabay, C.M.D.; Gül, E. The evaluation of oxidative stress and depresion levels in patients with inactive Behcet's disease. *Adv. Life Sci.,* **2014**, *4*(4), 207-212.

[279] Tong, J.J.; Schriner, S.E.; McCleary, D.; Day, B.J.; Wallace, D.C. Life extension through neurofibromin mitochondrial regulation and antioxidant therapy for neurofibromatosis-1 in Drosophila melanogaster. *Nat. Genet.,* **2007**, *39*(4), 476-485. http://dx.doi.org/10.1038/ng2004 PMID: 17369827

[280] Kamińska, T.; Szuster-Ciesielska, A.; Wysocka, A.; Marmurowska-Michałowska, H.; Dubas-Slemp, H.; Kandefer-Szerszeń, M. Serum cytokine level and production of reactive oxygen species (ROS) by blood neutrophils from a schizophrenic patient with hypersensitivity to neuroleptics. *Med. Sci. Monit.,* **2003**, *9*(7), CS71-CS75. PMID: 12883457

[281] Mollace, V.; Nottet, H.S.; Clayette, P.; Turco, M.C.; Muscoli, C.; Salvemini, D.; Perno, C.F. Oxidative stress and neuroAIDS: triggers, modulators and novel antioxidants. *Trends Neurosci.,* **2001**, *24*(7), 411-416. http://dx.doi.org/10.1016/S0166-2236(00)01819-1 PMID: 11410272

[282] Shah, D.; Mahajan, N.; Sah, S.; Nath, S.K.; Paudyal, B. Oxidative stress and its biomarkers in systemic lupus erythematosus. *J. Biomed. Sci.,* **2014**, *21*, 23. http://dx.doi.org/10.1186/1423-0127-21-23 PMID: 24636579

[283] Wang, S.Y.; Jin, W.N.; Wu, D. Mechanisms of juvenile neuronal ceroid lipofuscinosis (JNCL). *Yi Chuan,* **2009**, *31*(8), 779-784. http://dx.doi.org/10.3724/SP.J.1005.2009.00779 PMID: 19689937

[284] Aksenova, M.V.; Aksenov, M.Y.; Mactutus, C.F.; Booze, R.M. Cell culture models of oxidative stress and injury in the central nervous system. *Curr. Neurovasc. Res.,* **2005**, *2*(1), 73-89. http://dx.doi.org/10.2174/1567202052773463 PMID: 16181101

[285] Areti, A.; Yerra, V.G.; Naidu, V.; Kumar, A. Oxidative stress and nerve damage: role in chemotherapy induced peripheral neuropathy. *Redox Biol.,* **2014**, *2*, 289-295. http://dx.doi.org/10.1016/j.redox.2014.01.006 PMID: 24494204

[286] Matsushita, M.; Kumano-Go, T.; Suganuma, N.; Adachi, H.; Yamamura, S.; Morishima, H.; Shigedo, Y.; Mikami, A.; Takeda, M.; Sugita, Y. Anxiety, neuroticism and oxidative stress: cross-sectional study in non-smoking college students. *Psychiatry Clin. Neurosci.,* **2010**, *64*(4), 435-441. http://dx.doi.org/10.1111/j.1440-1819.2010.02109.x PMID: 20653910

[287] Fu, R.; Yanjanin, N.M.; Bianconi, S.; Pavan, W.J.; Porter, F.D. Oxidative stress in Niemann-Pick disease, type C. *Mol. Genet. Metab.,* **2010**, *101*(2-3), 214-218. http://dx.doi.org/10.1016/j.ymgme.2010.06.018 PMID: 20667755

[288] Yamada, S.; Won, D.J.; Yamada, S.M. Pathophysiology of tethered cord syndrome: correlation with symptomatology. *Neurosurg. Focus,* **2004**, *16*(2), E6. http://dx.doi.org/10.3171/foc.2004.16.2.7 PMID: 15209489

[289] Yamashita, T.; Ando, Y.; Obayashi, K.; Terazaki, H.; Sakashita, N.; Uchida, K.; Ohama, E.; Ando, M.; Uchino, M. Oxidative injury is present in Purkinje cells in patients with olivopontocerebellar atrophy. *J. Neurol. Sci.,* **2000**, *175*(2), 107-110. http://dx.doi.org/10.1016/S0022-510X(00)00296-3 PMID: 10831770

[290] Qi, X.; Lewin, A.S.; Sun, L.; Hauswirth, W.W.; Guy, J. Suppression of mitochondrial oxidative stress provides long-term neuroprotection in experimental optic neuritis. *Invest. Ophthalmol. Vis. Sci.,* **2007**, *48*(2), 681-691. http://dx.doi.org/10.1167/iovs.06-0553 PMID: 17251466

[291] Nagata, K.; Hasegawa, T.; Hirokado, Y.; Kiyama, K.; Honda, K.; Aoyama, Y. Endocrinological stress and oxidative stress of orthostatic hypotension. *Auton. Neurosci.,* **2007**, *135*(1), 44-45. http://dx.doi.org/10.1016/j.autneu.2007.06.060

[292] Rudić, M.; Milković, L.; Žarković, K.; Borović-Šunjić, S.; Sterkers, O.; Waeg, G.; Ferrary, E.; Bozorg, G.A.; Žarković, N. The effects of angiotensin II and the oxidative stress mediator 4-hydroxynonenal on human osteoblast-like cell growth: possible relevance to otosclerosis. *Free Radic. Biol. Med.,* **2013**, *57*, 22-28. http://dx.doi.org/10.1016/j.freeradbiomed.2012.11.023 PMID: 23261942

[293] Cutlip, RG.; Geronilla, KB.; Baker, BA.; Mercer, RR.; Hollander, M.; Alway, SE. Mechanisms of repetitive strain injury in an aging model. *NORA Symposium 2006: Research Makes a Difference!* April 18-26, **2006**, pp. 256-257.

[294] Hwang, O. Role of oxidative stress in Parkinson's disease. *Exp. Neurobiol.,* **2013**, *22*(1), 11-17. http://dx.doi.org/10.5607/en.2013.22.1.11 PMID: 23585717

[295] Fortunati, N.; Manti, R.; Birocco, N.; Pugliese, M.; Brignardello, E.; Ciuffreda, L.; Catalano, M.G.; Aragno, M.; Boccuzzi, G. Pro-inflammatory cytokines and oxidative stress/antioxidant parameters characterize the bio-humoral profile of early cachexia in lung cancer patients. *Oncol. Rep.,* **2007**, *18*(6), 1521-1527. http://dx.doi.org/10.3892/or.18.6.1521 PMID: 17982639

[296] Lee, H.Y.; Xu, Y.; Huang, Y.; Ahn, A.H.; Auburger, G.W.; Pandolfo, M.; Kwiecinski, H.; Grimes, D.A.; Lang, A.E.; Nielsen, J.E.; Averyanov, Y.; Servidei, S.; Friedman, A.; Van Bogaert, P.; Abramowicz, M.J.; Bruno, M.K.; Sorensen, B.F.; Tang, L.; Fu, Y.H.; Ptácek, L.J. The gene for paroxysmal non-kinesigenic dyskinesia encodes an enzyme in a stress response pathway. *Hum. Mol. Genet.,* **2004**, *13*(24), 3161-3170. http://dx.doi.org/10.1093/hmg/ddh330 PMID: 15496428

[297] Southwood, C.M.; Fykkolodziej, B.; Dachet, F.; Gow, A. Potential for cell-mediated immune responses in mouse models of pelizaeus-merzbacher disease. *Brain Sci.,* **2013**, *3*(4), 1417-1444. http://dx.doi.org/10.3390/brainsci3041417 PMID: 24575297

[298] Auré, K.; Dubourg, O.; Jardel, C.; Clarysse, L.; Sternberg, D.; Fournier, E.; Laforêt, P.; Streichenberger, N.; Petiot, P.; Gervais-Bernard, H.; Vial, C.; Bedat-Millet, A.L.; Drouin-Garraud, V.; Bouillaud, F.; Vandier, C.; Fontaine, B.; Lombès, A. Episodic weakness due to mitochondrial DNA MT-ATP6/8 mutations. *Neurology,* **2013**, *81*(21), 1810-1818. http://dx.doi.org/10.1212/01.wnl.0000436067.43384.0b PMID: 24153443

[299] Carozzi, V.A.; Canta, A.; Chiorazzi, A. Chemotherapy-induced peripheral neuropathy: What do we know about mechanisms? *Neurosci. Lett.,* **2015**, *2*(596), 90-107.

[300] Masao, K.; Hirokazu, T.; Mitsufumi, M. Evaluation of oxidative stress status in children with pervasive developmental disorder and attention deficit hyperactivity disorder using urinary-specific biomarkers. **2011**, *16*(1), 45-46.

[301] Grings, M.; Tonin, A.M.; Knebel, L.A.; Zanatta, A.; Moura, A.P.; Filho, C.S.; Wajner, M.; Leipnitz, G. Phytanic acid disturbs mitochondrial homeostasis in heart of young rats: A possible pathomechanism of cardiomyopathy in Refsum disease. *Mol. Cell. Biochem.,* **2012**, *366*(1-2), 335-343. http://dx.doi.org/10.1007/s11010-012-1311-1 PMID: 22527938

[302] Castellani, R.; Smith, M.A.; Richey, P.L.; Kalaria, R.; Gambetti, P.; Perry, G. Evidence for oxidative stress in Pick disease and corticobasal degeneration. *Brain Res.,* **1995**, *696*(1-2), 268-271. http://dx.doi.org/10.1016/0006-8993(95)00535-X PMID: 8574681

[303] Yang, X.; Jin, L.; Shimer, A.; Shen, F.; Li, X. Novel treatment of radiculopathy with fullerol nanoparticles. *Global Spine J.,* **2014**, *4*, 2. http://dx.doi.org/10.1055/s-0034-1376537

[304] Zhan, X.; Desiderio, D.M. Signaling pathway networks mined from human pituitary adenoma proteomics data. *BMC Med. Genomics,* **2010**, *3*, 13. http://dx.doi.org/10.1186/1755-8794-3-13 PMID: 20426862

[305] Ziegler, D.; Sohr, C.G.; Nourooz-Zadeh, J.; Jaffar, N.Z. Oxidative stress and antioxidant defense in relation to the severity of diabetic polyneuropathy and cardiovascular autonomic neuropathy. *Diabetes Care,* **2004**, *27*(9), 2178-2183. http://dx.doi.org/10.2337/diacare.27.9.2178 PMID: 15333481

[306] White, J.P.; Lloyd, R.E. Poliovirus unlinks TIA1 aggregation and mRNA stress granule formation. *J. Virol.,* **2011**, *85*(23), 12442-12454. http://dx.doi.org/10.1128/JVI.05888-11 PMID: 21957303

[307] Tews, D.S.; Goebel, H.H. Cell death and oxidative damage in inflammatory myopathies. *Clin. Immunol. Immunopathol.,* **1998**, *87*(3), 240-247. http://dx.doi.org/10.1006/clin.1998.4527 PMID: 9646833

[308] Gordon, T.; Hegedus, J.; Tam, S.L. Adaptive and maladaptive motor axonal sprouting in aging and motoneuron disease. *Neurol. Res.,* **2004**, *26*(2), 174-185. http://dx.doi.org/10.1179/016164104225013806 PMID: 15072637

[309] Beatriz, G.S.; Gabino, G.; Rene, D.; Fe, B.; Camilo, E. Hernández. Report of cases in patients with acute herpetic neuralgia using a Mangifera indica extract. *Rev. Bras. Farmacogn.,* **2011**, *21*(6), 1111-1117. http://dx.doi.org/10.1590/S0102-695X2011005000125

[310] Anichini, C.; Lotti, F.; Longini, M.; Proietti, F.; Felici, C.; Perrone, S.; Buonocore, G. Antioxidant effects of potassium ascorbate with ribose therapy in a case with Prader Willi Syndrome. *Dis. Markers,* **2012**, *33*(4), 179-183. http://dx.doi.org/10.1155/2012/425205 PMID: 22960339

[311] Brown, D.R. Neurodegeneration and oxidative stress: prion disease results from loss of antioxidant defence. *Folia Neuropathol.,* **2005**, *43*(4), 229-243. PMID: 16416388

[312] Aoyama, K.; Matsubara, K.; Kobayashi, S. Aging and oxidative stress in progressive supranuclear palsy. *Eur. J. Neurol.,* **2006**, *13*(1), 89-92. http://dx.doi.org/10.1111/j.1468-1331.2006.01139.x PMID: 16420399

[313] Xin, X.; Fan, B.; Flammer, J.; Miller, N.R.; Jaggi, G.P.; Killer, H.E.; Meyer, P.; Neutzner, A. Meningothelial cells react to elevated pressure and oxidative stress. *PLoS One,* **2011**, *6*(5), e20142. http://dx.doi.org/10.1371/journal.pone.0020142 PMID: 21611150

[314] Hübner-Woźniak, E.; Morgulec-Adamowicz, N.; Malara, M.; Lewandowski, P.; Okęcka-Szymańska, J. Effect of rugby training on blood antioxidant defenses in able-bodied and spinal cord injured players. *Spinal Cord,* **2012**, *50*(3), 253-256. http://dx.doi.org/10.1038/sc.2011.134 PMID: 22124350

[315] Jackson, A.C.; Kammouni, W.; Fernyhough, P. Role of oxidative stress in rabies virus infection. *Adv. Virus Res.,* **2011**, *79*, 127-138. http://dx.doi.org/10.1016/B978-0-12-387040-7.00008-1 PMID: 21601046

[316] Kolberg, C.; Horst, A.; Moraes, M.S.; Duarte, F.C.; Riffel, A.P.; Scheid, T.; Kolberg, A.; Partata, W.A. Peripheral oxidative stress blood markers in patients with chronic back or neck pain treated with high-velocity, low-amplitude manipulation. *J. Manipulative Physiol. Ther.,* **2015**, *38*(2), 119-129. http://dx.doi.org/10.1016/j.jmpt.2014.11.003 PMID: 25487299

[317] Miclescu, A.A.; Nordquist, L.; Hysing, E.B.; Butler, S.; Basu, S.; Lind, A.L.; Gordh, T. Targeting oxidative injury and cytokines' activity in the treatment with anti-tumor necrosis factor-α antibody for complex regional pain syndrome 1. *Pain Pract.,* **2013**, *13*(8), 641-648. http://dx.doi.org/10.1111/papr.12027 PMID: 23336526

[318] Sabine, G.S.; Damien, C.; Pierre, P.; Pierre, C.; Abdallah, G. Nicole, Sarda. Nitric oxide and sleep, Physiological review. *Sleep Med.,* **2005**, *9*(2), 101-113. http://dx.doi.org/10.1016/j.smrv.2004.07.004 PMID: 15716213

[319] Nikolaidis, M.G.; Paschalis, V.; Giakas, G.; Fatouros, I.G.; Koutedakis, Y.; Kouretas, D.; Jamurtas, A.Z. Decreased blood oxidative stress after repeated muscle-damaging exercise. *Med. Sci. Sports Exerc.,* **2007**, *39*(7), 1080-1089. http://dx.doi.org/10.1249/mss.0b013e31804ca10c PMID: 17596775

[320] Cikrikcioglu, M.A.; Hursitoglu, M.; Erkal, H.; Kınas, B.E.; Sztajzel, J.; Cakirca, M.; Arslan, A.G.; Erek, A.; Halac, G.; Tukek, T. Oxidative stress and autonomic nervous system functions in restless legs syndrome. *Eur. J. Clin. Invest.,* **2011**, *41*(7), 734-742.

http://dx.doi.org/10.1111/j.1365-2362.2010.02461.x PMID: 21250984

[321] Leoncini, S.; De Felice, C.; Signorini, C.; Pecorelli, A.; Durand, T.; Valacchi, G.; Ciccoli, L.; Hayek, J. Oxidative stress in Rett syndrome: natural history, genotype, and variants. *Redox Rep.,* **2011**, *16*(4), 145-153. http://dx.doi.org/10.1179/1351000211Y.0000000004 PMID: 21888765

[322] Abdin, A.; Sarhan, N. Resveratrol protects against experimental induced Reye's syndrome by prohibition of oxidative stress and restoration of complex I activity. *Can. J. Physiol. Pharmacol.,* **2014**, *92*(9), 780-788. http://dx.doi.org/10.1139/cjpp-2014-0251 PMID: 25162205

[323] Schrammel, A.; Mussbacher, M.; Winkler, S.; Haemmerle, G.; Stessel, H.; Wölkart, G.; Zechner, R.; Mayer, B. Cardiac oxidative stress in a mouse model of neutral lipid storage disease. *Biochim. Biophys. Acta,* **2013**, *1831*(11), 1600-1608. http://dx.doi.org/10.1016/j.bbalip.2013.07.004 PMID: 23867907

[324] López-Erauskin, J.; Galino, J.; Bianchi, P.; Fourcade, S.; Andreu, A.L.; Ferrer, I.; Muñoz-Pinedo, C.; Pujol, A. Oxidative stress modulates mitochondrial failure and cyclophilin D function in X-linked adrenoleukodystrophy. *Brain,* **2012**, *135*(Pt 12), 3584-3598. http://dx.doi.org/10.1093/brain/aws292 PMID: 23250880

[325] Hunter, J.W.; Mullen, G.P.; McManus, J.R.; Heatherly, J.M.; Duke, A.; Rand, J.B. Neuroligin-deficient mutants of C. elegans have sensory processing deficits and are hypersensitive to oxidative stress and mercury toxicity. *Dis. Model. Mech.,* **2010**, *3*(5-6), 366-376. http://dx.doi.org/10.1242/dmm.003442 PMID: 20083577

[326] Dr. Loges & Co. GmbH. Intravenous Vitamin C in the Treatment of Viral Infection, Especially in the Treatment of Shingles (168), Pascoe Pharmazeutische Praeparate GmbH **2012**.

[327] Stefanova, N.; Reindl, M.; Neumann, M.; Haass, C.; Poewe, W.; Kahle, P.J.; Wenning, G.K. Oxidative stress in transgenic mice with oligodendroglial alpha-synuclein overexpression replicates the characteristic neuropathology of multiple system atrophy. *Am. J. Pathol.,* **2005**, *166*(3), 869-876. http://dx.doi.org/10.1016/S0002-9440(10)62307-3 PMID: 15743798

[328] Pagano, G.; Castello, G.; Pallardó, F.V. Sjøgren's syndrome-associated oxidative stress and mitochondrial dysfunction: prospects for chemoprevention trials. *Free Radic. Res.,* **2013**, *47*(2), 71-73. http://dx.doi.org/10.3109/10715762.2012.748904 PMID: 23153390

[329] Yamauchi, M.; Kimura, H. Oxidative stress in obstructive sleep apnea: putative pathways to the cardiovascular complications. *Antioxid. Redox Signal.,* **2008**, *10*(4), 755-768. http://dx.doi.org/10.1089/ars.2007.1946 PMID: 18177236

[330] He, S.; Dayton, A.; Kuppusamy, P.; Werbovetz, K.A.; Drew, M.E. Induction of oxidative stress in Trypanosoma brucei by the antitrypanosomal dihydroquinoline OSU-40. *Antimicrob. Agents Chemother.,* **2012**, *56*(5), 2428-2434. http://dx.doi.org/10.1128/AAC.06386-11 PMID: 22314522

[331] Miwa, K.; Kishimoto, C.; Nakamura, H.; Makita, T.; Ishii, K.; Okuda, N.; Taniguchi, A.; Shioji, K.; Yodoi, J.; Sasayama, S. Increased oxidative stress with elevated serum thioredoxin level in patients with coronary spastic angina. *Clin. Cardiol.,* **2003**, *26*(4), 177-181. http://dx.doi.org/10.1002/clc.4960260406 PMID: 12708624

[332] Martín, I.; Gibert, M.J.; Pintos, C.; Noguera, A.; Besalduch, A.; Obrador, A. Oxidative stress in mothers who have conceived fetus with neural tube defects: the role of aminothiols and selenium. *Clin. Nutr.,* **2004**, *23*(4), 507-514. http://dx.doi.org/10.1016/j.clnu.2003.09.010 PMID: 15297086

[333] Jia, Z.; Zhu, H.; Li, J.; Wang, X.; Misra, H.; Li, Y. Oxidative stress in spinal cord injury and antioxidant-based intervention. *Spinal Cord,* **2012**, *50*(4), 264-274. http://dx.doi.org/10.1038/sc.2011.111 PMID: 21987065

[334] Bedreag, O.H.; Rogobete, A.F.; Sărăndan, M.; Cradigati, A.; Păpurică, M.; Roşu, O.M.; Dumbuleu, C.M.; Săndesc, D. Oxidative stress and antioxidant therapy in traumatic spinal cord injuries. *Rom. J. Anaesth. Intensive Care,* **2014**, *21*(2), 123-129. PMID: 28913444

[335] Hayat, E.Y. Spinal muscular atrophy: An oxidative stress response counteracted with curcumin. *Biomed. Aging Pathol.,* **2012**, *2*(2), 61-66. http://dx.doi.org/10.1016/j.biomag.2012.03.007

[336] Mano, T.; Katsuno, M.; Banno, H.; Suzuki, K.; Suga, N.; Hashizume, A.; Tanaka, F.; Sobue, G. Cross-sectional and longitudinal analysis of an oxidative stress biomarker for spinal and bulbar muscular atrophy. *Muscle Nerve,* **2012**, *46*(5), 692-697. http://dx.doi.org/10.1002/mus.23413 PMID: 22941760

[337] Guevara-García, M.; Gil-del Valle, L.; Velásquez-Pérez, L.; García-Rodríguez, J.C. Oxidative stress as a cofactor in spinocerebellar ataxia type 2. *Redox Rep.,* **2012**, *17*(2), 84-89. http://dx.doi.org/10.1179/1351000212Y.0000000005 PMID: 22564351

[338] Kasparová, S.; Brezová, V.; Valko, M.; Horecký, J.; Mlynárik, V.; Liptaj, T.; Vancová, O.; Ulicná, O.; Dobrota, D. Study of the oxidative stress in a rat model of chronic brain hypoperfusion. *Neurochem. Int.,* **2005**, *46*(8), 601-611. http://dx.doi.org/10.1016/j.neuint.2005.02.006 PMID: 15863238

[339] Rodrigo, R.; Fernández-Gajardo, R.; Gutiérrez, R.; Matamala, J.M.; Carrasco, R.; Miranda-Merchak, A.; Feuerhake, W. Oxidative stress and pathophysiology of ischemic stroke: novel therapeutic opportunities. *CNS Neurol. Disord. Drug Targets,* **2013**, *12*(5), 698-714. http://dx.doi.org/10.2174/18715273113120500015 PMID: 23469845

[340] Kadam, S.D.; Gucek, M.; Cole, R.N.; Watkins, P.A.; Comi, A.M. Cell proliferation and oxidative stress pathways are modified in fibroblasts from Sturge-Weber syndrome patients. *Arch. Dermatol. Res.,* **2012**, *304*(3), 229-235. http://dx.doi.org/10.1007/s00403-012-1210-z PMID: 22402795

[341] Hayashi, M.; Arai, N.; Satoh, J.; Suzuki, H.; Katayama, K.; Tamagawa, K.; Morimatsu, Y. Neurodegenerative mechanisms in subacute sclerosing panencephalitis. *J. Child Neurol.,* **2002**, *17*(10), 725-730. http://dx.doi.org/10.1177/088307380201701101 PMID: 12546425

[342] Ikeda, T.; Choi, B.H.; Yee, S.; Murata, Y.; Quilligan, E.J. Oxidative stress, brain white matter damage and intrauterine asphyxia in fetal lambs. *Int. J. Dev. Neurosci.,* **1999**, *17*(1), 1-14. http://dx.doi.org/10.1016/S0736-5748(98)00055-0 PMID: 10219955

[343] Liu, F.; Ma, F.; Kong, G.; Wu, K.; Deng, Z.; Wang, H. Zinc supplementation alleviates diabetic peripheral neuropathy by inhibiting oxidative stress and upregulating metallothionein in peripheral nerves of diabetic rats. *Biol. Trace Elem. Res.,* **2014**, *158*(2), 211-218. http://dx.doi.org/10.1007/s12011-014-9923-9 PMID: 24615552

[344] Cho, C.H.; Lee, H.J. Oxidative stress and tardive dyskinesia: pharmacogenetic evidence. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2013**, *46*, 207-213. http://dx.doi.org/10.1016/j.pnpbp.2012.10.018 PMID: 23123399

[345] Ufuk, Çakata Systemic Oxidative Stress and Degenerative Disorders. *Biochemistry,* **2015**, 30.

[346] Astrid, B.; Younge, B.R.; Luke, S.; Bettina, M.; Johannes, B. Reactive nitrogen intermediates in giant cell arteritis. *Am. J. Pathol.,* **2002**, *161*, 1.

[347] Cubí, R.; Candalija, A.; Ortega, A.; Gil, C.; Aguilera, J. Tetanus toxin Hc fragment induces the formation of ceramide platforms and protects neuronal cells against oxidative stress. *PLoS One,* **2013**, *8*(6), e68055. http://dx.doi.org/10.1371/journal.pone.0068055 PMID: 23826362

[348] Shatillo, A.; Koroleva, K.; Giniatullina, R.; Naumenko, N.; Slastnikova, A.A.; Aliev, R.R.; Bart, G.; Atalay, M.; Gu, C.; Khazipov, R.; Davletov, B.; Grohn, O.; Giniatullin, R. Cortical spreading depression induces oxidative stress in the trigeminal nociceptive system. *Neuroscience,* **2013**, *253*, 341-349. http://dx.doi.org/10.1016/j.neuroscience.2013.09.002 PMID: 24036374

[349] Landau, Y.E.; Steinberg, T.; Richmand, B.; Leckman, J.F.; Apter, A. Involvement of immunologic and biochemical mechanisms in the pathogenesis of Tourette's syndrome. *J. Neural Transm. (Vienna),* **2012**, *119*(5), 621-626.

http://dx.doi.org/10.1007/s00702-011-0739-x PMID: 22139323

[350] Achzet, L.M.; Davison, C.J.; Shea, M.; Sturgeon, I.; Jackson, D.A. Oxidative stress underlies the ischemia/reperfusion-induced internalization and degradation of AMPA receptors. *Int. J. Mol. Sci.,* **2021**, *22*(2), 717.

[351] Milhavet, O.; Lehmann, S. Oxidative stress and the prion protein in transmissible spongiform encephalopathies. *Brain Res.,* **2002**, *38*(3), 328-339.
http://dx.doi.org/10.1016/S0165-0173(01)00150-3 PMID: 11890980

[352] Rodríguez-Rodríguez, A.; Egea-Guerrero, J.J.; Murillo-Cabezas, F.; Carrillo-Vico, A. Oxidative stress in traumatic brain injury. *Curr. Med. Chem.,* **2014**, *21*(10), 1201-1211.
http://dx.doi.org/10.2174/09298673216661312171533 10 PMID: 24350853

[353] Louis, E.D.; Jurewicz, E.C.; Parides, M.K. Case-control study of nutritional antioxidant intake in essential tremor. *Neuroepidemiology,* **2005**, *24*(4), 203-208.
http://dx.doi.org/10.1159/000084713 PMID: 15802925

[354] Paiva, C.N.; Feijó, D.F.; Dutra, F.F.; Carneiro, V.C.; Freitas, G.B.; Alves, L.S.; Mesquita, J.; Fortes, G.B.; Figueiredo, R.T.; Souza, H.S.; Fantappié, M.R.; Lannes-Vieira, J.; Bozza, M.T. Oxidative stress fuels *Trypanosoma cruzi* infection in mice. *J. Clin. Invest.,* **2012**, *122*(7), 2531-2542.
http://dx.doi.org/10.1172/JCI58525 PMID: 22728935

[355] Reith, R.M.; Way, S.; McKenna, J., III; Haines, K.; Gambello, M.J. Loss of the tuberous sclerosis complex protein tuberin causes Purkinje cell degeneration. *Neurobiol. Dis.,* **2011**, *43*(1), 113-122.
http://dx.doi.org/10.1016/j.nbd.2011.02.014 PMID: 21419848

[356] Mikhaylova, O.; Ignacak, M.L.; Barankiewicz, T.J.; Harbaugh, S.V.; Yi, Y.; Maxwell, P.H.; Schneider, M.; Van Geyte, K.; Carmeliet, P.; Revelo, M.P.; Wyder, M.; Greis, K.D.; Meller, J.; Czyzyk-Krzeska, M.F. The von Hippel-Lindau tumor suppressor protein and Egl-9-Type proline hydroxylases regulate the large subunit of RNA polymerase II in response to oxidative stress. *Mol. Cell. Biol.,* **2008**, *28*(8), 2701-2717.
http://dx.doi.org/10.1128/MCB.01231-07 PMID: 18285459

[357] Ono, H.; Fukuhara, R. The evaluation of oxidative stress during ACTH therapy in West syndrome. *No To Hattatsu,* **2011**, *43*(2), 141-142.
PMID: 21409838

[358] Kalita, J.; Kumar, V.; Misra, U.K.; Ranjan, A.; Khan, H.; Konwar, R. A study of oxidative stress, cytokines and glutamate in Wilson disease and their asymptomatic siblings. *J. Neuroimmunol.,* **2014**, *274*(1-2), 141-148.
http://dx.doi.org/10.1016/j.jneuroim.2014.06.013 PMID: 25002079

[359] Onofre, A.P. *A Clinical Trial for AMN: Validation of Biomarkers of Oxidative Stress, Efficacy and Safety of a Mixture of Antioxidants*; Ministerio de Sanidad, Servicios Sociales e Igualdad Fundacion Hesperia, **2014**.

[360] Müller, C.C.; Nguyen, T.H.; Ahlemeyer, B.; Meshram, M.; Santrampurwala, N.; Cao, S.; Sharp, P.; Fietz, P.B.; Baumgart-Vogt, E.; Crane, D.I. PEX13 deficiency in mouse brain as a model of Zellweger syndrome: Abnormal cerebellum formation, reactive gliosis and oxidative stress. *Dis. Model. Mech.,* **2011**, *4*(1), 104-119.
http://dx.doi.org/10.1242/dmm.004622 PMID: 20959636