

# MRI in Early Detection of Neurodegenerative Disorders: A Comprehensive Review

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**Abstract:** *Progressive loss of neurons is a feature of neurodegenerative disorders such as Alzheimer's, Parkinson's, and Multiple Sclerosis. For prompt intervention, early detection is essential. A sensitive and non-invasive method, magnetic resonance imaging (MRI) can identify abnormalities in the brain before clinical symptoms manifest. For the purpose of early diagnosis, this study assesses both conventional and cutting-edge MRI methods, including volumetric analysis, diffusion tensor imaging, functional MRI, susceptibility-weighted imaging, and quantitative susceptibility mapping. We also talk about new MRI applications, difficulties, and opportunities. Objective: Examining how MRI can aid in the early diagnosis of neurodegenerative diseases such Multiple Sclerosis, Parkinson's disease, and Alzheimer's disease is the aim of this review. Aim: This study examines how sophisticated MRI methods—volumetric imaging, fMRI, and DTI—identify early brain alterations in neurodegenerative disorders, frequently prior to the onset of symptoms, emphasizing their use in directing therapy and assessing advantages and disadvantages. Discussion: MRI is essential for the early detection of neurodegenerative illnesses because it can spot anomalies in the brain, such as hippocampal shrinkage or white matter lesions, before symptoms appear. Although accessibility and expense are still barriers, it encourages early diagnosis and treatment planning. Conclusion: When neurodegenerative diseases are detected early, MRI is a useful tool for identifying abnormalities in the brain before significant symptoms manifest. Subtle structural and functional anomalies are revealed by advanced techniques like DTI, fMRI, and SWI, which help in early diagnosis and treatment. MRI is crucial for early screening and future treatment of various illnesses due to its advantages, even in the face of obstacles like cost and accessibility.*

**Keywords:** Multiple sclerosis, MRI, Alzheimer's disease, Parkinson's disease, and neurodegenerative illnesses

## 1. Introduction

Neurodegenerative diseases are a class of long-term, progressive illnesses that impact the central nervous system and cause the slow, irreversible loss of the structure and function of neurons. These illnesses are a major burden on people and their families, but they are also becoming a bigger worldwide public health concern, particularly as the population ages. Because neurodegenerative disorders are becoming more common as life expectancy rises globally, early detection and preventive measures are desperately needed [1].

The three most well-known neurodegenerative illnesses are Multiple Sclerosis (MS), Parkinson's disease (PD), and Alzheimer's disease (AD). While the underlying pathophysiology and clinical presentation of various conditions vary, they all have one thing in common: cognitive, behavioral, sensory, or motor deficits brought on by gradual harm to the nervous system [1].

Alzheimer's disease (AD) is the most prevalent cause of dementia and is typified by personality changes, disorientation, language difficulty, and progressive memory loss. Tau tangles and beta-amyloid plaques, two aberrant proteins, build up in the brain and induce cell death, especially in regions linked to memory and learning like the cortex and hippocampus. Since the illness process usually starts years before symptoms appear, early identification is essential for effective treatment [3].

Parkinson's disease (PD) is a neurological condition that worsens with time and mostly impacts movement. It is caused by dopamine-producing neurons in the substantia nigra, a part of the brain, degenerating. Tremors, rigidity, bradykinesia (slow movement), and balance issues are typical symptoms. Even though Parkinson's disease (PD) is mainly recognized for its motor symptoms, non-motor symptoms such as

depression, sleep disorders, and cognitive impairment also manifest, frequently in the early stages of the disease [3].

Multiple Sclerosis (MS) is an autoimmune condition where the immune system of the body targets the myelin coating that protects nerve fibers in the brain and spinal cord. Axonal injury, inflammation, and demyelination result from this, impairing brain-body connection. Numerous symptoms, such as weariness, numbness, vision abnormalities, and muscle weakness, can be caused by multiple sclerosis (MS), which frequently first manifests in young adulthood. Early brain lesions can develop without obvious symptoms; hence imaging is essential for an early diagnosis [2].

The fact that clinical symptoms frequently don't show up until after substantial brain damage has already happened is one of the main obstacles in managing neurodegenerative diseases. By the time a diagnosis is verified by clinical assessment, cognitive testing, or visible symptoms, the illness might have advanced past the stage at which early treatment would be most helpful. Patients may experience worse results as a result of this delay, and the efficacy of current treatments may be reduced. So, one of the main objectives in neurology and medical imaging is to identify these disorders early on, even before symptoms show up [3].

In this context, Magnetic Resonance Imaging (MRI) has emerged as one of the most valuable diagnostic tools. MRI is a non-invasive imaging technique that provides high-resolution, detailed images of the brain's anatomy and, in some applications, its function. It offers the ability to visualize even small structural changes in the brain, detect areas of tissue loss or damage, and observe how different parts of the brain are connected or affected by disease. Unlike other imaging methods such as CT scans, MRI does not use ionizing radiation, making it safer for repeated use and for long-term disease monitoring [3,4].

In order to identify small changes in the brain that take place long before clinical symptoms appear, MRI is essential. For instance, early-stage Alzheimer's disease can be used to identify high-risk individuals due to the hippocampus and entorhinal cortex shrinking. The deep brain areas involved in motor control can show anomalies in Parkinson's disease, according to MRI. Even before clinical symptoms of multiple sclerosis manifest, MRI is the gold standard for identifying white matter abnormalities. Doctors can begin treatment considerably sooner thanks to these early imaging indicators, which can halt the progression of the disease and enhance long-term results [1,3,5].

MRI is also being used more and more to monitor the course of diseases and the effectiveness of treatments, giving important insights into how the brain is evolving over time. Identifying at-risk groups, creating new treatments, and comprehending the natural course of neurodegenerative diseases are all areas in which it is crucial [4]. Even though MRI has many benefits, there are still obstacles preventing its widespread application. These include variations in image interpretation, the necessity for skilled specialists, the expensive expense of sophisticated imaging, and restricted access in some areas. But with continued advancements in technology and growing recognition of its benefits, MRI is anticipated to be even more included into early neurodegenerative disease diagnosis procedures [3,4].

MRI's vital role in the early diagnosis of neurodegenerative diseases will be examined in this review, with particular attention paid to its clinical uses, disease-specific results, and potential to revolutionize the way we identify and treat these ailments. This article emphasizes the value of imaging in enhancing patient care and results in the age of early and preventive neurology by highlighting the advantages and disadvantages of MRI and reviewing the available data [1-5].

### 1.1 Pathogenesis of Neurodegenerative Conditions

Neurons and their functions gradually disappear in neurodegenerative diseases. While each condition affects various parts of the nervous system, they all share a number of pathogenic processes, such as inflammation, oxidative stress, protein aggregation, and neuronal death [1,3,6]. The main neurodegenerative diseases' pathophysiology, causes, symptoms, and current treatment approaches are outlined below:

#### 1) Alzheimer's Disease (AD)

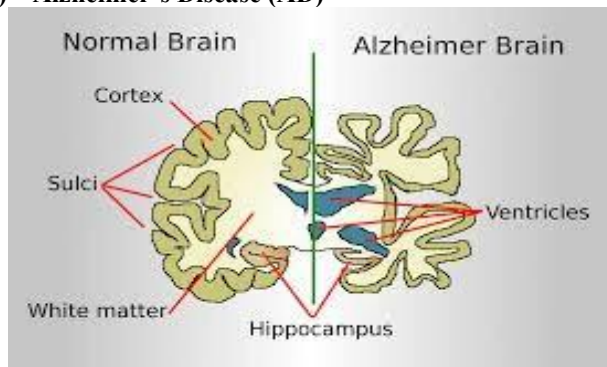


Figure 1: Alzheimer's Disease (AD) [8].

#### Pathophysiology:

The aberrant buildup of tau protein tangles and beta-amyloid plaques in the brain is the main cause of Alzheimer's disease. This accumulation results in synaptic dysfunction, neuroinflammation, and neuronal death. The cerebral cortex and hippocampal regions, which are essential for memory and cognition, show the most noticeable alterations [3,5].

#### a) Reasons:

- The main risk factor is aging.
- Genetic variables (APOE  $\epsilon 4$  allele, for example)
- Family background
- Risk factors for cardiovascular disease (obesity, diabetes, and hypertension)
- Lifestyle variables and head trauma

#### b) Signs and symptoms

- Early: Disorientation, memory loss, and trouble pronouncing words
- Intermediate: Mood swings, poor judgment, and confusion
- Late: Abnormal conduct, severe cognitive deterioration, and incapacity to carry out daily responsibilities

#### c) Therapy:

- Pharmacologic: NMDA receptor antagonists (Memantine), cholinesterase inhibitors (Donepezil, Rivastigmine)
- Non-pharmacologic: Support for caregivers, exercise, and cognitive treatment
- Anti-amyloid monoclonal antibodies, such as Aducanumab and Lecanemab, are emerging treatments [3,5,6].

#### 2) Parkinson's Disease (PD)

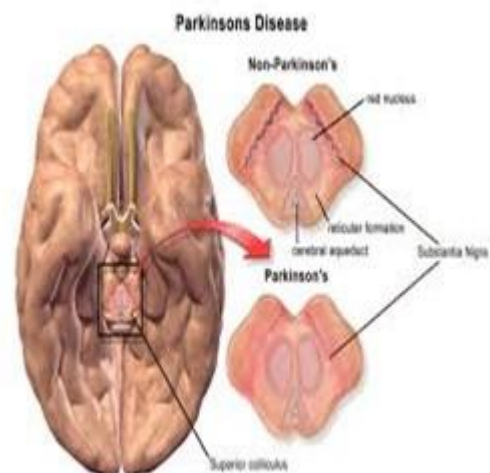


Figure 2: Parkinson's Disease (PD) [9].

#### Pathophysiology:

Parkinson's disease results in a reduction in dopamine levels in the basal ganglia due to the gradual degradation of dopaminergic neurons in the substantia nigra pars compacta. Coordination and motor control are compromised [3,6].

#### Reasons:

- Most of the time, idiopathic
- Genetic mutations, such as those in LRRK2, PARK7, and SNCA

- Exposures to the environment (such as insecticides)
- Both mitochondrial malfunction and oxidative stress

### Signs and symptoms

Motor symptoms: Postural instability, muscle rigidity, bradykinesia (slowness of movement), and resting tremor non-motor symptoms include constipation, depression, sleep issues, loss of smell, and later stages of cognitive deterioration [3,6].

### Therapy:

- Pharmacologic: MAO-B inhibitors (Selegiline), dopamine agonists (Pramipexole, Ropinirole), and levodopa/carbidopa
- Surgical: For certain individuals, deep brain stimulation (DBS)
- Occupational treatment, speech therapy, and physical therapy are supportive [3,6].

### 3) Multiple Sclerosis (MS)

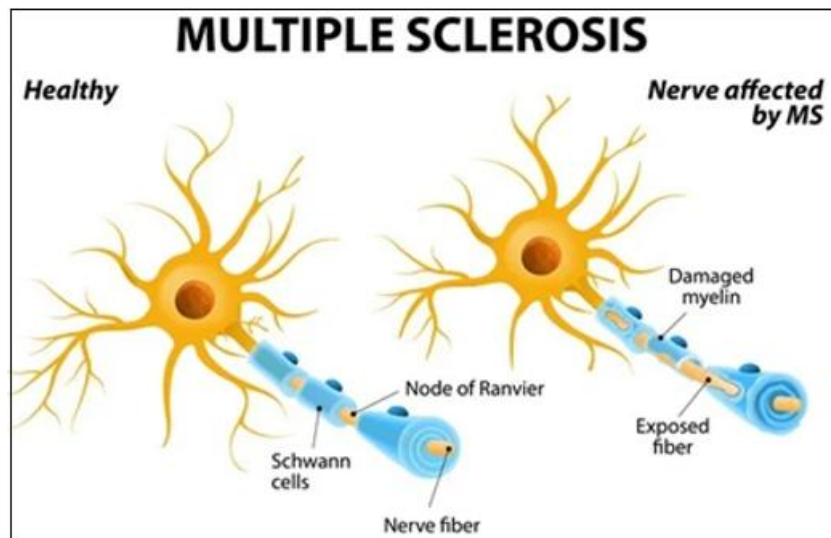


Figure 3: Multiple Sclerosis (MS) [10]

### Pathophysiology:

Axonal damage and demyelination result from the immune system attacking the myelin sheath that surrounds nerve fibers in the central nervous system in multiple sclerosis (MS), an autoimmune illness. Neurological impairment results from this disruption of nerve signal transmission [2,6,7].

### Reasons:

- Genetic susceptibility (gene HLA-DRB1)
- infections caused by viruses (e.g., Epstein-Barr virus)
- Lack of vitamin D
- Smoking
- Gender: female (greater risk)

### Signs and symptoms

- Sensory abnormalities (tingling, numbness)
- Motor symptoms, such as spasticity and muscular weakness
- Visual issues (double vision, optic neuritis)
- Cognitive alterations, fatigue, and bladder problems [2,7].

### Therapy:

High-dose corticosteroids, such as methylprednisolone, can cause an acute relapse.

DMTs, or disease-modifying treatments: Fingolimod, ocrelizumab, glatiramer acetate, and interferon-beta

Symptom management includes physical rehabilitation, antidepressants, and antispasticity medications [2,6].

This section demonstrates that MRI can identify early structural and functional alterations that are pertinent to all neurodegenerative diseases, even though they each impact different brain regions and exhibit unique clinical symptoms.

It is easier to choose the best imaging methods for early diagnosis and monitoring when one is aware of the underlying pathophysiology, causes, and symptom patterns [1-7].

### 1.1 Early detection using MRI techniques Identification

#### 1) Conventional MRI (T1, T2, FLAIR)

- Can identify white matter lesions and brain atrophy.
- Gray matter structures can be seen in T1-weighted pictures. FLAIR is a useful tool for detecting MS lesions [1,2,3,7].

#### 2) Volumetric MRI

- Measures the volume of particular areas of the brain.
- It is possible to identify early entorhinal and hippocampus atrophy in AD.
- Analysis is aided by automated software, such as FreeSurfer [3,5,6].

#### 3) Diffusion Tensor Imaging (DTI)

- uses the diffusion of water molecules to measure the integrity of white matter pathways.
- In the early stages of neurodegeneration, fractional anisotropy (FA) is downwards.
- In the impacted locations, the mean diffusivity (MD) is ↑.
- beneficial for MS, AD (cingulum, fornix), and early PD (substantia nigra) [3,4,6].

#### 4) Functional MRI (fMRI)

- Uses the blood-oxygen-level-dependent (BOLD) signal to measure brain activity.
- Changed connectivity in the Default Mode Network (DMN) in AD is detected by resting-state fMRI.

- Parkinson's disease motor networks.
- Promising in terms of preclinical change detection [4,6].

### 5) Weighed Imaging of Susceptibility (SWI) and QSM

- Find iron buildup in Parkinson's disease.
- When visualizing substantia nigra degeneration, SWI is helpful.
- Quantitative maps of tissue susceptibility, such as those in PD and MS, are provided by QSM [4,6].

### 6) MRI in Particular Conditions

#### a) Alzheimer's disease

- Atrophy of the hippocampal region is the first observable indication.
- White matter integrity loss in the parietal and fornix lobes is revealed by DTI.
- DMN connectivity is impaired in resting-state fMRI.
- Helpful in detecting AD's precursor, mild cognitive impairment (MCI) [3,5,6]

#### b) Parkinson's illness

- Iron accumulation in the substantia nigra is detected by SWI and QSM.
- DTI identifies microstructural alterations in the thalamus and basal ganglia.
- Even in early Parkinson's disease, FMRI shows aberrant motor circuit connection [4,6].

#### c) Multiple Sclerosis

- Periventricular white matter lesions are detected using FLAIR MRI.
- Early axonal damage is highlighted by DTI before lesions become apparent.
- Cortical lesions that are frequently overlooked by standard MRI can be seen with DIR sequences [2,7].

#### d) Restraints and Difficulties:

- Expensive and restricted: Advanced MRI methods, such as 7T, are only available at research facilities and are costly.
- Normative practices Problems: Reproducibility is impacted by variations in MRI methodology amongst facilities.
- Overlap of Imaging Results: A few alterations are not unique to a particular disease.
- Interpretation: Necessitates skilled neuroradiologists and appropriate computer programs [3,4,6].

### 1.5 The Clinical Consequences

Early disease-modifying treatment intervention is made possible by early diagnosis.

In order to monitor patients, patient stratification assists in grouping them into high-risk categories.

MRI can be used to monitor the course of an illness and the effectiveness of treatment [1-7].

## 2. Discussion

In line with earlier published research, this review shows that MRI is essential for the early diagnosis of severe neurodegenerative illnesses. According to Du L et al. [1] and

Li KR et al. [3], structural MRI and volumetric analysis are still very useful for detecting early cortical and hippocampal atrophy, especially in the early detection of Alzheimer's disease (AD).

In AD, Parkinson's disease (PD), and multiple sclerosis (MS), diffusion tensor imaging (DTI) provide sensitive indicators of microstructural white matter impairment. This review demonstrates that early decreases in fractional anisotropy and increases in diffusivity can be found even before overt lesions or considerable atrophy, which is consistent with the findings of Gill AJ et al. [2] and Akram AS et al. [6]. DTI demonstrates significant diagnostic utility in MS, supporting findings from Filippi M et al. [7].

In line with Chandrasekar SK et al. [4], functional MRI offers complementary value by identifying altered default mode network connection in early AD and diminished motor network activity in PD. Similarly, susceptibility-based imaging (SWI/QSM) is particularly promising in Parkinson's disease (PD), as it provides a more reliable visualization of early iron deposition in the substantia nigra than traditional MRI [4, 6].

Our results confirm MRI's long-standing position as the gold standard for MS diagnosis. According to Gill AJ et al. [2] and Filippi M et al. [7], FLAIR continues to be the most sensitive sequence for identifying early lesions.

Despite these advantages, there are also drawbacks, such as high expense, differences in imaging procedures, and the requirement for professional interpretation—problems that have also been brought to light by Du L et al. [1] and Chandrasekar SK et al. [4]. Nevertheless, MRI is an essential tool for early diagnosis, monitoring, and therapy planning across neurodegenerative illnesses, according to evidence from this study and earlier studies. Further advancements in ultra-high-field MRI and quantitative imaging are anticipated to improve diagnosis accuracy even more.

## 3. Conclusion

For the early diagnosis of neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, and Alzheimer's disease, magnetic resonance imaging, or MRI, is essential. These disorders frequently start with subtle alterations in the structure and function of the brain long before obvious symptoms appear. Such early changes, such as brain shrinkage, white matter lesions, and deep gray matter changes, can be seen by MRI and used to inform early diagnosis [1-7].

MRI is quickly taking the lead in clinical practice and research due to its superior soft tissue contrast and non-invasive nature. However, these obstacles should be solved by factors like cost and technology [3,4,6].

By using MRI in early screening and diagnostic procedures, medical professionals can better track the course of a disease, evaluate the effectiveness of treatment, and eventually enhance patient outcomes. Better clinical judgment is supported by early imaging, which also increases the



likelihood that disease-modifying treatments will be started when they are most effective [1-7].

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