

Oxidative Stress and Electroencephalography (EEG): Unravelling the Impact on Brain Wave Patterns: A Comprehensive Review

Dr. Animesh Dey^{1*}

^{1*}Department of Allied Health Sciences Brainware University Kolkata, West Bengal, India. Email Id- deyanimesh3@gmail.com

***Corresponding author:** Dr. Animesh Dey

^{*}Department of Allied Health Sciences Brainware University Kolkata, West Bengal, India. Email Id- deyanimesh3@gmail.com

Abstract:

Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defenses, profoundly impacts brain function due to the brain's high oxygen consumption and lipid-rich environment. This review explores how oxidative stress affects EEG patterns and its implications for understanding neurological diseases. ROS overproduction leads to neuronal damage through mitochondrial dysfunction, lipid peroxidation, protein oxidation, and DNA damage. EEG, a non-invasive method to measure brain electrical activity, reveals distinct brainwave patterns (delta, theta, alpha, beta, and gamma) that can be altered by oxidative stress. Oxidative stress modifies EEG patterns by reducing magnesium levels in cerebrospinal fluid, disrupting calcium balance, and impairing mitochondrial function. This results in increased slow-wave activity, disrupted alpha rhythms, and heightened beta and gamma activities, indicating cortical hyperexcitability and impaired brain connectivity. Various neurological conditions, including epilepsy, traumatic brain injury, and neurodegenerative diseases like Alzheimer's, exhibit these EEG changes linked to oxidative stress. Studies show correlations between oxidative stress and altered EEG patterns in conditions such as epilepsy, sleep deprivation, and stress. For instance, paradoxical sleep deprivation and cognitive stressors increase oxidative stress, leading to EEG alterations. Conversely, reducing oxidative stress through antioxidants can improve EEG patterns. This review synthesizes current literature to provide a comprehensive understanding of how oxidative stress affects EEG patterns, highlighting the need for further research to uncover underlying mechanisms and improve diagnosis and treatment of neurological conditions linked to oxidative stress.

Keywords- Electroencephalography (EEG), Oxidative stress, ROS,

Introduction:

When the production of ROS exceeds the capacity of the antioxidant defenses to scavenge them, oxidative stress occurs. Since the brain is characterized by high oxygen consumption and constitutes a lipid-rich environment, it is extremely sensitive to oxidative damage. The brain's electrical activity is recorded to obtain the data using EEG, which serves as an essential tool for understanding how oxidative stress affects oscillations and rhythms in neural activity.¹ The purpose of the review is to thoroughly analyze the impact of ROS on EEG patterns and explain how this might help understand neurological diseases.

Mechanisms of Oxidative Stress in the Brain:

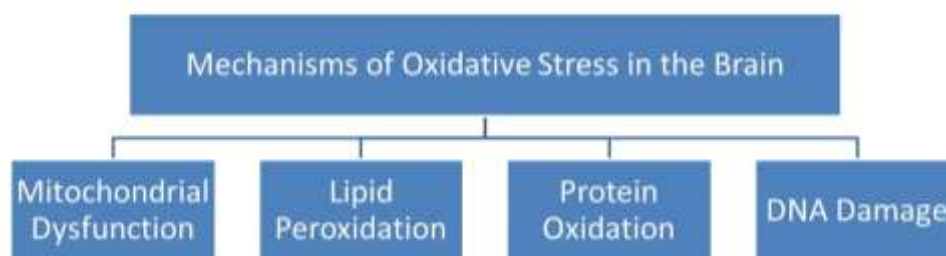


Fig-1: Mechanisms of Oxidative stress in Brain

The overproduction of ROS such as superoxide anions, hydrogen peroxide, and hydroxyl radicals occurs. These molecules can cause damage to lipids, proteins, and DNA through the oxidation process. Oxidative stress can result in mitochondrial dysfunction, lipid peroxidation, protein oxidation, and DNA damage in neurons.² These

reactive molecules can damage cellular components, including lipids, proteins, and DNA. In neurons, oxidative stress can lead to:

- **Mitochondrial Dysfunction:** Impairment of mitochondrial function results in reduced ATP production and increased ROS generation.
- **Lipid Peroxidation:** Oxidative degradation of lipids affects membrane integrity and function.
- **Protein Oxidation:** Modification of proteins can disrupt their structure and function, affecting cellular signaling pathways.
- **DNA Damage:** Oxidative modifications to DNA can lead to mutations and impaired cellular functions.

EEG and Brain Wave Patterns-



Fig: 2- EEG stages with details

EEG or electroencephalography is a highly used method for measuring and recording the electrical activity of the brain. It is a non-invasive approach that includes the use of electrodes placed on the scalp to catch and record the electrical signals that brain produces. These signals, also known as brainwaves, can give useful information about brain functioning and activity. Besides, according to the character in terms of frequency and amplitude, the EEG waves are divided into the following categories. It is necessary to underline that the frequency ranges are approximate and may vary a little from the one source to another. Also, factors such as age, mental condition, and specific clinical diseases, for example, can affect the existence and characteristics of these waves. Often experts seek EEG waves patterns to analyze the brain activity and make predictions if there are some anomalies or patterns that correlate with some neurological disorders or types of consciousness.

• **Delta waves** – delta is the slowest brain wave recorded on the EEG apparatus. It ranges from 0.5 to 4 Hz. This type of wave is usually associated with coma, deep slumber, or some other clinical condition, and it has a high amplitude. Healthy people's delta waves can be present when an individual is deeply relaxed and calm or when in a meditation state. However, a person's delta wave is less visible when they are up and about;

• **Theta waves** – Theta waves (frequency: 4 – 8 Hz) are more frequent during fatigue, daydreaming, or light slumber because they are slower than alpha waves. They can be seen in young children, hypnosis, or some forms of meditation. Increased theta activity in the brain may occasionally be related to memory loss or trouble focusing.

- Alpha waves (frequency: 8 – 13 Hz) occur when the individual is awake but relaxed with closed eyes. Alpha waves are most commonly seen in the occipital portion of the brain, and they have normal and rhythmic waveforms. Whenever the subject opens their eyes or activates mentally or visually, alpha waves will disappear or aggravate.
- Beta waves (frequency: 13 – 30 Hz) are associated with concentration, attentiveness, and alertness. Beta has a lower amplitude but a higher frequency than alpha waves. Beta waves are subdivided into two categories based on the number of frequency values they contain. Low beta wave having frequency from 13 to 17 Hz and high beta wave having frequency from 17 to 30 Hz. High beta activity increases when one is under tension or concerned. EEG's quickest wave,
- Gamma wave is the most acceptable term for it. The gamma wave frequency ranges from 30 to 100 Hz. They are associated with reasoning functions and attention to understanding sensations. Gamma waves are common in people who are working or in certain states of awareness.³

Impact of Oxidative Stress on EEG Patterns:

Oxidative stress affects EEG patterns by producing reactive oxygen species which alter magnesium's capacity to pass through the blood-brain barrier. For that reason, the amount of magnesium located within the cerebrospinal fluid diminished, resulting in a severe and fast decline of magnesium absorption.⁴ Consequently, Stress-mediated oxidative damage is mainly due to the increase in OH* generated during cellular destruction. Oxidative stress is a term used to describe a situation in which the organism's ability to detoxify reactive oxygen species (ROS) or fix the injury they cause is overwhelmed by their production. ROS are chemically reactive molecules that can damage DNA, lipids and other biological molecules. Oxidative stress occurs when the processes producing ROS exceed antioxidant protection mechanisms.⁵ Neuronal function is significantly affected by oxidative stress.⁶ It is taken into account that neurons have been especially vulnerable to oxidative stress due to their increased metabolic activity, high lipid content and minimal regenerative capabilities. The injury to biological components present in neurons, including the outer membrane, proteins, and DNA, are also appropriate. Neuronal energy can be impaired by oxidative stress and the normal function of these cells in the human body may be disrupted. Oxidative stress also impairs the mitochondria, the cells that make the energy required for living. ROS can destroy the mitochondrial DNA and the electron transport chain. Destruction of the mitochondria structure pursuant to this mechanism described above can eventually being not able to produce enough energy, boost ROS creation and cause oxidative stress to the structure of the neuron neuro-inflammation.⁷ Inflammatory processes that elicit the formation of ROS are doomed to failure. For the conventional situation for synaptic failure, antisynaptic neurotransmission and neuro-degeneration, neuro-inflammation becomes a factor. Excitotoxicity can be brought on or heightened by oxidative stress. When combined, ROS can disturb the calcium balance and create the feeling that neurons can be ruined by the overabundance of Ca²⁺ ions in this manner. One of the numerous disorders in which inhibitory mechanisms are important is excitotoxicity. Due to calcium and ROS, it has been the subject of study in many neurological illnesses. Neuronal excitability can be impaired by oxidative stress, causing oxidative damage.⁸ Oxidative stress can negatively affect synaptic plasticity. Disruption in the synaptic connection of various areas of the brain can have an adverse effect on cognitive activity again. All in all, oxidative stress impedes synaptic learning and memory capacity. Oxidative stress can have a negative impact on neurotransmission. Oxidative stress, for example, diminishes glutamate's removal from extracellular space, causing more substantial excitability. Excitotoxic therapeutic apoptotic cell death results from the increase in extracellular glutamate levels, and if levels are elevated enough, neurons lyse. Excitability caused by oxidative stress is not only dangerous per se but also capable of causing further neurodegenerative processes. Oxidative stress is considered a significant factor in neurodegenerative diseases. Neurodegenerative issues such as Alzheimer's, Huntington's and Parkinson's illnesses are characterized by a progressive loss of neurons and memory function loss. Some previously performed post-mortem autopsies demonstrated oxidative stress energy production malfunctions.⁹ The role of oxidative stress in the digenesis of neurological disorders can be highlighted by reviewing EEG deviations throughout the course of the illness. EEG analyses can provide additional information about the disease's course and severity. Epilepsy is a disease in which neuronal malfunction due to neurotransmitter systems perpetually leads to episodes of seizures.¹⁰ It has been demonstrated that oxidative stress is the erector and accelerator of epilepsy. Researchers may use the information from here to study how oxidative stress affects epilepsy by comparing EEG. The secondary damage on Traumatic brain injury

can be heavily reliant on oxidative stress and may lead to death if not permanently treated. ROI may mutate into anoxic due to straightforward blow weakening if not healed, which may be an irreversible life-severity issue. Due to the significant factors address, it can cause a bad influence on EEG depending on the duration. The sections are only contemplated to present the readers with the idea; also, note without any medical or biology the provisions may sound challenging; therefore, it is best to provide research for better understanding.¹¹

Several studies have explored the connection between EEG and oxidative stress. For example, Taguchi et al. undertook a study in mice and discovered that low neuronal Irs2 preserve stable superoxide dismutase (Sod) levels in the brain throughout feeding. According to these results, there is a link between brain signalling pathways and oxidative stress.¹² Another study revealed a correlation between the down-regulation of Wrn and redox homeostasis, glucose metabolism, and oxidative stress. It also proved an association between Wrn expressions and increasing levels of oxidative stress caused by the loss of sleep.¹³ Other research has proven a significant association between this syndrome and oxidative stress. For example, epileptic encephalopathy accompanied by severe EEG anomalies and drug-resistant seizures has been connected with oxidative stress. Additionally, oxidative stress was found to be relevant to COVID-19, a common viral infection that can target the central nervous system. Pro-inflammatory cytokines infiltrate the central nervous system, causing seizures, stroke, electrolyte imbalance, and mitochondrial dysfunction, which all contribute to oxidative stress. Another factor affecting oxidative stress in the brain is sleep deprivation.¹⁴ Singh et al. have shown that paradoxical sleep deprivation enhances oxidative stress in the brain, affecting various parameters, such as a decrease in glutathione levels and superoxide dismutase activity, in a brain-region-dependent pattern. Similarly, stress has a significant impact on oxidative metabolism and brain activity.¹⁵ It has been noted that in disturbed animals are transferred to a novel cage in the control group and display a noticeable increase in body temperature and a reduction in locomotors activity accompanied by an overall increase in EEG power. This EEG intensity anomaly vanished at the end of the stressful situation. Subordinates animals' brain activity changed during the social stress test, and this was accompanied by a slow, stable reduction in EEG power in the 4.2–30 Hz frequency. Moreover, a strong, transient raise in delta-wave activity was detected, which was followed by an increase in EEG power after social stress when animals were placed back in their own cage. The power of neither group was changed in EEG gamma oscillations due to social stress interaction, but in the defeat animals, it increased following the operation. Defeated subordinate animals show a decrease in EEG power and slow-wave activities, which may indicate higher brain activity and higher oxidative metabolism. Since the brain has a high metabolic rate and is susceptible to ischemic injury, it is especially vulnerable to oxidative damage. Stroke, traumatic brain injury, and neurodegenerative diseases are all connected to oxidative stress. Hence, there is a solid need to understand the role of oxidative stress in various brain pathologies for intervention and potential treatments. In conclusion, multiple studies have demonstrated the relationship between EEG and oxidative stress. All of the previously presented studies proposed that alterations in brain activity, neurological conditions, and sleep deprivation influence oxidative stress variables. Since these are only correlative, it is imperative to determine the etiological basis of oxidative stress in the brain in the years to come to develop an appropriate intervention.¹⁶

This review is intended to present a general understanding of how oxidative stress affects EEG pattern changes through synthesizing the published literature. Future research can be directed toward understanding the underlying mechanism and filling gaps. The same sections of this knowledge will eventually improve diagnosis and treatment of neurological conditions linked to oxidative stress. EEG patterns can be changed in different ways due to the effect of oxidative stress, demonstrating the influence on the organism's brain activity. The EEG alterations that have shown a connection with oxidative stress include: 1. Increased slow-wave activity, oxidative stress has been shown to increase slow-wave activity in the EEG, likely reflecting damaged or dysfunctional neurons. 2. Disruption of alpha rhythm, the alpha rhythm is a characteristic EEG oscillation frequency that occurs at approximately 8–13 HZ and indicates an alert and relaxed state of mind. Furthermore, oxidative stress can alter the frequency, coherence, or power of the alpha rhythm. 3. An increase in beta and gamma activity is another change in the EEG, which is the effect of oxidative stress on the beta 14–30 Hz and gamma bands. These alterations represent cortical activity or cortical hyperexcitability.¹⁷ EEG patterns may change as a result of oxidative stress in a variety of ways, reflecting changed brain activity. Here are a few EEG changes linked to oxidative stress that have been noticed:

Increased slow-wave activity: It has been demonstrated that oxidative stress increases the EEG's slow-wave (delta and theta) activity. This increase in slow-wave activity can be a sign of damaged or dysfunctional neurons. Alpha

rhythm disruption: The alpha rhythm is a noticeable EEG oscillation that happens at about 8 to 13 Hz and is connected to a calm and aware state. Oxidative stress can throw off the alpha rhythm, which can result in changes to its frequency, coherence, or power. An increase in beta and gamma activity is another effect of oxidative stress on the EEG's beta (14–30 Hz) and gamma (30–100 Hz) frequency bands. These changes can represent cortical activation or hyperexcitability.¹⁸

According to EEG coherence or synchronization analyses, oxidative stress might impair the functional connectivity between various brain regions. This break in connection may be a result of poor information integration or communication across different brain regions. It's significant to highlight that oxidative stress-induced changes in EEG patterns can occur in a variety of neurological diseases and are not exclusive to any one disorder. In order to make correct assessments, EEG patterns should be analyzed in conjunction with clinical symptoms and other diagnostic procedures. EEG patterns offer vital information about how the brain is functioning. Several diseases, including neurodegenerative diseases, aging, and psychiatric disorders.¹⁹ They have investigated the effects of oxidative stress on EEG patterns. For example, recreational ecstasy and MDMA users, who are known to experience increased oxidative stress, have been found to display altered EEG patterns.¹⁹ These findings suggest that oxidative stress can have a detrimental impact on EEG activity. On the other hand, there is evidence that reducing oxidative stress can have positive effects on EEG patterns. Furthermore, studies have investigated the effects of different stressors on EEG activity. Cognitive stressors have been shown to result in reduced alpha and increased beta power in task-related brain areas.¹⁸ Paradoxical sleep deprivation, which is known to induce oxidative stress, has been found to produce brain region-specific changes in oxidative stress parameters, including decreases in glutathione levels.¹² Sleep deprivation has also been associated with altered levels of cytokines, lymphocytes, and oxidative stress markers.²⁰ In summary, oxidative stress can have significant effects on EEG patterns. Increased oxidative stress has been associated with altered EEG activity in recreational ecstasy/MDMA users and lipopolysaccharide-induced sepsis. On the other hand, reducing oxidative stress through interventions such as antioxidant therapy or reducing insulin-like signaling can have positive effects on EEG patterns. Different stressors, including cognitive stressors and sleep deprivation, have also been shown to influence EEG activity. Further research is needed to fully understand the mechanisms underlying these effects and to explore potential therapeutic interventions for oxidative stress-related alterations in EEG patterns.²⁰

Different mechanisms may be responsible for the changes in EEG patterns brought on by oxidative stress. According to the study tailored nanoparticles (NP) are responsible for one process that results in reactive oxygen species (ROS). ROS formation and consequent oxidative stress can be caused by changes in the structural and physicochemical characteristics of NP, such as changes in particle surface, size, composition, and metal content.²¹ According to this study, this oxidative stress can then influence cellular reactions such as mitochondrial respiration, NP-cell contact, and immune cell activation, all of which lead to ROS-mediated damage. The part that oxidative stress plays in neurodegenerative disorders is another mechanism. Alzheimer's disease (AD) has been linked to oxidative stress, and NADPH oxidase activation, a significant ROS generator, has been seen in the brains of AD patients.²² The connection between oxidative stress and neurodegeneration raises the possibility that it potentially plays a role in changes to EEG rhythms. Additionally, oxidative stress has been linked to central nervous system alterations and mental tiredness. According to studies, mental exhaustion can cause changes in resting-state EEG power, which may be an indication of abnormalities in brain systems linked to oxidative stress.²³ In schizophrenia and other associated illnesses, oxidative stress has also been connected to changes in antioxidant defense mechanisms, which can affect EEG patterns.²⁴

Overall, oxidative stress-induced changes in EEG patterns can be attributed to a number of mechanisms, including the production of ROS by engineered nanoparticles, its role in neurodegenerative diseases, its effect on mental fatigue, and its association with particular conditions like aortic valvular stenosis and exposure to air pollution. For the purpose of creating predictive models and potential therapies for EEG changes brought on by oxidative stress, it is essential to comprehend these pathways.

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