

## MENTAL DISORDER ASSOCIATED WITH NEUROLOGICAL DISEASES

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### ABSTRACT

Central Nervous System disorder are the among the leading causes of morbidity and mortality worldwide. One of the main causes of India's burden of communicable and non-communicable diseases is neurological disorder, both deadly and non-fatal. In this review, we will focus on various neurological diseases, such as ADHD, Autism, Alzheimer, Parkinson's disease, neurofilament proteins have become one of the most significant bodily fluid biomarkers of neuro-axonal damage.

### INTRODUCTION

The rapidly developing fields of neuroscience, neurology, and psychiatry seek to comprehend the intricate mechanisms underlying brain function and malfunction in addition to creating efficient treatments for a range of neurological and mental conditions. Twelve excellent submissions from authors worldwide were accepted for the special issue.<sup>[1]</sup> These submissions covered a wide range of subjects and conditions, including bipolar disorder, depression, anxiety, autism, addiction, pain, epilepsy, Parkinson's disease, Huntington's disease, Alzheimer's disease, and SCZ. The brain ailment known as stroke.

Global mental health has emerged as a significant new viewpoint on mental illnesses and their management in the twenty-first century. This new field builds on developments in implementation science, mental epidemiology, human rights movements, and cross-cultural psychiatry.<sup>[2]</sup> Advances and criticisms in the subject have focused especially on psychiatric nosology. The Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM- III), was crucial because it offered a method that tried to avoid employing many etiology models and instead concentrated on trustworthy diagnostic criteria.<sup>[3]</sup> These concepts were frequently employed in psychiatric research on mental illness, epidemiological studies of mental illness. A significant amount of nosological science work has been included into and given momentum by the World Health Organization's (WHO) most recent versions of the DSM (DSM-5) and the International Classification of Diseases (ICD-11). The WHO was founded in 1948 and has since grown to become a major proponent of global health, embodying the fundamental principles of this approach,

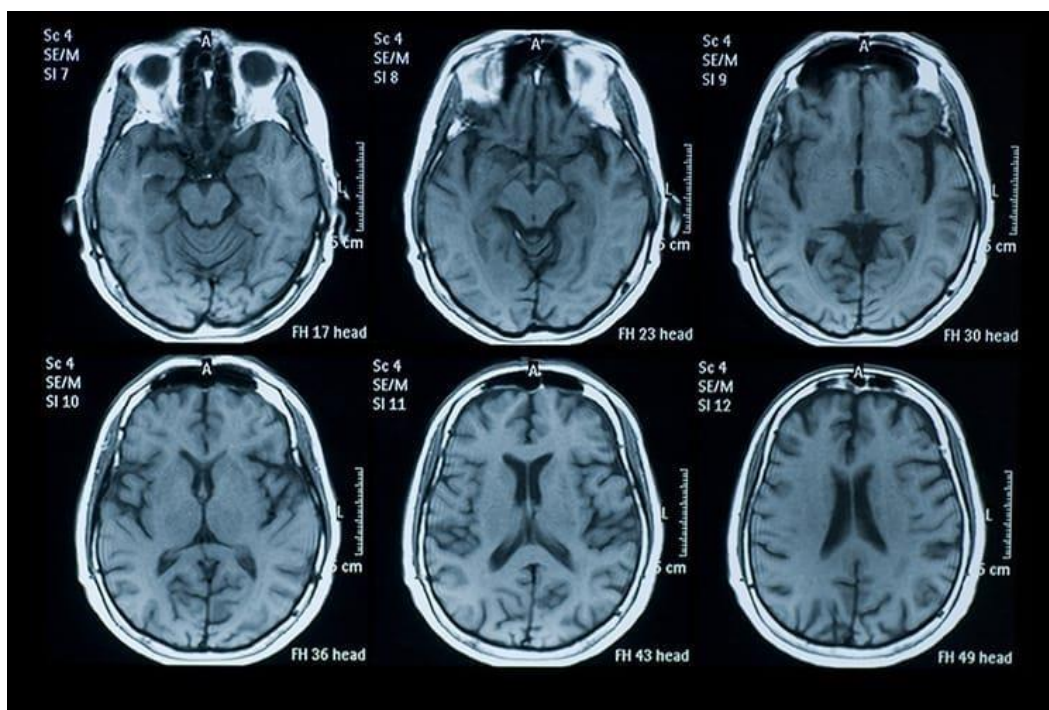
such as the understanding that health is a public good that requires assistance from all governmental sectors, that health encompasses a spectrum from wellness to illness, and that biological, sociocultural, and environmental factors determine health.<sup>[4][5]</sup>

### Mental Functioning

To a certain degree, a neurological examination can evaluate how neurological disease and damage affect brain function in terms of behavior, memory, or cognition. This field is the specialty of behavioral neurology. Furthermore, clinical neuropsychology use neuropsychological evaluation to accurately detect and monitor mental functioning issues, typically following a neurological impairment or brain injury.<sup>[6]</sup> Numerous conditions, including neurological disorders, mental health disorders, trauma, and substance addiction, can affect mental functioning, resulting in behavioral changes, mood swings, and cognitive impairments. In order to properly diagnose, treat, and support people who are having cognitive or emotional difficulties, it is essential for both the neurological and psychiatric sectors to comprehend mental functioning and how it is disrupted. The fields are specialized in behavioral neurology. Additionally, neuropsychological testing is used in clinical neuropsychology. Mental functioning can be disrupted by various factors, such as neurological diseases, mental health disorder, trauma, or substance abuse, leading to cognitive impairments, mood disturbance, and behavioral change. Mental functioning in relation to neurological disorder can be significantly affected, depending on the specific disorder and the areas of the brain involved. Here are some key aspects:<sup>[7]</sup>

**1. Cognition:** Disorder like Alzheimer's and other dementias can leads to impaired memory, problem -

- solving skills, and decision-making abilities.
- 2. Attention:** Condition such as ADHD can result in difficulty focusing, maintaining attention and organizing tasks.
  - 3. Language:** Aphasia, often seen in stroke patients, affects the ability to speak or understand language.
  - 4. Executive Functioning:** Disorders like frontal lobe damage can impact planning, reasoning and self-control
  - 5. Mood and Emotion:** Neurological condition can lead to changes in mood regulation, resulting in anxiety, depression, or emotional instability
  - 6. Perception:** Conditions such as visual processing disorders can affect how individuals interpret sensory information
  - 7. Social Cognition:** Neurological disorders can impact social skills, empathy, and understanding social cues.
  - 8. Behavior:** Changes in behavior, such as impulsivity or aggression, can occur in condition like frontal lobe injuries or autism spectrum disorderS.



#### • Pathophysiology

Neurological disorders arise from various mechanisms that disrupt the normal framework and function of the brain and nervous system.

Several molecular mechanisms are involved in this process, depending on the type of cell death, including apoptosis, necrosis, autophagy, and necroptosis.

#### Here's an overview of these key mechanisms

Neurological diseases often involve various forms of cell death, contributing to neurodegeneration. This process occurs in diseases like Alzheimer's and Parkinson's, often triggered by misfolded proteins or mitochondrial dysfunction.

Necrosis is another form of cell death, characterized by an uncontrolled process due to trauma, ischemia or oxidative stress, leading to inflammation, commonly seen in stroke and traumatic brain injuries.<sup>[8]</sup> Autophagy is a cellular process that degrades damaged organelles and proteins, acting protectively in early stages of neurodegeneration but potentially leading to cell death if excessively misfolded proteins or mitochondrial

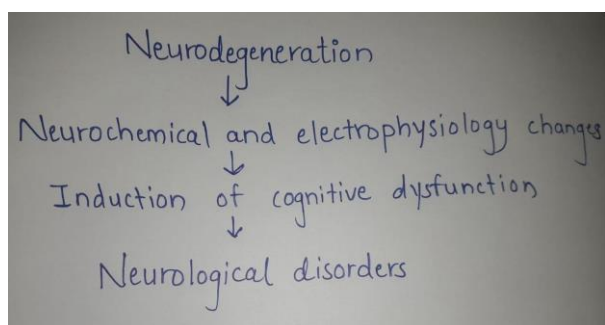
dysfunction. Autophagy is a cellular process that degrades damaged organelles and proteins, acting protectively in early stages of neurodegeneration but potentially leading to cell death if excessively activated. Finally, necroptosis is a regulated form of necrosis mediated by RIPK1, RIPK3, and MLKL, which drives inflammation and plays a role in conditions such as ALS and multiple sclerosis.<sup>[9]</sup>

This pathway is regulated by the family of anti- and pro-apoptotic B cell lymphoma-2 (BCL-2) protein family members, which can be divided into three subgroups according to their structure and function and the presence of conserved areas known as BCL-2 homology (BH) motifs. Among these are the BH3-only proteins, the anti-apoptotic proteins, and the essential effectors of apoptosis that form oligomers that cause mitochondrial outer membrane permeabilization (MOMP), which releases apoptogenic factors that encourage the activation of caspase (aspartate-specific cysteine proteases).<sup>[10]</sup> The complex and multifactorial mechanisms are:

Disrupted excitable domains: This can affect the nervous

system's axonal structures, myelination, and mitochondrial distribution

Cellular homeostasis changes: These changes can include excitotoxicity, cytoplasmic Ca overload, overproduction of reactive oxygen and nitrogen species, energy failure, and inflammation.



### • CAUSES

**Neurological disorders can be caused by a variety of factor including**

- Genetic Factors : Inherited mutation can lead to conditions like Huntington's disease and certain forms of muscular dystrophy.
- Infection :Viral or bacterial infections, such as meningitis or Lyme disease, can affect the nervous system.
- Trauma : Head injuries from accidents can result in conditions like traumatic brain injury (TBI) or post-concussion syndrome.
- Degenerative Disease : Conditions such as Alzheimer's Parkinson's and amyotrophic lateral sclerosis (ALS) involve progressive degeneration of nerve cells.
- Autoimmune Disorder : Conditions like multiple sclerosis occur when the immune system mistakenly attacks nerve tissues.
- Environmental Factors : Exposure to toxins (like heavy metals or pesticides) can contribute to neurological issues
- Vascular Issues : Stroke or vascular malformations can lead to neurological deficits.
- Metabolic Disorder : Imbalances in the body's metabolic processes, such as in diabetes or thyroid disorders, can affect brain function.
- Development Disorders : Conditions like autism spectrum disorder and attention – deficit hyperactivity disorder (ADHD) arises during brain development.
- Lifestyle Factors : Poor diet, lack of exercise, and substance abuse can contribute to the risk of developing neurological condition.

### • Symptoms of Neurological Disorder

One of the most common manifestation is persistent headaches, which can vary from tension – type

headaches to debilitating migraines. Seizures are another critical symptom, characterized by abnormal electrical activity in the brain, leading to convulsions or loss of consciousness. Motor function impairments are prevalent, with individuals experiencing weakness, paralysis, or difficulties with coordination and balance, often affecting their ability to perform daily tasks. Sensory disturbances, such as numbness, tingling or hypersensitivity, may arise, indicating issues with nerve signaling. Cognitive symptoms can include memory loss, confusion, and difficulties with concentration or problem-solving, often impacting academic or occupational performance. Emotional and behavioral changes are also common, with many individuals facing depression, anxiety, or mood swings. In more severe cases, symptoms can escalate to include altered consciousness or profound cognitive decline, significantly affecting the individual's quality of life and necessitating comprehensive medical evaluation and intervention. Understanding these symptoms is crucial for timely diagnosis and effective management of neurological disorder.<sup>[11]</sup>

- Motor issues: Weakness, tremors, coordination problems, or paralysis.
- Sensory Changes : Numbness, tingling, or loss of sensation in certain body parts.
- Cognitive Changes : Memory loss, difficulty concentrating, confusion, or impaired judgment.
- Seizures: Episodes of abnormal electrical activity in the brain, leading to convulsions or loss of consciousness.
- Speech Difficulties : Trouble speaking, slurred speech, or difficulty understanding language.
- Emotional Change : Mood swings, anxiety, depression, or change in behavior.
- Sleep Disturbances : Insomnia, excessive sleepiness, or disrupted sleep patterns.
- Headaches : Frequent or severe headaches, including migraines.
- Loss of Coordination : Difficulty with balance or performing fine motor tasks.

### • Common Preventions of Neurological disorders

Regular physical activity can help keep your heart healthy, improve your mood and sleep, and lower your risk of depression and anxiety. Managing chronic condition such as hypertension, diabetes and high cholesterol is also crucial, as they are significant risk factors for many neurological disorders. Vaccination against infections like meningitis and encephalitis, as well as good hygiene practices, helps prevent neuro-infectious diseases. Additionally, wearing protective gear during high -risk activities, like helmets when biking, can prevent traumatic brain injuries. Early detection and regular check- ups, particularly for those with a family history of neurological conditions, play key role in mitigating the progression of diseases like Alzheimer's and Parkinson's. Public health efforts, such as education on stroke symptoms and prompt treatment, are also essential in reducing the long-term impact of



neurological disorder.<sup>[12]</sup>

- **Major Diseases involved in Neurological Disorder ADHD**

Attention-deficit/hyperactivity disorder (ADHD) is a developmental disorder that affects a person's behaviour: The neurological and neurodevelopmental illness known as ADHD is typified by recurrent patterns of hyperactivity, impulsivity, restlessness, and inattention that start in childhood. Originally identified as a clinical diagnostic in the 1930s, ADHD is widely known in the pediatric population. However, attention is now being paid to the diagnosis and treatment of the illness in adults. The prevalence of ADHD in adults is estimated to be between 2 and 3%. Furthermore, a number of mental problems, such as mood disorders, oppositional and antisocial personality disorders, substance misuse, and self-harm, have been found to be substantially associated with ADHD. These disorders dramatically increase the burden on families and society. Due mostly to the absence of established, reliable diagnostic criteria, adult ADHD has received less attention in epidemiological studies than ADHD in children.<sup>[13]</sup>

- **Symptoms**

People with ADHD may have trouble paying attention,

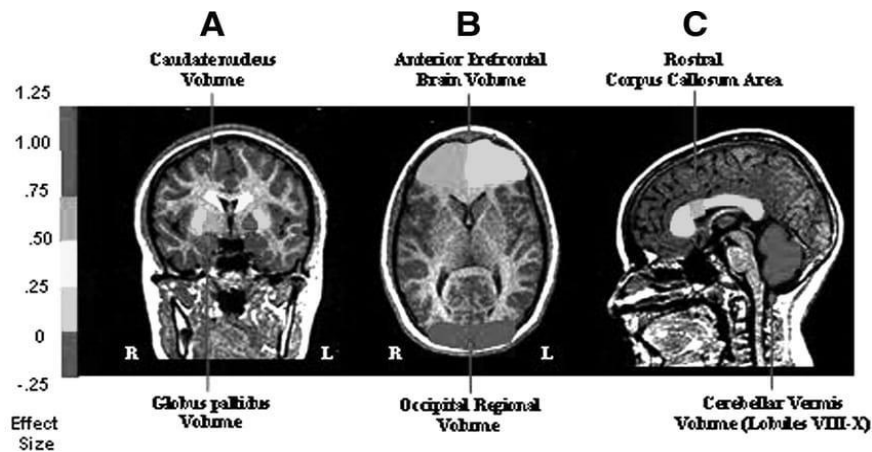
be hyperactive or act impulsively. Other symptoms include disorganization, forgetfulness, and difficulty completing tasks.

- **Treatment**

The cornerstone of care for patients with ADHD is still pharmaceutical therapy. The cornerstone of ADHD treatment is stimulants. About 70% of patients find them to be effective. Two is the number that needs to be treated. Every subtype of stimulant has several formulations, such as sustained release, long-acting, immediate-release, and extended-release. Blood pressure fluctuations, a decrease in appetite and sleep, and the possibility of dependency are among side effects of stimulants.<sup>[14][15]</sup>

- **Risk factors and causes**

Risk factors and causes of ADHD The reason of ADHD is unknown to specialists. Studies indicate a major hereditary component to the illness. If it is inherited, you can have a higher chance of having it. Additionally, you may have a higher chance of having it if you: suffered a brain injury. were born to a mother who drank or smoked when she was carrying you. Were born prematurely or with low birth weight.



- **ASD**

The neurological disorder known as autism spectrum disorder is typified by communication difficulties, repetitive activities, and social skills issues. The word "spectrum" refers to the broad range of symptom types and intensities that people with autism experience.<sup>[17]</sup>

- **Sign and Symptoms**

ASD symptoms typically become noticeable in early childhood, often before age 3. These symptoms can include:

- Social communication difficulties : Repeating words or phrases, hand-flapping, rocking, or insisting on following certain routines.
- Sensory sensitivities : overreaction or underreaction to sensory stimuli like sounds, lights, textures, or smells.

- Genetics : Research has identified multiple gene therapy.
- Environmental factors : Certain prenatal exposures, such as advanced parental age or maternal infections during pregnancy, may increase the risk.
- Brain development : Abnormalities in brain development and connectivity might also play a role.<sup>[18][19]</sup>

- **Diagnosis**

**Common step included**

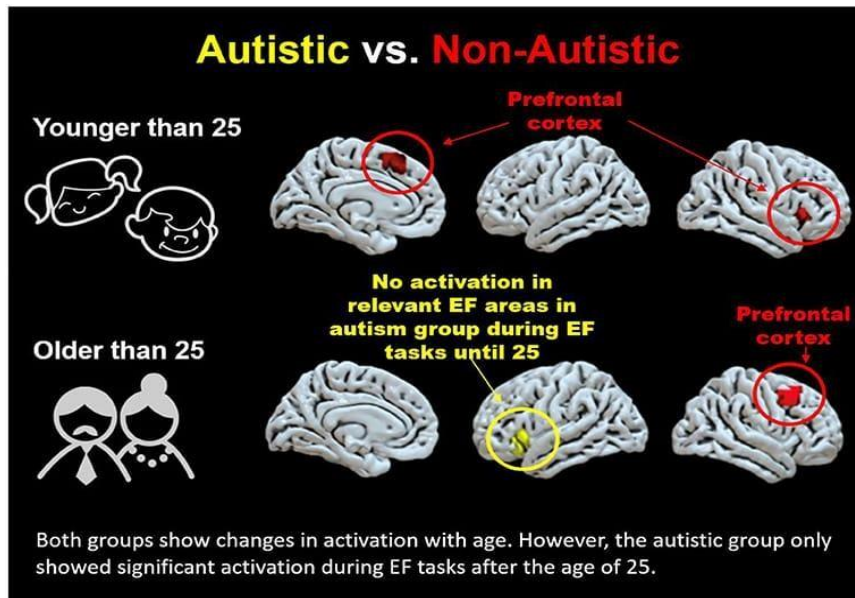
- Development screening : Checking if a child is reaching developmental milestones.
- Comprehensive diagnostic evaluation : Involves physical exams, cognitive assessment, and parent interviews. A multidisciplinary team, including neurologists, psychologists and speech therapists,

may be involved.<sup>[20]</sup>

- **Treatment and Management**
- Behavioral therapy : Most widely used therapies in teaching social, communication, and learning skills.
- Occupational therapy : Assists in developing everyday skill such as dressing, eating and

interacting with the environment.

- Medications : Though there is on specific medication for autism, certain medication may be used to manage symptoms such as anixety, hyperactivity or mood disorder.<sup>[21]</sup>



- **Bipolar disorder**

Extreme mood fluctuations, including manic and depressive episodes, are hallmarks of bipolar disorder, a psychiatric illness. While primarily classified as a psychiatric disorder, research increasingly suggests that neurological factors also play a significant role. When bipolar disorder occurs in the context of a neurological disease, diagnosis can be particularly challenging. Therefore, distinguishing between primary psychiatric conditions and mood changes secondary to neurological illness require careful clinical assessment. Diagnostic evaluation often includes a through history of the patient's neurological condition.

Additionally, mood symptoms in these patients may be a typical or present with a rapid cycling pattern. Cognitive impairment and other neuropsychiatric symptoms associated with the underlying neurological disease may further complicate diagnosis. Clinicians need to consider both neurological and psychiatric dimensions to ensure appropriate treatment and management of bipolar disorder in these cases.<sup>[22]</sup>

- **Symptoms**

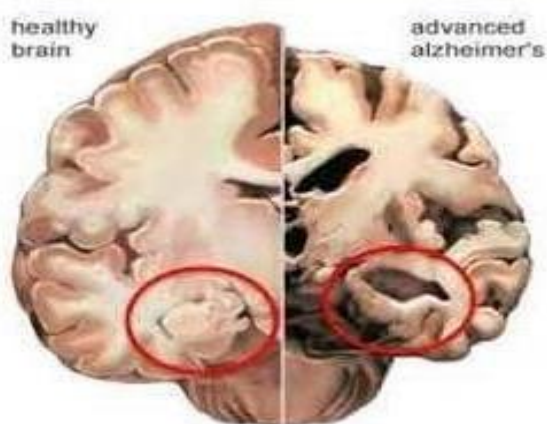
The symptoms of bipolar disorder are marked by extreme mood fluctuations. Depressive episodes bring overwhelming sadness, fatigue, feelings of worthlessness, and even thoughts of suicide. The shifts between these mood states can be rapid or spaced out over months or years.<sup>[23]</sup> Diagnosis involves comprehensive psychiatric evaluation, where a clinician

assesses the patient's mood history, behavior, and family background. Tools like the Mood Disorder Questionnaire or clinical interviews can help in identifying patterns of mania and depression. In some case, brain imaging or blood tests may be conducted to rule out other medical condition that can mimic mood disorder, such as thyroid problem or neurological diseases.<sup>[24]</sup>

- **Treatment**

Treatment of bipolar disorder is multifaceted, combining medication, psychotherapy, and lifestyle management. During periods of depression, mood stabilizers and selective serotonin reuptake inhibitors or other antidepressants may be used sparingly to avoid manic episodes.<sup>[25]</sup> Cognitive-behavioral therapy in particular helps individuals learn coping mechanisms and control their mood fluctuations. Long-term stability also depends on lifestyle changes including avoiding alcohol or drugs, controlling stress, and keeping a regular sleep routine.<sup>[26]</sup>

- **Alzheimer's Disease**



After stroke, AD was the sixth most common cause of death prior to the COVID-19 pandemic. Late-onset AD (LOAD) is the term for AD that usually appears after the age of 65.

About 5% of AD patients have early-onset AD (EOAD), which is less prevalent and manifests before the age of 65. A more aggressive course of the disease results from EOAD's frequently unusual symptoms and delayed diagnosis.<sup>[27]</sup>

- **Causes**

Although a number of theories have been put forth to explain AD, two are thought to be the primary ones: some contend that cholinergic dysfunction is a major risk factor for AD, while others propose that changes in the synthesis and processing of amyloid  $\beta$ -protein serve as the primary trigger. Nevertheless, there is currently no recognized theory to explain the pathophysiology of AD.<sup>[28]</sup>

- **Biological Factors**

- Amyloid Plaques: Accumulation of beta-amyloid protein fragments forms plaques in the brain, disrupting cell communication.<sup>[29]</sup>
- Neurofibrillary Tangles: Hyperphosphorylated tau protein leads to the formation of tangles inside neurons, contributing to cell death.
- Neuroinflammation which lead to the growth of diseases.

### 3. Environmental Factors

- Factors such as head trauma, cardiovascular health, and exposure to toxins may increase risk.

- **Symptoms**

Symptoms of Alzheimer's disease can be categorized into cognitive and behavioral symptoms:

#### 1. Cognitive Symptoms

- Memory Loss: Difficulty remembering recent events or newly learned information (short-term).

- Memory Disorientation: Confusion about time or place, getting lost in familiar locations.
- Difficulty in Problem-Solving: Challenges in planning, organizing, or completing familiar tasks.

#### 2. Behavioral and Psychological Symptoms

- Changes in Mood and Personality: Increased anxiety, depression, apathy, or irritability.
- Hallucinations or Delusions: In some cases, individuals may experience false beliefs or see things that aren't there.
- Changes in Sleep Patterns: Sleep disturbances, including insomnia or excessive daytime sleeping.<sup>[30]</sup>

- **Diagnosis**

Diagnosing Alzheimer's disease involves several steps:

#### 1. Clinical Assessment

- Medical History: Gathering information on symptoms, duration, and family history.
- Cognitive Tests: Standardized assessments such as the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment are used to assess cognitive processes, including memory and problem-solving skills.<sup>[31]</sup>

#### 2. Neurological Examination

- Evaluating reflexes, coordination, and sensory responses to rule out other neurological conditions.

#### 3. Imaging Studies

- MRI or CT Scans: To lead other causes of dementia it observe structural changes in the brain.
- PET Scans: Can identify amyloid plaques in the brain.<sup>[32]</sup>

- **Treatment**

#### 1. Medications

- Cholinesterase Inhibitors: By raising levels of acetylcholine, a neurotransmitter important in memory and learning, drugs such as galantamine (Razadyne), rivastigmine (Exelon), and donepezil (Aricept) can assist enhance cognitive performance.
- NMDA Receptor Antagonist: Memantine (Namenda) helps control glutamate levels, which can be harmful in excess, and is used to treat moderate to severe Alzheimer's disease.<sup>[33]</sup>

#### 2. Supportive Care

- Cognitive Therapy: Engaging in cognitive activities, memory training, and structured routines can help maintain cognitive function.
- Behavioral Interventions: Addressing behavioral symptoms through structured activities and support.

#### 3. Support for Caregivers

- Education and support services for caregivers are essential to manage the stress and challenges of caring for someone with Alzheimer's.<sup>[34]</sup>

- **Parkinson's Diseases**

Movement is the main symptom of Parkinson's disease (PD), a progressive neurological illness. Degeneration of dopamine-producing neurons in the substantia nigra, a region of the brain essential to movement control, is its defining feature.<sup>[35]</sup>

- **Causes**

- Genetic mutations can play a role in familial forms of Parkinson's disease. Some known genetic mutations include:
  - LRRK2: Causes gene mutation.
  - PRKN (Parkin): Associated with early-onset PD.

## 2. Environmental Factors

- Toxins: There is evidence linking exposure to specific toxins, like pesticides and herbicides, to a higher risk of Parkinson's disease.
- Occupational Exposures: Certain jobs that expose individuals to chemicals or heavy metals may increase the risk.

## 3. Age

As people age, especially after the age of 60, their risk of getting (PD) increases.

## 4. Other Factors

**Inflammation:** Prolonged inflammation in the brain may be a factor in neuronal degeneration.

**Oxidative Stress:** Cells, especially neurons, can be harmed by an imbalance between the body's antioxidants and free radicals.<sup>[36]</sup>

- **Symptoms**

Parkinson's disease symptoms can be categorized into motor and non-motor symptoms:

Motor Symptoms:

1. Bradykinesia: Slowness of movement, making everyday tasks more difficult.
2. Rigidity: Pain and limited range of motion caused by stiffness and inflexibility in the trunk and limbs.
3. Instability: Reduced coordination and balance, which raises the possibility of falls.
4. Changes in Gait: stumbling gait, less arm swing, and trouble starting a movement.

### Non-Motor Symptoms

1. Cognitive Changes: Memory, attention, and executive function impairments that may eventually lead to dementia.
2. Sleep Disturbances: Difficulty falling asleep, frequent awakenings, and REM sleep behavior disorder.
3. Autonomic Dysfunction: Conditions like constipation, urinary issues, and orthostatic hypotension.
4. Sensory Symptoms: Changes in smell (hyposmia) and pain or discomfort in the limbs

- **Diagnosis**

### 1. Clinical Assessment

- Neurologists look for the characteristic motor symptoms and may assess the response to dopaminergic medications.

### 2. Neurological Examination

- To assess motor function, balance, coordination, and cognitive capacities, a thorough neurological examination is performed.

### 3. Imaging Studies

- Although there are no definitive tests, imaging studies such as an MRI or a dopamine transporter (DAT) scan can help rule out other conditions and may support the diagnosis.<sup>[37]</sup>

- **Treatment**

#### Medications

1. Dopaminergic Medications:
  1. - Levodopa: The best drug for managing symptoms is levodopa, which the brain converts to dopamine.
  2. - Dopamine Agonists: Medications like pramipexole (Mirapex), ropinirole (Requip), and bromocriptine stimulate dopamine receptors in the brain.
  3. - COMT Inhibitors: By stopping levodopa's breakdown, COMT Inhibitors such as Entacapone and Tolcapone can prolong the effects of the drug.

### 2. Anticholinergics

- Medications like trihexyphenidyl may help control tremors, particularly in younger patients, but are less commonly used due to potential side effects.

### 3. Amantadine

An antiviral medication that may help with mild motor symptoms and dyskinesias. Non-Pharmacological Treatments:

#### 1. Physical Therapy

- Focused on improving mobility, balance and flexibility through exercise programs tailored to individual needs.

#### 2. Occupational Therapy

- With the use of adaptive techniques and technology, patients are helped to continue their everyday activities and enhance their quality of life.

#### 3. Speech Therapy

- Addresses communication and swallowing difficulties often experienced by individuals with PD.

#### 4. Dietary Changes

- A well-balanced diet can help manage symptoms. Staying hydrated and having regular meals can also improve medication effectiveness.



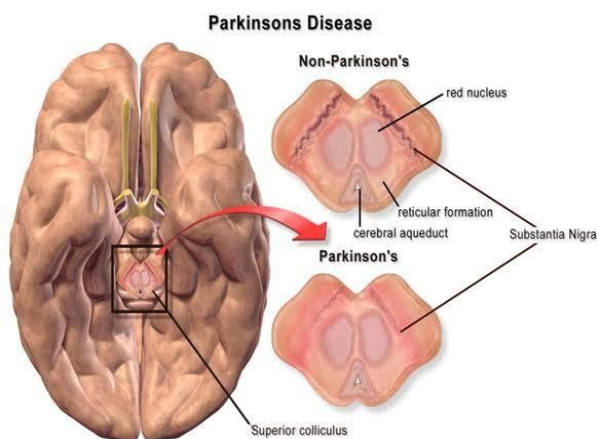
## Surgical Treatments

### 1. Deep Brain Stimulation (DBS)

- A surgical procedure that entails implanting a device that sends electrical impulses to particular brain regions may be beneficial for patients who do not react well to medication.
- A surgical procedure that involves implanting a device that sends electrical impulses to particular brain regions may be beneficial for patients who do not respond well to medication.

### 2. Other Surgical Options

- Less common procedures, such as lesioning techniques, may be considered for certain patients.<sup>[38]</sup>



### • Conclusion on Neurological Disorders

Neurological disorders are conditions that impact the nervous system, which comprises the brain, spinal cord, and peripheral nerves. These conditions can provide a variety of serious public health issues. These disorders can vary significant public health challenge. The high degree of pleiotropy indicates that therapeutic techniques may be beneficial across diagnostic borders, and the neurodevelopment continuum highlights the need for novel and adaptable approaches to diagnosis and patient classification.<sup>[39]</sup>

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