Role of Oxidative Stress in the pathogenesis of neurodegenerative disorders

Essay
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List of abbreviations

A beta PP	**:**	Amyloid beta precursor protein.
Abeta	**:**	Amyloid beta peptide.
AChRs	**:**	Nicotinic acetylcholine receptors.
AGEs	**:**	Advanced glycated end products.
ALS	**:**	Amyotrophic lateral sclerosis.
ALS/PDC	**:**	Amyotrophic lateral sclerosis/parkinsonism-dementia complex of Guam.
ApoE	**:**	Apolipoprotein e.
APP	**:**	Amyloid precursor protein.
AS	**:**	Alpha-synuclein.
ATP	**:**	Adenosine-5'-triphosphate.
Aβ	**:**	B-amyloid.
BBB	**:**	The blood–brain barrier.
Bcl-2	**:**	Apoptosis regulator.
BDNF	**:**	Brain-derived neurotrophic factor.
CBD	:	Corticobasal_degeneration
CCR2b	**:**	C-c chemokine receptor type 2.
CCR5	**:**	C-c chemokine receptor type 5.
CCS	**:**	Copper chaperone.
CGIs	**:**	Cytoplasmic Glial inclusions
CNS	**:**	Central nervous system.
COMT	**:**	Catechol-o-methyltransferase.
COX	**:**	Cyclooxygenase.
Cp	**:**	Ceruloplasmin.

Cu	**:**	Copper.
DA	**:**	Dopamine.
DAT	**:**	Da uptake transporter.
DATATOP	**:**	Deprenyl and tocopherol antioxidative therapy of parkinsonism is a placebo-controlled clinical trial.
DLBs	**:**	Dementia with lewy bodies.
DOPA	**:**	3 4-dihydroxy-phenylalanine.
DOPAL	**:**	3 4-dihydroxyphenylacetaldehyde.
DRLPA	**:**	Dentatorubral-pallidoluysian atrophy.
EAE	**:**	Experimental autoimmune encephalomyelitis.
EDSS	**:**	Expanded disability status scale.
EGCG	**:**	Epigallocatechin-3-gallate.
Egr-1	**:**	Early growth response-1.
ER	**:**	Endoplasmic reticulum.
fALS	**:**	Familial amytrophic lateral sclerosis.
Fe-S	**:**	Ferrous sulfide.
18F	**:**	Fludeoxyglucose.
FLD-MND type:		Frontal lobe degeneration (FLD), Motor neuron disease (MND) type.
FRDA	**:**	Friedreich ataxia.
FTDP 17	**:**	Frontotemporal dementia with parkinsonism-17.
GAs	**:**	Golgi apparatus.
GDNF	**:**	Glial-derived neurotrophic factor.
GPx	**:**	Glutathione peroxidase.
GSH	**:**	Glutathione.
GSH	**:**	Reduced glutathione.
GSS	**:**	Gerstmann-Sträussler-Scheinker disease.

GSSG	**:**	Oxidized glutathione.
HD	**:**	Huntington's disease.
HLA-DR	**:**	Is a major histocompatibility complex class ii cell surface receptor encoded by the human leukocyte antigen complex.
HNE	**:**	4-hydroxy-2-nonenal.
HNE	**:**	4-hydroxy-2-transnonenal.
HO-1	**:**	Heme oxygenase-1.
Hsp26	**:**	Heat shock protein 26.
Hsp27	**:**	Heat shock protein 27.
HSPs	**:**	Heat shock proteins.
ILBD	**:**	Incidental lewy body disease.
iNOS	**:**	Inducible nitric oxide synthase.
IRP / IRE	**:**	The iron regulatory protein / iron-responsive element.
JNK	**:**	C-jun n-terminal protein kinase.
JNKs	**:**	C-jun n-terminal kinases.
LB	**:**	Lewy bodies.
LBs	**:**	Lewy bodies.
LPS	**:**	Lipopolysaccharide.
MAO	**:**	Monoamine oxidase.
MBP	**:**	Myelin basic protein.
MCI	**:**	Mild cognitive impairment.
MDA	**:**	Malonaldialdehyde.
MIP -	**:**	Macrophage inflammatory protein.
MMPs	**:**	Matrix metalloproteinases.
MnSOD	**:**	Manganese superoxide dismutase.
MOBP	**:**	Myelin-associated basic glycoprotein.
MOG	**:**	Myelin oligodendrocytes glycoprotein.

MPP+	**:**	1-methyl-4-phenyl-2 3-dihydropyridium ion.
MPT	**:**	Mitochondrial permeability transition.
MPTP	**:**	MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a neurotoxin precursor to MPP+,.
MS	**:**	Multiple sclerosis.
MSA	**:**	Multiple system atrophy.
MSTD	:	Multiple system tauopathy with presenile dementia
MutSOD1	**:**	Mutant Superoxide dismutase 1.
NAC	**:**	N-acetylcysteine.
NFTs	**:**	Neurofibrillary tangles.
NF-κB	**:**	Nuclear factor kappa-light-chain-enhancer of activated b cells is a protein complex that controls the transcription of DNA.
NGF	**:**	Nerve growth factor.
NM	**:**	Neuromelanin.
nNOS	**:**	Neuronal nitric oxide synthase.
6-OHDA	**:**	6-hydroxydopamine., also known as Oxidopamine is a neurotoxic syntheticorganic compound used by researchers to selectively estroy dopaminergic and noradrenergic neurons in the brain.
(8OHG)	**:**	Hydroxyguanosine. A nucleic acid modification
ONOO•−	**:**	Peroxynitrite.
OS	**:**	Oxidative stress.
p75NTR	**:**	75-kda neurotrophin receptor.
PAK	**:**	P21-activated kinase.
PBN	**:**	A-phenyl-n-tertbutylnitrone.
PCD	**:**	Programmed cell death.

PCS	**:**	Prospective cohort studies.
PD	**:**	Parkinson’s disease.
PET	**:**	Positron emission tomography.
PLO	**:**	The protein lipid overlay.
PLP	**:**	Proteolipid protein.
PMA	**:**	Phorbol myristate acetate.
PPARs	**:**	Peroxisomal proliferation-activated receptors.
PPND	:	pallido-ponto-nigral degeneration.
PSP	**:**	Progressive supranuclear palsy.
RNS	**:**	Reactive nitrogen species.
ROS	**:**	Reactive oxygen species.
sALS	**:**	Sporadic amytrophic lateral sclerosis.
SCAs	**:**	Spinocerebellar ataxias.
SN	**:**	Substantia nigra.
SNc	**:**	Substantia nigra compacta.
SNpr	**:**	Substantia nigra pars reticulata.
SOD	**:**	Superoxide dismutase.
TBARS	**:**	Thiobarbituric acid reactive substances.
TCA	**:**	Tricarboxylic acid.
TCR	**:**	T-cell receptor.
TH	**:**	Tyrosine hydroxylase.
THC	**:**	Tetrahydrocurcumin.
THP1	**:**	(Human acute monocytic leukemia cell line): This product is used to test leukemia cell lines in immunocytochemical analysis of protein-protein interaction, and immunohistochemistry.
TNF	**:**	Tumor necrosis factor.

TQ	**:**	Thymoquinone.
UA	**:**	Uric acid.
Ub	**:**	Ubiquitin.
UPDRS	**:**	Unified parkinson’s disease rating scale.
UPP	**:**	Ubiquitin–proteasomal pathway.
UPR	**:**	Unfolded protein response.
UPS	**:**	Ubiquitin–proteasomal system.
VEGF	**:**	Vascular endothelial growth factor.
YAC	**:**	Yeast artificial chromosome.

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List of Glossary

Advanced glycation end products **:** (AGEs) are proteins or lipids that become glycated after exposure to sugars.

Aggresome **:** Correct folding requires proteins to assume one particular structure from a constellation of possible but incorrect conformations.

Alpha-synuclein **:** (α-syn) is a small soluble protein expressed primarily at presynaptic terminals in the central nervous system.

A quinine **:** Is a class of organic compounds that are formally "derived from aromatic compounds [such as benzene or naphthalene].

Carbonylation **:** Refers to reactions that introduce carbon monoxide into organic and inorganic substrates.

Chaperones **:** Proteins that assist the non-covalent folding or unfolding and the assembly or disassembly of other macromolecular structures.

Cybrid cells **:** A cytoplasmic hybrid (or cybrid, a portmanteau of the two words) is a eukaryotic cell line produced by the fusion of a whole cell with a cytoplast. Cytoplasts are enucleated cells.

Dimerization **:** A regulatory mechanism in signal transduction.

Epitope **:** Is the part of an antigen that is recognized by the immune system, specifically by antibodies, B cells, or T cells.

Fenton reaction **:** Transition metals such as Iron and Copper donate or accept free electrons intracellular reactions and help in creating free radicals.

Fibrillogenesis : Is the development of fine fibrils normally present in collagen fibers of connective tissue.

Flavonoids : (**or Bioflavonoids**) (from the Latin word flavus meaning yellow, their colour in nature) are a class of plant secondary metabolites.

Frataxin : Is a protein that in humans is encoded by the FXN gene.

Ginkgo biloba : known as the maidenhair tree, is a unique species of tree with no close living relatives.

Haber-Weiss reaction
: Generates (hydroxyl radicals) from H2O2 (hydrogen peroxide) and superoxide. This reaction can occur in cells and is therefore a possible source for oxidative stress.

Hallervorden-Spatz Disease
: (HSD) is a rare disorder characterized by progressive extrapyramidal dysfunction and dementia

Idebenone : Is a drug that was initially developed by Takeda Pharmaceutical Company for the treatment of Alzheimer's disease and other cognitive defects. This has been met with limited success.

Isoprostanes : Are prostaglandin-like compounds formed in vivo from the free radical-catalyzed peroxidation of essential fatty acids

Lipid peroxidation: Refers to the oxidative degradation of lipids. It is the process in which free radicals "steal" electrons from the lipids in cell membranes, resulting in cell damage.

Metalloprotease : Is any protease enzyme whose catalytic mechanism involves a metal.

Neurotrophins : Are a family of proteins that induce the survival, development, and function of neurons.

Oligomer : A molecule that consists of a few monomer unit in contrast to a polymer that, at least in principle, consists of a nearly unlimited number of monomers. Many oils are oligomeric, such as liquid paraffin.

Perikaryal : Related to perikaryon which is the cell body of a neuron, containing the nucleus and organelles.

Phytochemicals : Chemical compounds that occur naturally in plants.

Plasma membrane blebbing
: A **bleb** is an irregular bulge in the plasma **membrane** of a cell caused by localized decoupling of the cytoskeleton from the plasma **membrane**.

Polyphenols : Are a structural class of mainly natural, but also synthetic or semisynthetic, organic chemicals characterized by the presence of large multiples of phenol structural units.

Proteasomes : Are protein complexes inside all eukaryotes and archaea, and in some bacteria. In eukaryotes, they are located in the nucleus and the cytoplasm.

Redox-active : Protein which possesses at least one active center which mediates its participation in redox reactions, usually via reversible oxidation of a cysteine residue leading to a cysteine-sulfenic acid that can either be stabilized, or react with an unmodified cysteine residue and form a stable but reversible disulfide bond.

Siderophores : Are small, high-affinity iron chelating compounds secreted by microorganisms such as bacteria, fungi and grasses.

Spin quantum: In atomic physics, the spin quantum number is a quantum number that parameterizes the intrinsic angular momentum (or spin angular momentum, or simply spin) of a givenparticle. .

Thymoquinone : Is a phytochemical compound found in the plant Nigella sativa.

Turmeric (Curcuma longa)
: Is a rhizomatous herbaceous perennial plant of the ginger family, Zingiberaceae.

Ubiquitination : Is an enzymatic, protein post-translational modification (PTM) process.

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Introduction

Oxidative stress is caused by an imbalance between the production of reactive oxygen and a biological system's ability to readily detoxify the reactive intermediates or easily repair the resulting damage. All forms of life maintain a reducing environment within their cells. This reducing environment is preserved by enzymes that maintain the reduced state through a constant input of metabolic energy. Disturbances in this normal redox state can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. ***(Valko et. al, 2005)***

Free radicals can be overproduced or the natural antioxidant system defenses weakened, first resulting in oxidative stress, and then leading to oxidative injury and disease. Examples of this process include heart disease, cancer, and neurodegenerative disorders. Oxdation of human low-density lipoproteins is considered an early step in the progression and eventual development of atherosclerosis, thus leading to cardiovascular disease. Oxidative DNA damage may initiate carcinogenesis. Environmental sources of reactive oxygen species are also important in relation to oxidative stress and disease. A few examples include: UV radiation, ozone, cigarette smoke, and others are significant sources of oxidative stress. Current hypotheses favor the idea that lowering oxidative stress can have a health benefit***. (Yuan et. al, 2006)***

Compelling support for the involvement of free radicals in disease development originates from epidemiological studies demonstrating that an enhanced antioxidant status is associated with reduced risk of several diseases. Vitamins C and E, in the prevention of cardiovascular disease, are a notable example.