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A BRIEF REVIEW OF CNS DISORDERS AND THEIR PATHOPHYSIOLOGY, VARIOUS TYPES OF TREATMENTS TO TREAT DISORDERS AND SOME PRECAUTIONS

Mohd Abid[1]*, Nadir Khan[1], Mohd Yunus[1], Alimuddin[1], Hemant Singh[1], Sheeba Naaz[2], Mohd Faizan[1], Nazar Khan[1], Ishanul Haque[1]

[1]Department of Pharmacology, Janta college of Pharmacy, Noorpur, Bijnor, 246734, U.P., India.
[2]Department of Pharmacology, RVIT, Bijnor, 246701, U.P., India.

***Corresponding Author: Dr. Mohd Abid**
Professor, Janta College of Pharmacy, Noorpur, Bijnor, 246734, U.P., India.
Email ID: fromabid@yahoo.com

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ABSTRACT

A mental illness is a health problem that significantly touches how a person impressions, reflects, behaves, and interrelates with other people. Advance in science and skill has funded to an enormous improvement in the excellence of life of humankind. However, up-to-date life stress, related trials and tribulation are responsible for the surge in the incidence of a variety of psychiatric disorders. Central nervous system disorders are various types and grades of severity. Some of the main types are depression, anxiety, schizophrenia, bipolar mood disorder, personality disorders, and eating disorders. Mental and behavioral disorders are not limited to, any singular group: they are present in people of all areas, countries and all humanity's. About 450 million people hurt from mental disorders. One person in four will grow one or more mental or behavioral disorders With unipolar depressive disorders, bipolar affective disorder, schizophrenia, epilepsy, alcohol and nominated drug use disorders, Alzheimer's and other dementias, post-traumatic stress disorder, obsessive and compulsive disorder, panic disorder and primary insomnia during their lifetime.

KEYWORDS: Central nervous system, schizophrenia, epilepsy, alcohol, Alzheimer's and dementias etc.

INTRODUCTION

A mental illness is a health problem that significantly touches how a person impressions, reflects, behaves, and interrelates with other people. Advance in science and skill has funded to an enormous improvement in the excellence of life of humankind. However, up-to-date life stress, related trials and tribulation are responsible for the surge in the incidence of a variety of psychiatric disorders.

Central nervous system disorders are various types and grades of severity. Some of the main types are depression, anxiety, schizophrenia, bipolar mood disorder, personality disorders, and eating disorders.

Mental and behavioral disorders are not limited to, any singular group: they are present in people of all areas, countries and all humanity's. About 450 million people hurt from mental disorders.[1] One person in four will grow one or more mental or behavioral disorders With unipolar depressive disorders, bipolar affective disorder, schizophrenia, epilepsy, alcohol and nominated drug use disorders, Alzheimer's and other dementias, post-traumatic stress disorder, obsessive and compulsive disorder, panic disorder and primary insomnia during their lifetime.[2] Mental and behavioral disorders are current at any point in time in about 10% of the adult population universal. One fifth of teenagers below the age of 18 years suffer from developmental, emotional or behavioral problems.[3] Five of the ten foremost causes of disability worldwide are psychiatric conditions, including depression, alcohol use, schizophrenia and compulsive disorder.[4]

Neuropsychiatric conditions account for 13% of disability adjusted life years (DALYs), intentional injuries for 3.3% and HIV/AIDS for the extra 6%. These latter two have a behavioral constituent linked to mental health. Moreover, behind these oft-repeated figures lie enormous human suffering.

- More than 150 million persons suffer from depression at any point in time;
- Nearly 1 million commit suicide every year;
- About 25 million suffer from schizophrenia;
- 38 million suffer from epilepsy; and
- More than 90 million suffer from an alcohol- or drug-use disorder

Abuse of alcohol and other materials continues to be one of the most serious public health problems in both developed and developing countries. Worldwide, alcohol accounted for 4% of the full burden of diseases in 2000.

In Latin American countries, alcohol was the foremost risk factor for the global burden of diseases in 2000. Of an estimated 246,000 alcohol-related deaths in this region, about 61,000 were due to accidental and intentional injuries.[5]

One in four adults−about 61.5 million Americans−experiences mental illness in a given year. One in 17−about 13.6 million−live with a serious mental illness such as schizophrenia, major depression or bipolar disorder.[6]

About 18.1 percent of Americans adults−about 42 million people−live with anxiety disorders, such as panic disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), generalized anxiety disorder and phobias.[7]

1.1 Correlation of Mental disorders with other disorders

It is becoming increasingly clear that mental functioning is fundamentally interconnected with animal and social functioning and health outcomes. For example, depression is a risk factor for cancer and heart diseases. Mental disorders such as depression, anxiety and material use disorders in patients who also suffer from physical disorders may result in poor compliance and failure to adhere to their treatment schedules.

Furthermore, a number of actions such as smoking and sexual activities have been linked to the growth of physical disorders such as carcinoma and HIV/AIDS. Among the 10 leading risk issues for the global burden of disease measured in DALYs, as identified in the World Health Report 2002, there were mental/ behavioral (unsafe sex, tobacco use, alcohol use) and three others were significantly affected by mental/behavioral factors (overweight, blood pressure and cholesterol).[5]

2. Anxiety

Anxiety disorders, the most prevalent psychiatric illnesses in the universal community are present in 15 to 20 percent of medical clinic patients. Anxiety, defined as a subjective sense of unease, dread or forbidding, can indicate a primary psychiatric condition, or it can be a constituent of, or reaction to, a primary medical disease. The primary anxiety disorders are classified according to their period and the course and the life and nature of precipitants.[8] About one-third of medical patients awarding with anxiety have an organic etiology for their psychiatric symptoms, but an anxiety disorder can also present with somatic symptoms in the deficiency of diagnosable medical condition.[9]

The biological bases of fear and anxiety are now recognized, and the major brain structures and neuronal circuits involved in emotional information processing and behavior are delineated. Emotional and cognitive processes cannot be dissociated, even when considering such a basic emotion as fear. The cognitive apprehension of events and situations is critically involved in emotional experiences and also influences coping strategies or defense mechanisms.[10]

2.1 Etiology and pathophysiology

Anxiety disorders are thought to result from deviations in benzodiazepine receptor and GABA (A) receptor/chloride ion channel regulation. Benzodiazepines are thought to bind two discrete GABA receptor sites type I, which has broad neuro-anatomic distribution and type II, which is focused on the hippocampus, striatum and neocortex. Pharmacological differences in sensitivity to benzodiazepine receptor subtypes are related to drug differences in sedation, memory impairment and anti-anxiety efficacy. Serotonin also appears to have a role in the neurobiology of anxiety.[11]

3. Depressive Disorders

Major depression is defined as depressed mood on a daily basis for a smallest duration of two weeks. An episode may be categorized by sadness, indifference or apathy, or irritability and is usually related to changes in the number of neurovegetative functions, including sleep patterns and hunger and weight, motor agitation or retardation, fatigue, impairments in concentration and choice making, feelings of shame or guilt, and thought of death or dying. Patients with endogenous depression have a profound loss of choice in all enjoyable activities, exhibit early morning awakening, and feel that the dysphoric mood state is qualitatively different from sadness.[12]

3.1 Etiology and pathophysiology

The neurobiology of depression is ill understood. It has been suggested that neural networks involving prefrontal cortex and the basal ganglia may be primary sites of deficit. Involvement of the serotonin system is recommended by findings of lower plasma tryptophan levels, a decreased cerebra-spinal fluid level of 5-hydroxyindolacetic acid (the major metabolite of serotonin in the brain), and reduced platelet serotonergic transporter binding. A growth in brain 5HT receptors in suicide victims is also described.[13]

4. Stress disorders

Stress is a state of threatened homeostasis or disharmony caused by intrinsic or extrinsic adverse forces and is counter-acted by a complicated repertoire of physiologic and behavioral responses that aim to re-establish the challenged body equilibrium. The adaptive stress response is contingent upon an elaborate neuroendocrine, cellular, and molecular infrastructure, the stress system. Crucial functions of the stress system response are mediated by the hypothalamic-pituitary-adrenal (HPA) axis and the central and peripheral mechanisms of the autonomic nervous system (ANS).[15]

4.1 Pathophysiology of stress

Animals exposed to distressing actions over which they have no control response by releasing corticosteroids. The sympathetic branch of the nervous system is ongoing, also releasing epinephrine and norepinephrine. Thus, if prolonged, lead to structural deviations in the brain. Changes occur in neurons and their synapses in the hippocampus and medial prefrontal cortex. These produce damages in working memory and spatial memory, as well as increased aggression. Total, the hypothalamus releases corticotrophin releasing hormone (CRH) and vasopressin, which start the HPA axis. CRH cause to release corticotrophin from anterior pituitary, which travels through the bloodstream to the adrenal cortex, where corticotrophin then up regulates cortisol production. Vasopressin another hormone stimulates the cortical collecting ducts of the kidneys to growth, uptake of water, resulting in lesser volumes of urine formed. As the next unit will illuminate, corticosteroids such as cortisol act across the entire body to circulate the stress response.[15]

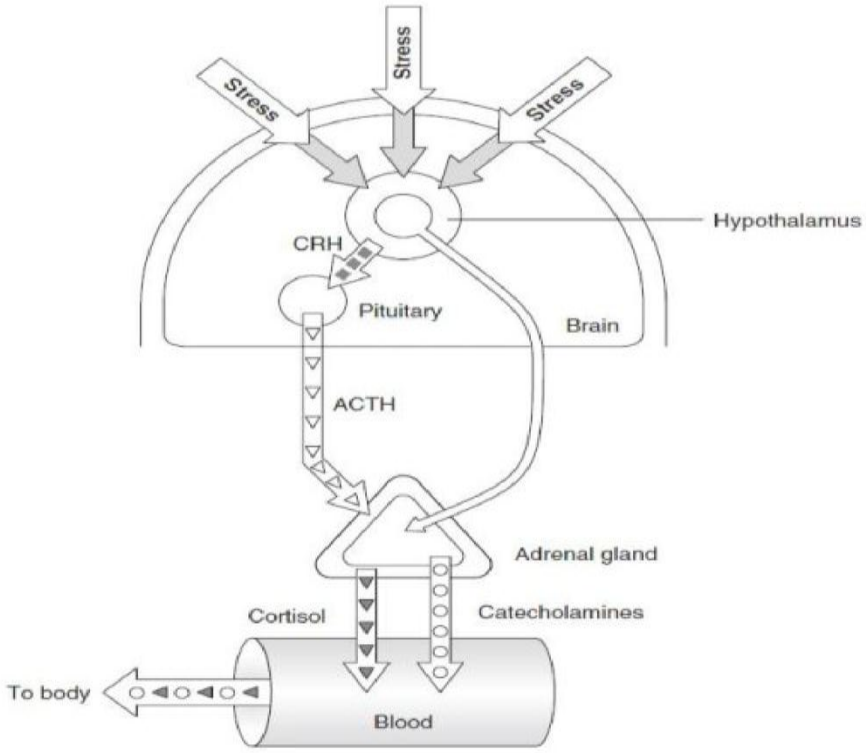

Fig. 1: Schematic diagram of how stress affects the body.[16]

5. Alzheimer

Alzheimer's disease (AD), also known as Alzheimer disease, or just Alzheimer's, interpretation for 60% to 70% of cases of dementia. A chronic neurodegenerative disease that usually starts slowly and becomes worse over time. The most common early symptom is difficulty in remembering new events (short-term memory loss). As the disease developments, symptoms can include: problems with language, disorientation (including easily getting lost), mood swings, loss of motivation, not managing self-care, and behavioral issues.[17]

5.1 Pathophysiology of Alzheimer

5.1.1 Neuropathology

Alzheimer's disease is characterized by loss of neurons and synapses in the cerebral cortex and certain sub cortical areas. This loss results in gross atrophy of the affected areas, with degeneration in the temporal lobe and parietal lobe, and parts of the frontal cortex and cingulate gyrus.

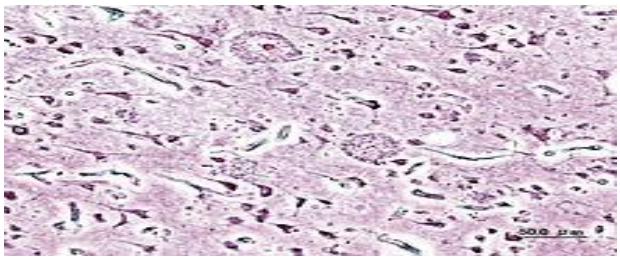

Fig. 2: Histopathologic image of senile plates seen in the cerebral cortex of a person with Alzheimer's disease of presenile onset. Silver impregnation.

Together amyloid plaques and neurofibrillary tangles are clearly visible by microscopy in brains of those troubled by AD. Signs are dense, mostly insoluble deposits of beta-amyloid peptide and cellular material outside and around neurons. Twists (neurofibrillary tangles) are aggregates of the microtubule-associated protein tau, which has become hyperphosphorylated and accumulate inside the cells themselves. While many older individuals develop some plates and tangles as a

consequence of ageing, the brains of people with AD have a greater number of them in specific brain regions such as the temporal lobe.[18]

Alzheimer's disease has been identified as a protein misfolding disease (proteopathy), caused by plate accumulation of abnormally folded amyloid beta protein, and tau protein in the brain.

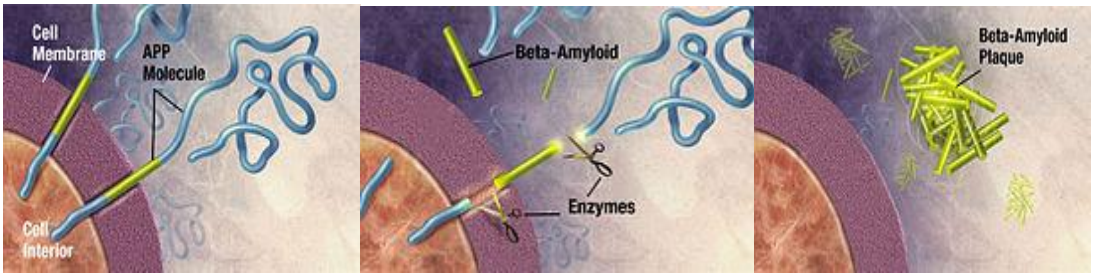

Fig. 3: Enzymes act on the APP (amyloid precursor protein) and cut it into fragments. The beta-amyloid fragment is crucial in the creation of senile plaques in AD.[19]

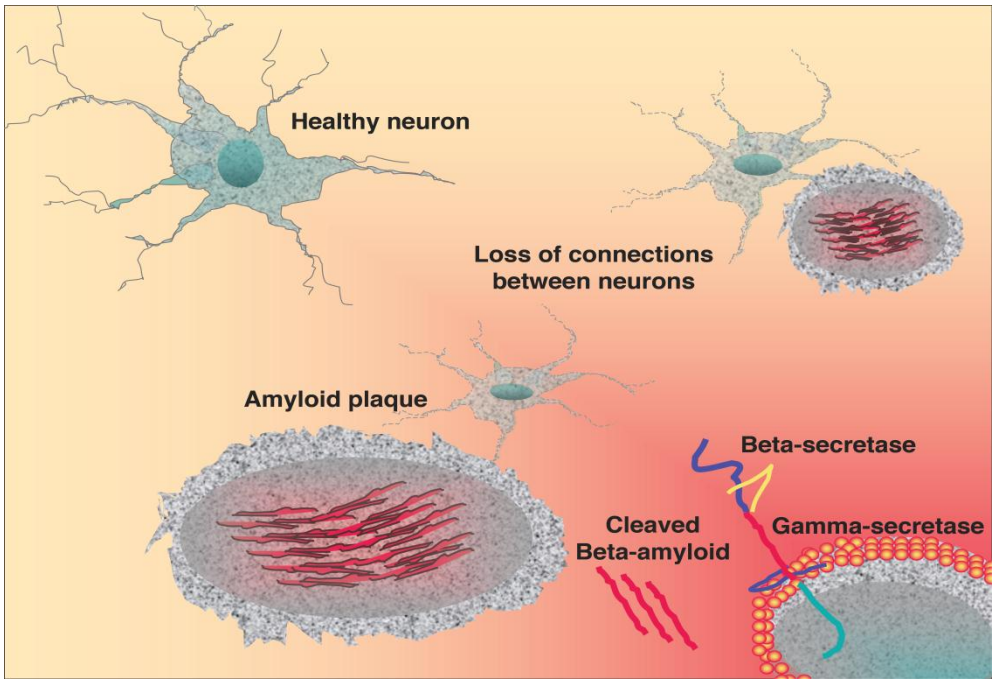

Fig. 4: Amyloid precursor protein (APP) is an integral membrane protein, highly expressed throughout the body. Extracellular amyloid plaques produce loss of connections between neurons and decreased neuronal activity.

As research continues to discover details of the disease process of dementia and AD, previously known pathophysiology is coming to the head of treatment; the roles of tau proteins in neurofibrillary tangles and beta amyloid in neuritic plates (also known as amyloid or senile plaques) is being explored. Neurofibrillary twists and plates are found mostly in AD, but are also present in fronto-temporal dementia and other diseases. Together the tangles and plaques occur naturally in the aging process, but are seen in excess in AD. In the creation of plaques, the large precursor protein known as amyloid precursor protein (APP) is cleaved into smaller protein fragments.[20,21,22]

6. Epilepsy

Epilepsy (from Ancient Greek), is a common and different set of chronic nervous disorders characterized by seizures. Some definitions of epilepsy require that seizures are recurrent and unprovoked.[23] But others require only a single seizure combined with brain alterations which increase the chance of a future. Epileptic seizures result from abnormal, excessive or hyper synchronous neuronal activity in the brain seizures.[24] About 50 million people worldwide have epilepsy and nearly 90% of epilepsy occurs in developing countries.[25] Onset of new cases occurs most frequently in infants and the elderly.[26]

6.1 Pathophysiology

Glutamate, an excitatory neurotransmitter, may therefore be released from these neurons in large amounts, which — by compulsory with close glutamatergic neurons triggers excessive calcium (Ca^{2+}) release of these post-synaptic cells. Such excessive calcium release can be neurotoxic to the affected cell. The hippocampus, which contains a large capacity of just such glutamatergic

neurons (and NMDA receptors, which are permeable to the Ca2+ entry after binding of both glutamate and glycine), is especially exposed to epileptic seizures, subsequent spread of excitation and possible neuronal death. Another possible mechanism involves mutations leading to ineffective GABA (the brain's most common inhibitory neurotransmitter) action. Epilepsy-related mutations in some non-ion channel genes have also been identified. Much like the channelopathies in voltage-gated ion channels, several ligand-gated ion channels have been linked to some types of frontal and generalized epilepsies.[27,28]

7. Parkinsonism

Parkinson's disease (PD) is a progressive neurodegenerative movement disorder that is likely to affect approximately 1% of the population older than 65 years of age.

The pathological hallmarks of Parkinson's disease (PD) are marked loss of dopaminergic neurons in the substantia nigra pars compacta (SNc), which causes dopamine depletion in the striatum, and the presence of intracytoplasmic inclusions known as Lewy bodies in the remaining cells. It remains unclear why dopaminergic neuronal cell death and Lewy body formation occur in PD. The pathological changes in PD are seen not only in the SNc but also in the locus coeruleus, pedunculo pontine nucleus, raphe nucleus, dorsal motor nucleus of the vagal nerve, olfactory bulb, parasympathetic as well as sympathetic post-ganglionic neurons, Mynert nucleus, and the cerebral cortex. Widespread neuropathology in the brainstem and cortical regions are responsible for various motor and non-motor symptoms of PD. Although dopamine replacement therapy improves the functional prognosis of PD, there is currently no treatment that prevents the progression of this disease. Previous studies provided possible evidence that the pathogenesis of PD involves complex interactions between environmental and multiple genetic factors. Exposure to the environmental toxin MPTP was identified as one cause of parkinsonism in 1983. In addition to MPTP, other environmental toxins, such as the herbicide paraquat and the pesticide rotenone have been shown to contribute to dopaminergic neuronal cell loss and parkinsonism. In contrast, cigarette smoking, caffeine use, and high normal plasma urate levels are associated with lower risk of PD. Recently, Braak and coworkers proposed the "Dual Hit" theory, which postulated an unknown pathogen accesses the brain through two pathways, the nose and the gut. Subsequently, a prion-like mechanism might contribute to the propagation of α- synuclein from the peripheral nerve to the central nervous system. Approximately 5% of patients with clinical features of PD have clear familial etiology. Therefore, genetic factors clearly contribute to the pathogenesis of PD. Over the decade, more than 16 loci and 11 causative genes have been identified, and many studies have shed light on their implication in, not only monogenic, but also sporadic forms of PD. Recent studies revealed that PD-associated genes play important roles in cellular functions, such as mitochondrial functions, the ubiquitin-proteasomal system, autophagy-lysosomal pathway, and membrane. In this chapter, we review the investigations of environmental and genetic factors of PD.[29]

7.1 Pathophysiology of Parkinsonism

It was reported that mitochondrial dysfunction, oxidative stress[32] and impairment of the Ubiquitin-Proteasome System (UPS) might represent the principal molecular pathways that commonly underlie the pathogenesis of PD.[29]

7.2 Oxidative free radicals

Free radicals, namely sensitive oxygen species (ROS) and reactive nitrogen species (RNS) are known to cause damage to lipids, proteins, enzymes and nucleic acids important to cell or tissue injury occupied in the procedure of elderly. Wide range of degenerative diseases, including inflammation, cancer, atherosclerosis, diabetes, liver injury, Alzheimer, Parkinson, and coronary heart pathologies is due to these free radicals and oxidative stress.[33]

Cells generally defend themselves against ROS damage with enzymes such as superoxide dismutase and catalase. Minor molecule antioxidants such as ascorbic acid (vitamin C), uric acid, and glutathione also play important roles as cellular antioxidants. Also, polyphenol antioxidants assist in preventing ROS damage by thorough free radicals. The negative effects of ROS on cell metabolism include roles in programmed cell death and apoptosis, while positive effects include induction of host defense genes and organization of ion transport systems. In specific, platelets involved in wound repair and blood homeostasis release ROS to recruit extra platelets to sites of injury. These also carry a link to the adaptive immune system via the occupation of leukocytes. Sensitive oxygen species are involved in cardiovascular disease, hearing impairment via cochlear damage induced by elevated sound levels, ototoxicity of drugs such as cisplatin and in congenital deafness in both animals and humans.[35]

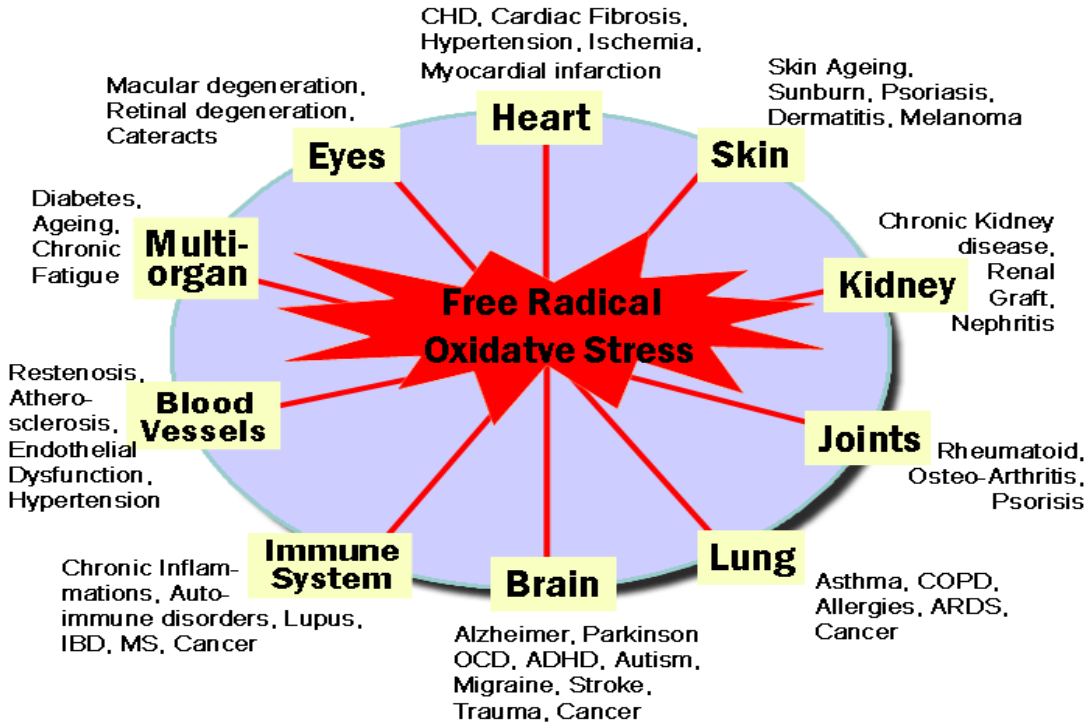

Fig. 5: Oxidative free radical complications.[36]

Careful systems against free radicals /Anti oxidants:
All aerobic systems of lifecycle continue elaborate anti-free-radical defense systems, also known as antioxidant systems.

Enzymes: The safety enzyme, superoxide dismutase (SOD), takes hold of molecules of superoxide – a mainly destructive free radical-and variations them to a much less reactive form. SOD and another important antioxidant enzyme set, the glutathione system, work inside the cell. Flowing biochemical reacts like uric acid and ceruloplasmin with free radicals in the intercellular spaces and bloodstream.

Self-repairing: The body also has systems to repair or replace damaged building blocks of cells. Most protein parts in the cell are completely changed every few days. Scavenger enzymes break used and damaged proteins into their piece parts for reuse of the cell. Nutrients: Vitamins and other nutrients neutralize the Oxy radicals' and help as a second line of cover. Among the many substances used are Vitamins C and E, beta-carotene, and bioflavonoid.[37]

7.3 Cerebral Ischemia/Reperfusion

Brain damage as a result of reduced blood flow, e.g. stroke and cerebral ischemia; represents a complex pathological event which has been extensively investigated. Furthermore, the release of excitatory neurotransmitters, such as glutamate, induces a cascade of reactions in the postsynaptic neurons that stimulates the release and metabolism of arachidonic acid via lipoxygenase pathways resulting in the formation of ROS. The liberation of ROS during the oxidation of dopamine by monoamine oxidase in the nerve terminals of dopaminergic neurons may produce an increment of oxidative stress in brain regions, such as substantia nigra. Neurons are nonreplicating cells and any damage to brain tissues by the ROS tends to be cumulative over time, depending on the density of such neurons, this could cause localized lesions in the nervous system.

Two types of cerebral ischemia could be discriminated viz. global and focal cerebral ischemia. Both types may share common pathway of cell death, but the sequence of events that triggers tissue damage may be completely different.

Global cerebral ischemia characterized by affecting the entire forebrain, being severe of short duration and followed by recirculation. Moreover, tissue damage in this type is usually confined to the neuronal population and cell death is characteristically delayed by hours or days.

Focal cerebral ischemia localized to a part of the brain, encompassing a densely ischemic core (focus) and a less densely ischemic perifocal zone, which is known as the penumbra zone. Focal ischemia may be of long duration or even permanent, producing infarction of all the tissue elements within the involved vascular territory.

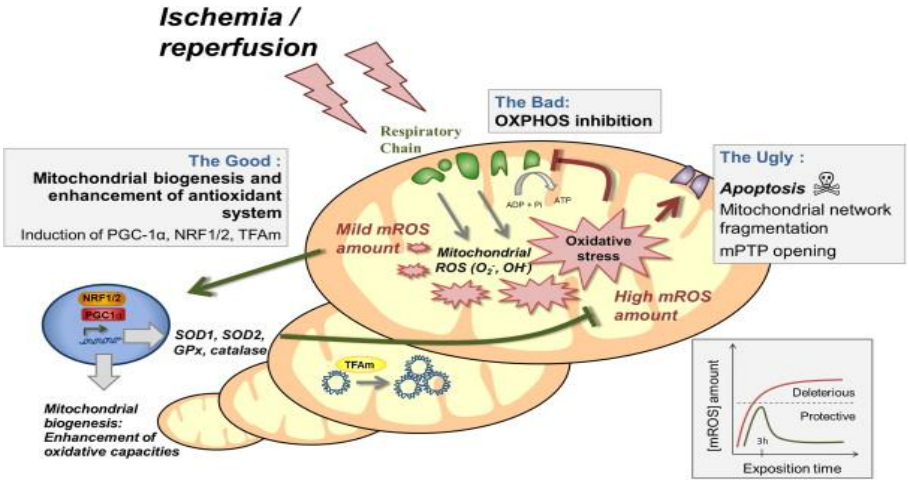

Fig. 6: Pathopysiologyo I/R inury.

Over the past decade, research has demonstrated that the consequences of cerebral ischemia result in two temporally distinct processes of neuronal cell death, which in turn affect surrounding brain tissue. Each of them has characteristic defining morphologic and molecular features, and the distinction between the two processes is based on morphologic findings on electron microscopy. Apoptosis or programmed cell death, a process associated with genomic fragmentation, is characterized by cell shrinkage, chromatin aggregation, and preservation of cell membrane integrity and mitochondria without inflammation and injury to surrounding tissue). Conversely, necrosis, a process that is not ‘‘regulated or programmed,’’ is typically observed as a consequence of severe cerebral ischemia and characterized by disruption of cellular homeostasis from energy failure due to severe mitochondrial injury.[38]

8. Recent advancement in treating CNS disorders

8.1 Gene therapy

CNS illnesses are very hard to treat with present therapy used due to the complication of the nervous system. Vector-mediated gene transfer is a not like method to treat CNS disorders that holds much benefit.

Parkinson’s disease (PD) is a neurological disease formed by the loss of dopaminergic neurons in the substantia nigra and the striatum. It was found that by a gene therapy process, delivering some neurotrophic factors improve the motor purpose in-patient.[39]

8.2 Advancement in diagnosis and therapy of neurodegenerative disorders

Dr. Andreas Weiss is studying about misfolded proteins and biomarker/translational assays, which would be beneficial as diagnostic tools to inform about disease progression, patient stratification and therapeutic effect.

8.3 Neurotrophins and neurodegenerative diseases

Neurotrophic reasons or neurotrophins group consists of nerve growth factor (NGF), neurotrophin 3 (NT3), brain-derived neurotrophic factor (BDNF), and neurotrophin 4 (NT4). They take ability to regulate differentiation and to care growth during growth of the vertebrate nervous system. There is a considerable number of psychiatric and neurodegenerative disorders are linked to altered NGF and BDNF levels and with changed expression of their receptors. For example, neurodegenerative Alzheimer’s disease (AD) is experimental in a mouse model in which antibodies neutralized almost half of the NGF level.[41] Extra neurodegenerative disorder, Down’s syndrome (DS), exhibits similar NGF signaling shortages in the same region of the brain.[40] In fact, Neurotrophins have a good role in preventing cell death of basal forebrain cholinergic neurons (BFCNs). This accomplishes that Neurotrophin-based therapies may be useful to treat neurodegenerative diseases.

8.4 Brain Stimulation Techniques

There are 50 million obsessive-compulsive illness (OCD) patients worldwide. Current studies on the epidemiology of estimate 50 million suffer from OCD, thus creation it a global problem. The treatment of OCD has changed significantly with introduction of careful serotonin reuptake inhibitors; approximately 60% of patients get improved. However, some patients remain hardy to the standard pharmacological and behavioral treatments. Besides pharmacological, behavioral, and neurosurgical approaches, unlike brain stimulation methods—transcranial magnetic stimulation, deep brain stimulation, and electroconvulsive therapy—have been investigated. Yet, positive result regarding efficacy, tolerability, and non-invasiveness and/or reversibility of these methods has increased interest in investigating their usage in treatment-resistant OCD.[41]

8.5 Transcranial magnetic stimulation (TMS)

TMS offers the magnetic field over the surface, producing powerful but brief magnetic fields that induce electrical currents in the brain, radically differs from the presently popular use of low-level static magnetic fields as alternative therapies.[42]

Although TMS is able to affect many brain functions, including movement, visual perception, memory, attention, speech, and mood, but the mechanism how it

works, remains unclear. Numerous animal studies exposed about the understanding of the mechanism of TMS. For example, TMS enhances apomorphine-induced stereotypy and reduces immobility in the Porsolt swim test.[43] It reported that TMS significantly modified the monoamines and their receptors in the brain cortex after electroconvulsive therapy (ECT).[44]

8.6 Vagus nerve stimulation (VNS)

8.6.1 History

For some years, scientists have been paying careful in whether and how motivation of cranial nerves might food vary in developed cortex. In the year 1930s, Bailey and Bremer exposed that stimulation of the vagus nerve in cats produced, organized activity in the cortex of the orbital gyrus.[45] VNS in the neck may perhaps quiet the muscle reduction in the abdomen that reasons vomiting, that is, convulsive reduction this study was done by Dr. Zabara at Temple University. Coming this idea comes into the question of whether recurrent valgus inspiration might also improve epilepsy. In 1985, Zabara recognized the anticonvulsant action of VNS on trial removals in dogs.[46]

8.7 Deep brain stimulation (DBS)

8.7.1 Technique

In this technique, a thin electrode is inserted directly into the brain. Then, unlike currents are applied at varying depths until the desired effects is created. Newly, DBS at different targets within the basal ganglia has developed an appealing therapeutic alternative in late stage Parkinson's disease. High incidence (> 80Hz) electrical stimulation of the mid thalamus or subthalamic nucleus has been found effective in this chronic neurological disorder.[47]

8.8 Synthetic nanoscale Vesicles

A side of Ben-Gurion University (BGU) scientists in Beersheva, Israel, has produced a system of, called V-Smart drug delivery technology, to allow oral medications to pass complete biological membranes, target sites in the brain and selectively release the drugs.

The nano-sized vesicles are made of definitely designed structures called bolaamphiphiles. The synthetic sacs, which are highly stable, control the release of the drugs that permit through biological barriers and target the place where the drug will be released in the brain and reduce side effects by making the medications extra open at target locations.

"The achievement of this V-Smart therapeutic should ultimately provide extra effective treatment for patients with CNS sicknesses and improve their lives," Dr. Heldman concluded.[48]

8.9 Ultrasound

The scholars of the Queensland University used the application of multiple iterations of scanning, ultrasound of the mouse brain to eliminate Amyloid beta (Aβ) plaque. It was observed that microloglial cells were activated by the high-frequency sound waves generated by the ultrasonic equipment which digest and eliminate the amyloid plaques that destroy brain synapses meanwhile this technique is able to temporarily open the blood-brain barrier that clear toxic protein clumps and restoring memory functions. To check the efficacy of this treatment, the scientists used spinning disk confocal microscopy and high-resolution three-dimensional reform to confirm that the ultrasound treatment had meaningfully reduced the extent of the Aβ toxic plaques. Noninvasive Alzheimer's treatment restores memory-using ultrasound 2015.[49]

9. Nutrition/diet, exercise and wellness in the treatment of CNS disorders

Nutrition and Wellness would be a source /method in the treatment of CNS disorders because good nutrition provides the base for a good mood. Several studies demonstrating that depression are more common when a population is consuming a high fat, refined diet through a low intake of fruit and vegetables. Whereas, a more natural diet with lots of fruit, vegetables and fish seems to offer extra relief.[50]

There is a connection between our brain and digestive structure via Vagus nerve and they are constantly in contact with one another. If the brain were not healthy, stomach would not be the healthy leading to weakness other organ of the body, mainly CNS because of insufficient absorption and supply of the nutrition from the diet or any other source. This moves overall mood and leads to systemic inflammation, which directly affects hormones and immune regulation. This can lead to inflammation in the brain, which directly impacts the hypothalamus affecting the areas of sleep, stress, weight, in addition to impacting the sympathetic nervous system.[51]

Healthy diets, such as those rich in omega-3 fatty acids and curcumin, have been shown to raise levels of particles important for daily brain function, for example, brain-derived neurotrophic factor which considered commonly beneficial for maintaining neuronal function and for promoting.[52,53] Dietary supplementation with nutrients such as omega-3 fatty acids and those of the herb curcumin can exert their influences on repair, controlling cellular energy metabolism and repairs of neural circuits important for learning and memory and for locomotion.[54]

Polyphenols are a large group of chemical substances found in plants characterized by the presence of multiple phenol groups. Polyphenols have great antioxidant properties, and some of the major groups described for their effects on the CNS are curcuminoids and flavonoids. Curcumin is the principal curcuminoid found in the Indian plant turmeric, which has gotten a reputation for its strong medicinal capacity. Flavonoids are created in many fruits and vegetables or their

subproducts, such as berries (e.g., blueberries, strawberries), tea, and red wine. Flavonoids can take positive effects on cognition for the treatment of brain diseases and brain injury.[55] The mechanisms by which flavonoids exert their movements in neural healing are diverse, for example, by promoting neuronal signaling and by increasing, making of anti-oxidant and anti-inflammatory agents. Like to higher dietary intake of omega-3 fatty acids, increased consumption of berry fruit shows a positive impact on dipping cognitive decay in aged rodents.[56]

Curcumin has been shown to advantage the brain by providing protection, through multiple mechanisms, against neurologic disorders. As an antioxidant, anti-inflammatory, and antiamyloidal agent, curcumin can increase cognitive purpose in patients with Alzheimer disease (AD). Amusingly, the even use of turmeric in India has been likely as one of the main reasons for the low percentage of clinical cases of AD in India[57] (Chandra V *et al*., 2001). In an animal study, curcumin has been shown to assist recovery after cerebral ischemia/reperfusion injury by preventing blood– brain barrier damage.[58]

9.1 Fasting and exercise

It is stated that fasting every other day has been observed to protect neurons in the hippocampus against excitotoxicity-induced death.[59] It was practiced in one study, rats that were placed on an every-other-day fasting diet for 2–4 months, showed better-preserved memory than rats fed ad libitum. The fact that fasting can increase levels of brain brain-derived neurotrophic factor, which influences metabolic agents on brain plasticity.[60]

Exercise exerts the properties of the brain and spinal cord by supporting the maintenance of the synaptic structure[61] axonal elongation[62] and neurogenesis in the adult brain.[63] Exercise has the size to enhance learning and memory under a variety of conditions, from selection to counteract the mental decline with age. It was observed that exercise is a significant strategy to provide protection against mental disorders and to slow the degenerative effects of aging.[64]

10. Reason of CNS Disorders

Apart from the nutrition/diet, exercise, etc. there are a number of over-all factors, which affects the normal life/mental disturbance by the humans like loss of beloved, loss in business, workload in job, accident, dispute in the Home, ages etc.

10.1 Medication

There are so various drugs, which directly or indirectly affect the CNS, they are as follows: Effects of benzodiazepines, with lorazepam are fatigue, drowsiness, amnesia, memory impairment, confusion, disorientation, depression, unmasking of depression, disinhibition, euphoria, suicidal ideation/attempt, ataxia, asthenia, extrapyramidal symptoms, convulsions/seizures tremor, vertigo etc.[65]

10.2 Antibiotics

Although sepsis is one of the main risk factors for delirium, antibiotics and anti-infective agents may also produce changes in mental status.[66,67] Inhibition of GABA may be involved in fluoroquinolone- and penicillin-induced delirium. Penicillin can induce psychosis and encephalopathy.[68]

This class includes drugs with known anticholinergic properties such as the first-generation, sedating antihistamines (eg, diphenhydramine, hydroxyzine, chlorpheniramine, meclizine), antispasmodics (eg, belladonna, diphenoxylate, clinidium, dicyclomine, hyoscyamine), oxybutynin, trazodone, ipratropium bromide, tricyclic antidepressants (which are discussed separately under antidepressants), phenothiazines (eg, thioridazine, prochlorperazine, promethazine, chlorpromazine, fluphenazine), muscle relaxants (cyclobenzaprine, orphenadrine), mydriatics (atropine, homatropine, tropicamide), diphenoxylate/atropine, antiparkinsonian agents (eg, benztropine, trihexyphenidyl), and antiarrhythmics (eg, disopyramide, quinidine, procainamide). Further, other drugs which may have possible anticholinergic effects include codeine, colchicine, warfarin, digoxin, furosemide, haloperidol, isosorbide dinitrate, meperidine, nifedipine, cimetidine, ranitidine, prednisolone, quinidine, and theophylline.[69,70] Many drug classes starting with the prefix "anti" have anticholinergic properties (eg, antihistamines, antidepressants, antipsychotics, antispasmodics, antiparkinsonian drugs, and some antihypertensives) and may help alert the practitioner to drugs that may be a source of confusion in their patients.[71]

10.3 Anticholinergic

Anticholinergic agents have been causally linked to the development of memory impairment in healthy subjects. Memory impairment may be associated with basal forebrain cholinergic pathways, whereas changes in consciousness seen in delirium may be attributable to alterations in pontine cholinergic pathways projecting into the frontal cortex and brain stem. Acetylcholine is also involved with attention, the sleep-wake cycle, and other aspects of cognitive functioning.[72]

10.4 Anticonvulsants

All anticonvulsants can affect cognition, even in the presence of therapeutic drug levels. They may cause drug-induced delirium or dementia.

10.5 Antidepressant

It is significant to note that in the elderly, depression may extend as pseudodementia. So, the disease process itself can induce cognitive impairment. However, tricyclic antidepressants are notorious for producing adverse CNS side effects such as delirium, disorientation, and memory

injury in the elderly owing to their highly anticholinergic properties. The most common and specific feature of tricyclic-induced cognitive injury in the elderly is impaired short-term recall memory.[73] Other types of injury include reduced reaction time, reduced retrieval from secondary memory, and reduced information processing.[74]

10.6 Antiparkinsonisms Drugs

Approximately 20% to 30% of patients with Parkinson's disease have an attendant dementia.[74] As with patients with other neuropsychiatric conditions, Parkinson's patients may be especially prone to the growth of drug-induced cognitive impairment. One of the drugs that are most often associated with changes in mental status is levodopa. About 5% of patients grow delirium from the use of this drug Cummings, 1991), although cognitive symptoms may occur in up to 60% of patients.[75]

10.7 Antipshychotics

As with other psychoactive medications, the risk of developing drug-induced cognitive impairment may be dose related. However, age may also be a significant risk factor for the growth of this condition. Various traditional antipsychotics possess anticholinergic properties (eg, thioridazine, chlorpromazine, trifluoperazine), which may partly explain the predisposition of this class of drugs to the growth of delirium and faster cognitive decline. One of the fresher atypical, clozapine is also highly anticholinergic. Other atypical that are devoid of important anticholinergic effects, such as respiration, appear less likely to reason drug-induced delirium.[76]

10.8 Corticosteroids

One of the proposed theories of what causes delirium is improved CNS cortisol levels. Exogenously administered corticosteroids may produce a comparable effect. Corticosteroids can induce together delirium and chronic cognitive impairment as well as psychosis. Use of high-dose steroids (> 80 mg/day of prednisone), long period of use, or the abrupt discontinuation of these hormonal agents can induce mental position changes. Even brief exposure to high doses of steroids can reversibly affect neuronal activity in the hippocampus, the part of the brain associated with memory; with continued use, permanent wound occurs. Overall, there is a medium risk of cognitive-induced damage secondary to this class of drugs.

Amongst the antihypertensive that historically have been associated with significant adverse CNS things (both delirium and dementia) is methyldopa. This drug products cognitive injury and decreased visual motor performance.[77] Methyldopa acts like a false neurotransmitter being changed to alpha-methyl-noradrenaline. In general, centrally acting antihypertensive such as clonidine and guanabenz is associated with more adverse cognitive effects. Reserpine irreversibly damages noradrenergic storage granules, thereby inducing altered mental function.[78]

10.9 Alcohol and related drugs

Alcohols produce depression and insomnia.

Marijuana decreased motivation, depression, paranoia, impaired memory.

Steroids anabolic/Andreno-genius (roids, juice) causes aggressiveness and mood swings.

Solvents-Inhalants like Acetone, Freon’s, nitrous oxide leads to brain damage.

Depressants like Alcohol, ladies, barbiturates etc. produces convulsions, depression, disorientation, insomnia

Stimulant drugs like Cocaine, crack, amphetamines, diet pills cause headaches, depression; malnutrition, anorexia, strokes, seizures.

Narcotics- Smack, codeine, heroine produces sleepiness.[79]

12. CONCLUSION

This review article may be helpful for the brief study of CNS disorders and their pathophysiology, various types of treatments to treat disorders, some precautions like life style, maintaining diet and exercise and in the last drugs induced the CNS disorders.

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14. CONFLICTS OF INTEREST

There are no conflicts of interest.

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