Journal of Neurol Neurophysiol 2022, Vol. 13, Issue 5, 001-002

Mini Review

Alzheimer's Disease: Oxidative Stress

Pragati Singh*

Department of Biotechnology, Graphic Era University, India

Corresponding Author*

Pragati Singh,

Editor office

Department of Biotechnology, Graphic Era University,

India,

E-mail:singhpragati330@gmail.com

Received: 2-May-2022, Manuscript No. jnn-22-66091; **Editor assigned:** 9-May-2022, PreQC No. jnn-22-66091 (PQ); **Reviewed**: 13-May-2022, QC No. jnn-22-66091 (Q); **Revised**: 19-May-2022, Manuscript No. jnn-22-66091(R); **Published**: 27-May-2022, DOI. 10.35248/2471-268X.22.13.583

Abstract

Alzheimer's Disease (AD) is the leading cause of impairment among people over the age of 65 across the world. Amyloid (A) peptide deposition abnormalities, the intracellular buildup of hyperphosphorylated protein neurofibrillary tangles, and dementia are all symptoms of Alzheimer's disease. The neurotoxic oligomer A peptide, which is the disease's neuropathological diagnostic criteria, and protein are mediators of neurodegeneration, which is one of the primary causes. However, oxidative stress, which is defined as an imbalance between antioxidants and oxidants that favours oxidants, is the primary cause and aggressor of these symptoms. Increased free radicals or a reduction in antioxidant defence can cause this imbalance. Free radicals are species with one or more unpaired electrons in their outer shell. Understanding the pathophysiology of Alzheimer's disease is becoming more focused on oxidative balance.

Oxidative damage has been seen in both characteristic diseases (senile plaques and neurofibrillary tangles) and normal-appearing pyramidal neurons in the brains of Alzheimer's patients. While this shows that oxidative stress is a proximal event in the aetiology of Alzheimer's disease, the mechanisms by which redox equilibrium is disrupted in the illness are unknown. Determining which of the proposed sources of free radicals, such as mitochondrial dysfunction, amyloid-L-mediated processes, transition metal accumulation, and genetic factors like apolipoprotein E and presenilins, are responsible for redox imbalance will help researchers better understand Alzheimer's disease pathogenesis and develop new therapeutic approaches.

Keywords: Alzheimer's disease; oxidative stress; β-amyloid; tau; metals; antioxidants

Introduction

Understanding the pathophysiology of Alzheimer's disease is becoming more focused on oxidative balance. Oxidative damage has been seen in both characteristic diseases (senile plaques and neurofibrillary tangles) and normal-appearing pyramidal neurons in the brains of Alzheimer's patients. While this shows that oxidative stress is a proximal event in the aetiology of Alzheimer's disease, the mechanisms by which redox equilibrium is disrupted in the illness are unknown. Determining which of the proposed sources of free radicals, such as mitochondrial dysfunction, amyloid-L-mediated processes, transition metal accumulation, and genetic factors like apolipoprotein E and presenilins, are responsible for redox imbalance will help researchers better understand Alzheimer's disease pathogenesis and develop new therapeutic approaches. Since metal catalyses redox reactions, one of the most important forms of antioxidant defence is storing and transporting iron in forms that do not catalyse the formation of reactive radicals, as is the case during tissue injury, when iron availability increases, potentially speeding up free radical reactions.

"Because metal catalyses redox reactions, one of the most important forms of antioxidant defence is storing and transporting iron in forms that do not catalyse the formation of reactive radicals, as is the case during tissue injury, when iron availability increases, potentially speeding up free radical reactions. The role of oxidative stress and free radical damage in the aetiology of Alzheimer's disease has been demonstrated [1-2]

Because metal catalyses redox reactions, one of the most important forms of antioxidant defence is storing and transporting iron in forms that do not catalyse the formation of reactive radicals, as is the case when tissue injury increases iron availability, potentially speeding up free radical reactions. It has been proven that oxidative stress and free radical damage play a part in the genesis of Alzheimer's disease. lesions, neurotransmitter deficiencies, and identification of AD as a single entity In the 1980s and 1990s, molecular biology methods and other new technology provided insight into the molecular changes in Alzheimer's disease, paving the way for a prospective understanding of the disease's pathogenetic pathways. The most frequent kind of dementia in adults is Alzheimer's disease. According to a community-based survey, almost 4 million Americans suffer from Alzheimer's disease. According to the findings, Alzheimer's disease affects 3% of people aged 65 to 74, 18.7% of those aged 75 to 84, and 47.2% of people aged 85 and more. In this nation, it is the fourth or fifth most common cause of death. 3 Unless prevention treatments are developed, it is anticipated that around 9 million people will have Alzheimer's disease by 2040, due to the ageing of society [3].

In adults, Alzheimer's disease is the most common form of dementia. Nearly 4 million Americans have Alzheimer's disease, according to a community-based poll. 2 Alzheimer's disease affects 3% of persons aged 65 to 74, 18.7% of those aged 75 to 84, and 47.2% of people aged 85 and more, according to the study's findings. It's the fourth or fifth leading cause of death in the United States. Due to the ageing of civilization, it is expected that around 9 million individuals will have Alzheimer's disease by 2040 unless preventative medicines are produced. Hyperphosphorylation of tau is linked to NFT pathology in Alzheimer's. Tau is a microtubule-associated protein in neurons that is controlled by protein kinases. Normally, there are two to three moles of phosphates per mole of tau, but in AD, this protein is three to four times hyperphosphorylated. This abnormally hyperphosphorylated tau loses its ability to assemble microtubules, resulting in the formation of PHF-containing neurofibrillary tangles. Membrane-associated-Amyloid Precursor Protein (APP) is proteolytically cleaved to generate. Two primary protease routes are involved in APP processing. The amyloidogenic route for processing APP to generate A is represented by the cleavage of APP at the N-terminus of the A region by secretase and at the C-terminus by secretase which cleaves inside the A sequence but does not generate Aβ, and may also digest APP. Because they have three copies of a chromosome, which contains the APP gene, patients with Down syndrome typically acquire AD in middle life. Despite its abundance of biometals and lipids, the brain has a high oxygen demand and contains a large number of peroxidation-prone lipid cells. Furthermore, liberated iron ions cannot be bound by the cerebral fluid. As a result, oxidative stress in nerve tissue can cause substantial brain damage through a variety of processes, including an increase in intracellular free Ca_2+, the release of excitatory amino acids, and neurotoxicity. Reactive Nitrogen Species (RNS), such as Nitric Oxide (NO) and peroxynitrite, are other important sources or modulators of oxidative stress, as they can be extremely reactive with proteins, lipids, nucleic acid, and other molecules, causing further structural and/or functional changes in the brain [4].

Oxidative Damage

Oxidative stress is defined as the oxidative system overwhelming the antioxidative defence system. Free radicals, also known as Reactive Oxygen Species (ROS), are created by unpaired electrons in oxygen and nitrogen-based compounds. The general mechanism of free radical production. Free radicals are very reactive and unstable because of their unpaired electrons. Free radicals take electrons from other molecules to produce paired electrons. The donor molecules become unstable after losing their electrons, and they are transformed into free radicals.

Oxidative stress is a term that refers to a wide range of molecules and free radicals that are produced by molecular oxygen. The outer shell of these free radicals has one unpaired electron. In its ground state, molecular oxygen is a bi-radical with two solitary electrons sharing the same spin in the outer shell. As a result, because the oxygen molecule can only react with one electron at a time, it is not particularly reactive with the electrons in chemical bonds. As a result, each of the two electrons spins when one of them is stimulated. The two electrons have opposite spins and can react fast with other electron pairs, especially double bonds. Free radicals created by the body are harmful, and if they are not eliminated or neutralised, they react with lipids, proteins, and nucleic acids, causing cellular damage. Membrane features such as fluidity, ion transport, enzyme activity, and protein cross-linking are all affected when cellular components are damaged by oxidative stress. Cell death occurs when there is too much oxidative damage. Furthermore, antioxidants turn O_2 into a hydroxyl radical (OH), which is one of nature's most powerful oxidants. Reduced transition metals catalyse this reaction, which may then be reduced again by O_2, allowing the process to continue. Furthermore, under the regulation of the rate of diffusion of the two radicals, O2 interacts with other radicals such as NO to generate peroxynitrite, a very potent oxidant that drives RNS oxidants. As a result, ROS and/or RNS are the primary actors, which cause oxidative stress in the absence of adequate antioxidant defences. Intracellular signalling, cell growth, and survival are all aided by ROS and/or RNS. Experiments and human brain research are increasingly pointing to oxidative stress as a factor in neuronal loss in Alzheimer's disease. Increased oxidative stress in AD is a result of soluble A, A fibrils, NFT, mitochondrial abnormalities, and ageing. Imbalances in oxidative homeostasis, which result in increased lipid peroxidation, have been identified as key variables in neurodegenerative diseases including Alzheimer's disease. In vivo, however, O_2 is created by mitochondria, which are controlled by enzymatic and non-enzymatic mechanisms.

The mitochondrial electron transport chain comprises a variety of redox centres that leak electrons to oxygen and is the predominant source of O_2 in most tissues. NADPH oxidases, which are found in many cell membranes, including polymorphonuclear, macrophages, and endothelial cells, as well as cytochrome P450 and HO_2-dependent oxygenases, are the principal enzymatic sources of O_2 [5]. The proteolytic conversion of xanthine dehydrogenase to xanthine oxidase is another enzymatic source of O_2 as an OH source. The direct transfer of oxygen by reduced coenzymes or prosthetic groups, such as flavin, and iron-sulphur clusters, or by xenobiotics following a prior reduction by enzymes, such as anticancer drugs or herbicides, is referred to as non-enzymatic generation of O_2.

References

1. Smith, M.A., et al. "Advanced Maillard reaction end products are associated with Alzheimer disease pathology". Proc Natl Acad Sci.91.12(1994):5710-5714.
2. Ledesma ,M.D., et al. "Analysis of microtubule-associated protein tau glycation in paired helical filaments". J Biol Chem. 269.34(1994):21614-216149.
3. Sayre ,L.M., et al. "4 - Hydroxynonenal - derived advanced lipid peroxidation end products are increased in Alzheimer's disease". J Neurochem. 68.5(1997):2092-2097.
4. Cras ,P., et al. "Neuronal and microglial involvement in beta-amyloid protein deposition in Alzheimer's disease". Am J Pathol. 137.2(1990):241.
5. Lockhart , B.P., et al. "Inhibitors of free radical formation fail to attenuate direct β - amyloid25–35 peptide - mediated neurotoxicity in rat hippocampal cultures". J Neurosci Res.39.4(1994):494-505.

Cite this article: Singh P. Alzheimer's Disease: Oxidative Stress. J Neurol Neurophysiol. 2022, 13(5), 001-002.