MODEL TO DETECT EARLY DEMENTIA RELATED COMMON DISORDER USING DEEP NEURAL NETWORK

A Thesis

Submitted in the partial fulfillment of the requirements

for the Award of the Degree

of

DOCTOR OF PHILOSOPHY (PhD)

in

COMPUTER APPLICATION

By

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LOVELY PROFESSIONAL UNIVERSITY

PUNJAB

2022

Certificate

It is to certify that. Harsimran Guram (registration no.-41800618), Department of Computer Application has carried out research work entitled **"**Model to detect early dementia related common disorder using deep neural network", for the award of degree of Doctor of Philosophy in Computer Application, Faculty of Technology and Sciences, Lovely Professional University, Punjab, India.

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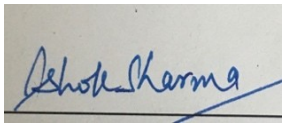

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Declaration

The work embodied in the thesis entitled "Model to detect early dementia related common disorder using deep neural network"submitted to the Faculty of Technology and Sciences, Lovely Professional University, Punjab, India, for the award of degree of Doctor of Philosophy in the subject of Computer Application has been carried out by me.

The thesis is entirely based on my original piece of work and has not submitted fully or partially elsewhere for the award of any degree. All the ideas and references have been duly acknowledged.

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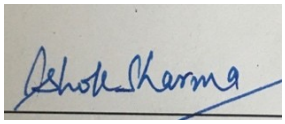

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Abstract

Dementia has developed into a significant health problem for many over the age of 50. Numerous kinds of dementia develop gradually and incrementally. Previous researchers have received reports from persons of various ages who have had memory loss and subsequent recall from long-term memory loss as a result of this neurodegenerative illness. Memory loss that is both gradual and irreversible characterises the disorder known as dementia. Although it is more common in the elderly, an increase in cases among the younger population has raised experts' eyes and encouraged them to explore the neuro-disorder, which causes memory loss and a barrier in recalling information from memory. Dementia can slow down to some extent if diagnosed early enough. Deep learning and an additional tree classifier are used to extract information from brain MRI images and classify dementia at an early stage. When segmenting MRI images, deep learning cells based on BI-LSTM base memory aid in the process. Features can then be gleaned. The suggested architecture uses a combination of Resnet and CNN to map non-linear space and extract useful domain features. An additional tree classifier is used to enhance class-wise learning of dementia stages during the learning process. It has been reported in the previous researches that the brain is predominately composed of two proteins. Abnormally high levels of beta-amyloid form one of plaques that obstruct cellular activities. There's also a protein known as tau, which can accumulate outside of the neuron's transportation framework and result in neurofibrillary tangles, which impair cell measure.

Magnetic resonance imaging (MRI) has been used to classify the causes of brain disease, according to this thesis. For more precise prediction, an attention-based transfer learning method (retrieves variable elements of patterns from magnetic resonance imaging (MRI) images) was applied, and features were then taught and used to sort fMRI data into different categories. In order to discover various patterns of dementia risk, hyper-parameters resulting from XGboost were obtained and assessed. Gradient boosting is commonly used to do variable extractions from independent to dependent variables, and the resulting derived variables are the result of this process. The ADNI database is used to populate the system's MRI. Most features can be extracted at acceptable speeds utilising the Feature Extractor's method. The experimental findings show

that the proposed method may be used to classify output in the correct manner. Precision and accuracy would rise by (nearly) 4.2 percent using this strategy, while recall would remain at (almost) 94.6 percent.

The entire study project is divided into several chapters, the majority of which are seven, and a chapter-by-chapter summary is provided elsewhere in this chapter.

Chapter-1: This section provides an overview of Alzheimer's disease and dementia. It explains the symptoms, stages, causes and the types of dementia. It covers the brain imaging along with the clinical diagnosis of Dementia. This chapter also includes a detailed discussion and explanation of the study's purpose, relevance, justification, and scope.

Chapter-2: This chapter includes a complete literature review with a huge collection of literature in terms of articles and journals written by a number of experts in the field. The study of dementia literature, gap analysis, and study goals have all been covered.

Chapter-3: This chapter presents a relative framework based on the implementation of the grey wolf-based optimization approach for optimizing feature of images. This chapter describes various algorithms, research methodology, and the data used in the process.

Chapter-4: In this chapter designing of a hybrid CNN-based approach for dementia early detection (CNAT-TRXG) have been discussed. This chapter also examines the impact of various tools mostly on implementation of specific research approaches for categorization, like CNN using attention layers and transfer learning.

Chapter-5: In this chapter a comparison of optimized feature optimized approach with existing approaches has been discussed. It entails analysing outcomes based on the optimised approach's performance.

Chapter-6: This chapter demonstrates the comparison of CNAT-TRXG (Proposed-2) approach with existing approaches. It involves the analysis of results based on the performance of the existing and the proposed approach.

Chapter-7: Here in this chapter, the conclusion drawn from the present research and the future scope in terms of the existing and proposed approaches for the analysis of dementia is discussed. The chapter's last section closes with a number of findings that point to the optimal approach being used.

Abbreviations

AD	Alzheimer's Disease
ADNI	Alzheimer's Disease Neuroimaging Initiative
BEHAVE-AD	Behavior Pathology in Alzheimer's Disease Rating Scale
BPSD	Behavioral and psychological symptoms of dementia
bvFTD	Behavioural Fronto-Temporal (lobe) Dementia
BVE	bovine spongiform encephalopathy
CAD	Computer Aided Technology
CDR	Clinical Dementia Rating
CNN	Convolution Neural Network
CJD	Creutzfeldt– Jacob Disease
iCJD	Iatrogenic Creutzfeldt– Jacob Disease
CT	Computerized Tomography
DBN	deep belief networks
DLB	Dementia with Lewy Bodies
EKG	Electrocardiogram
FTD	Fronto-Temporal (lobe) Dementia
GDS	Global Deterioration Scale
GOC	Goals Of Care
GWO	Grey Wolf Optimizer
LB	Lewy Body
MCI	Mild Cognitive Impairment
MD	Mild Dementia
MDD	Major Depressive Disorder
MMD	Moderate Dementia
MMDNN	Multi-Scale Deep Neural Network
MOST	Medical Orders for Scope of Treatment
MRI	Magnetic Resonance Imaging
MLP	Multi-Layer Perceptron
ND	No dementia
OCR	Optical Character Recognition
PPA	Primary Progressive Aphasia
PDD	Parkinson's Disease Dementia
PET	Positron Emission Tomography
PMCA	Polymerase Chain Reaction
PSP	Progressive Supranuclear Palsy
REM	Rapid Eye Movement
RF	Random Forest
SAE	Stacked Auto-Encoder

SAE	Sparse Autoencoder
SIFT	Scale Invariant *Feature* Transform
SPECT	Single Photon Emission Computed Tomography
SVM	Supported Vector Machine
VaD	Vascular Dementia
vCJD	variant CJD

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CHAPTER 1
INTRODUCTION

1.1 Overview

Dementia seems to be a clinical illness characterised by a steady decline in mental function. Language, Memory, decision making, reasoning, visuospatial function, focus, and orientation are all cognitive functions that might be harmed by dementia [37,45,55]. Cognitive impairments are frequently accompanied with personality, social behaviour, and affective management abnormalities in dementia patients [61,76]. Furthermore, the behavioural and cognitive changes that accompany dementia disrupt employment, relations, and social activities, as well as impede a person's ability to complete daily tasks.

Dementia has many reversible and irreversible causes. Depressive disorders, dietary inadequacies, endocrine and metabolic diseases (for instance, hypothyroidism), normal pressure hydrocephalus, space-occupying lesions (e.g., brain tumours), or drug misuse are all secondary causes of reversible dementias (pseudo-dementias). Certain medicines may cause cognitive impairment in older people (e.g., anticholinergic, psychotropics, analgesics, sedative-hypnotics). Degenerative and/or vascular processes in the brain cause irreversible dementias. Alzheimer's disease (AD) is by far the most prevalent example of irreversible dementia, accounting to 70% of cases in the United States. Primary dementias include vascular dementia (10-20%), Parkinson's dementia, Lewy body dementia, and front temporal dementia. Dementia has major consequences for individuals, their families, and society as a whole [28,52,74,79].

Dementia-related disorders are expected to affect about 139 million individuals globally by 2050, according to experts [1,73,97]. Because of the anticipated pace, healthcare, fiscal, and care service prices have seen a steady increase in public policy. Concerns about longevity are now commonplace, especially in countries where the population has more than doubled in life expectancy. According to predictions, the number of individuals with dementia in low-income

and middle-income nations will outpace those in higher-income nations over the next two decades. After its identification as an independent syndrome, researchers have investigated a wide range of issues pertaining to Alzheimer's disease, including its pathophysiological and restorative relationships. Studies of structural improvements in maturity level cognitive impairments using neuropathology and neuroimaging show a labelled temporal lag between the occurrence of neuropathologic features and the onset of symptoms. AD is a progressive neurodegenerative disease associated with ageing [36,39,77]. The present medications help with a few of the symptoms and indicators of Alzheimer's disease, but they don't deal with the underlying pathology; these are referred to as "symptomatic" therapies. The delayed-start, alternatively referred to as randomized-start, is often descriptive research in which patients are randomly assigned to receive a similar active treatment yet begin at different times. This refers to two treatment stages: a placebo-controlled phase followed by a delayed-start phase. During the placebo-controlled cycle, patients may gain either a placebo or an active treatment.

Dementia may be caused by a variety of both the irreversible and reversible factors. Reversible dementias (also called "pseudo-dementias") remain uncommon but theoretically curable. They arise as a result of another medical problem, such as anxiety, nutritional deficiencies (for example, vitamin B12), space-occupying lesions (for example, brain tumour), endocrine and metabolic disorders (for example, hypothyroidism), drug abuse or natural pressure hydrocephalus. Many drug groups often have the potential to cause cognitive dysfunction in elderly people (e.g., psychotropics, anticholinergic, sedative-hypnotics, analgesics). Irreversible (principal) dementias are caused by vascular processes and/or brain neurodegenerative. Main dementias involve Parkinson's disease-related dementia, vascular dementia (10-20% of cases), front temporal dementia, and Lewy body dementia. Given the major consequences of dementia for patients, theirrelatives, and community, possibly the best physicians should have a firm grasp on the subject [28,52,74,79].

1.2 Alzheimer's Dementia (AD)/Dementia

According to the Merriam-Webster Dictionary, dementia is characterised as severe impairment of cognitive abilities, particularly in the ability to socialise. Dementia is affected by infections

that attack brain cells, causing the cell death that causes dementia. Dementia can affect the way people act, think, and feel. Blood supply to a part of the brain may be affected after a stroke, leading to vascular dementia. Additionally, hydrocephalus and Parkinson's disease are risk factors for dementia. AD [16,83] is often an example of dementia with beta-amyloid build-up in the brain.

The bulk of AD patients report symptoms of mental illness. In some situations, the irregular spectrum of behavioural patterns manifests itself during the disease's later stages. Such signs, which are referred to as psychological and behavioural symptoms of dementia, are infrequent in nature instead of being progressive [81]. Patients experience reduced well-being, a diminished standard of living, and a significant burden on caregivers. Behavioral and psychological symptoms of dementia (BPSD) sometimes results in short-term hospitalisation or moving to a care home. This has been debated that even the easiest advantages will improve life and create a distinction between staying at institutionalization or at home. The care home workers as well as other residents are exposed to extremely high levels of stress of BPSD [50]. Because of the increased proportion of BPSD, many people with Alzheimer's disease are treated using antidepressants, sedatives, and neuroleptics. It triggered a major conversation about the misuse of psychoactive medication in nursing homes. Disruption and frustration are major signs of Alzheimer's disease. Generally, agitation is treated pharmacologically with a neuroleptic medication, that leads to inadequacy in several patients and common symptoms with the newest atypical neuroleptics.

Nonpharmacological therapies have received limited attention in comparison to pharmaceutical care, mainly because of a lack of reliable studies. In this area, studies are often focused on insufficient case or topic reports. There has also been a great deal of variation in non-pharmacological interventions. By evaluating nonpharmacological intervention methods, it is possible to conclude that: a specific evaluation of the clinical benefits of nondrug interventions in dementia care is not possible.

Music therapy is a non-pharmaceutical method of treatment. The methodical application of songs, noises, and gestures is one such treatment. To help persons with BPSD achieve therapy goals, the therapist uses specialised sounds or melodies, or the intrinsic audio quality created largely during therapies [50]. The majority of patients with AD are able to engage in therapy,

that improves their standard of living. Music therapy [12] has been shown to increase patient involvement and thus decrease patients' feelings of isolation (Svansdottir & Snaedal 2006).

This objective is to assist promoters in optimising the therapeutic medication for the treatment of many phases of AD that occur prior to the onset of severe dementia [44,46]. This guidance addresses the FDA's latest theory on patient selection for clinical studies when they have premature AD or are predisposed to grow AD. The suitable recommendation helps in the selection of endpoints for clinical trials in these communities and helps in elucidation of disease alteration. Dementia and Natural ageing are frequently confused with Alzheimer's disease [46,60]. Severe memory loss, which is a marker of Alzheimer's disease, is not seen in the ageing process. Strong ageing can result in the progressive loss of weight, hair, muscle mass, and height. The other symptom of healthy ageing is bone density loss, fragile skin, a reduced metabolic rate, and a diminished hearing and vision ability. Additionally, there may be memory loss, resulting in a delay in recalling information. However, cognitive decline that interferes with daily tasks is not a natural aspect of the ageing process.

1.3 Symptoms, Stages, and Causes of Dementia

1.3.1 Stages of dementia

In the majority of cases, dementia is gradual, meaning that it becomes worse with time. Dementia develops differently in each person. Even so, the majority of the population exhibit consistent with the preceding stages of the disease [40, 86]:

Mild cognitive impairment

Elderly individuals can experience MCI i.e., mild cognitive impairment but never experience dementia or another form of mental impairment. MCI patients may also experience loss of memory, difficulty remembering words, and difficulties with short-term memory.

Mild dementia

Mild dementia patients may well be able to work independently at this point. Among the symptoms are [42] the following:

- lapses in working memory.

- changes in personality, such as anger or stress.
- trouble with complicated tasks or major issue.
- trouble expressing ideas and feelings.

Moderate dementia

Individuals affected by this stage of the disease may require help from a beloved one or care taker. This is because dementia can now impair everyday tasks and activities. Symptoms include the following [86]:

- unwise decision.
- escalating confusion and anger.
- impaired memory that extends far enough into the past.
- the need for assistance with daily activities such as bathing and dressing.
- severe personality shifts.

Severe dementia

In this advanced phase of dementia, both physical and mental symptoms appear to deteriorate. Symptoms include the following [64,75]:

- failure to manage body processes, such as moving and gradually chewing and bladder control.
- Lack of ability to speak.
- Requiring extra aid.
- high risk of any kind of infection.

Advanced Dementia

- Advanced dementia [35,56,78] is indeed a primary cause of deaths in the U.S. Symptoms include severe memory problems (for example, failure to remember family), failure to

function everyday tasks, impairment of ambulatory capacity, limited verbal comprehension, and faecal and urinary incontinence.

- The most frequently seen medical problems are food disorders and diseases, which necessitate managerial decisions.
- Treatment preparation in advance is important. Treatment choices must be driven by care goals; upwards of 90% of health care proxy statements note that the primary goal is patient comfort [35,80].
- Experimental findings indicate that tube feeding has little value for patients with dementia, and tube feeding is therefore not suggested.
- Observational studies demonstrate a number of hospice care's advantages. If palliative and hospice care are available, these must be provided to patients with advanced dementia [35].

1.3.2 Causes of dementia

Dementia is the result of a number of different causes. The dysfunction of various body functions interferes with the output of neurons. Alzheimer's disease can be caused by a variety of factors, including brain abnormalities. Alzheimer's disease and Vascular dementia are the two most common kinds of dementia. The term "neurodegenerative" [86] refers to neurons that progressively stop working or act incorrectly, ultimately dying. This has an impact on synapses, which are the links between neurons that allow signals to travel through your brain. This separation can lead to a variety of problems. The following are some of the most common dementia causes.

Neurodegenerative diseases

- Alzheimer’s disease
- Parkinson’s disease with dementia
- Chronic alcoholism
- Vascular dementia
- Medication side effects
- Certain infections or tumours of the brain

Another component is frontotemporal lobar degradation, which refers to a group of illnesses affecting the frontal and temporal lobes of the brain. The following are the details:

- Pick’s disease
- Frontotemporal dementia
- Corticobasal degeneration
- Supranuclear palsy

Other dementia causes

Other conditions that may induce dementia include:

- systemic brain disorders including subdural hematoma and normal-pressure hydrocephalus.
- metabolic problems including deficiency of vitamin B-12, hypothyroidism, and liver and kidney problems.
- Toxic substances, like lead.

It's possible that each of these dementias may be reversed. If diagnosed early, these curable causes of dementia may well be able to counteract symptoms. Several researchers have evidenced that a patient should see their physician and have a health check as quickly as you notice symptoms.

1.4 Types of AD/DEMENTIA

Parkinson's disease (PD) and Alzheimer's disease (AD) are two prominent neurodegenerative diseases that mostly appear in the elderly. Despite the fact that PD and AD are typically used as chronic conditions, recent research has shown a rising number of people with PD who still have AD, as well as the increasing number of individuals with dementia who have PD. A type of degenerative dementia is also considered an important background for this specific type of dementia: Dementia with Lewy Bodies (DLB) (characterized by progressive and intermittent cognitive dysfunction, extrapyramidal, and psychoses characteristics), is seen in other

degenerative dementias, including Alzheimer's disease and vascular dementia. Dementia may be caused by a host of disorders and illnesses, including Alzheimer's and multiple sclerosis [9, 85].

1.4.1 Alzheimer's Disease (AD)

Around 50% to 60% of dementia cases are considered to be caused by Alzheimer's disease. It is a physical condition that affects the brain's structure. Proteins form "tangles" and "clumps" in the brain cells, causes damage. The prevalence of Alzheimer's disease is universal, but this category of dementia is intensively researched.

Alzheimer's disease affects people starting at the age of 65, but it can also affect people as young as 45. As a basic function of AD which is suggested to differentiate the illness, the image shifts pervasively.

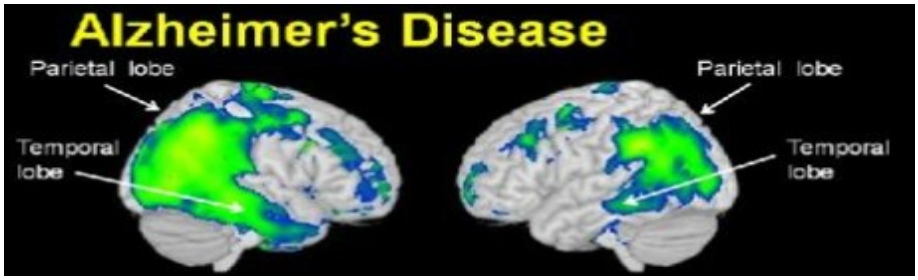


Figure 1.1 Alzheimer's disease brain MRI [90**]**

The following conditions are included in this:

- Dementia can indeed be diagnosed by psychiatric assessments recorded by the Blessed dementia scale, Mini Mental State Review, or a similar examination, and verified by neuropsychological testing.
- If there are deficits in more than two cognitive areas.
- If memory as well as other cognitive functions decline over time.
- If there is no delirium.
- If it happens between the ages of 40 and 90, mostly after 65 years of age.
- If there are no systemic disorders or any other cerebral diseases that can self-govern gradual memory and cognition decline.

It is critical that such deficits have an effect on everyday performance activities. Relevant assessments are included in the neuropsychological evaluation [18] to reach all functional processes. This is covered in greater depth later in the text. Sexual changes, mood disorders, hallucinations, appetite changes, and delirium, indifference and apathy, disinhibition, disruptions in psychomotor behaviour, and disrupted sleep are some of the other behavioural changes that take place during the disease. Loss of topographic orientation, Memory loss, language disturbances, and personality changes, are all common symptoms of Alzheimer's disease.

1.4.2 Vascular Dementia (VaD)

VaD seems being the second most common form of dementia, contributing for around 20% of all cases [4]. This type of dementia happens after a stroke or a small vessel disease occurs. This factsheet discusses VaD (Kotila et al. 1986). When it comes to VaD, a deficiency in blood supply in the brain is thought to lead to a number of dementia syndromes. Binswanger disease is caused by a variety of lesions, including small vessel disease, thromboembolic disorders, single lesions in main areas, chronic alterations of cerebral circulation, lacunar infarcts, amyloid angiopathy, intercerebral hemorrhagic lesions, and extreme white matter modifications. Main and secondary avoidance are both possible because VaD is related to cerebrovascular compromise. There is a large variance in the rate of VaD between different populations. According to a Canadian report 11, VaD accounts for 19 percent of dementia cases. The typical clinical definition of VaD is characterised by a rapid onset, typically as a result of a Transient Ischemic Attack (TIA), or stroke (CVA) with gradual progress or permanent decline, and a step - wise fluctuating presentation. Additionally, focal neurological signs such as ataxia, hemiparesis, hemianopsia, hemiparesis, and aphasis are often diagnosed with hemineglect. Magnetic resonance and brain CT exams are widely used to reveal like brain infarcts, but other considerations are being used to accelerate the mechanism of differential diagnosis. The Hachinski scale may be used to supplement the diagnosis. Scores of seven or higher suggest a greater chance of Alzheimer's and other degenerative dementias, while scores of five or lower show a higher risk of cardiovascular attack (heart disease and stroke) [17].

Symptoms of VaD

The symptoms vary according to the area of the brain impacted mostly by stroke. While Alzheimer's disease is characterized by memory difficulties, VaD is characterized by impaired judgement, as well as difficulty preparing, managing, and making choices.

Additional symptoms can include the following [87]:

- Memory issues that interfere with your loved one's everyday activities.
- Difficulty in understanding or speaking voice.
- Difficulty remembering familiar sights and sounds.
- Confusion or agitation.
- Personality and mood changes.

Numerous small strokes and perhaps other conditions affecting nerve fibres and blood vessels deep within the brain may result in far more incremental cognitive changes as the damage settles. Early signs of severe small vessel disease involve impaired judgement and planning, uncontrollable laughter and weeping, deteriorating ability to concentrate, trouble getting the correct words, and impaired social function [88].

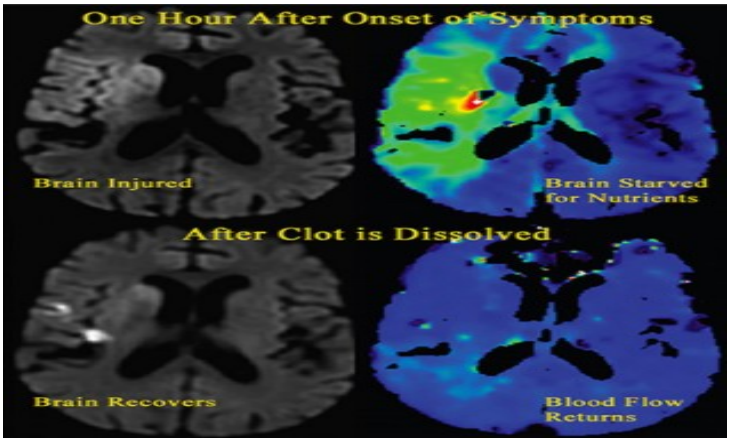


Figure 1.2 Brain MRI with VaD [88]

Credit: National Institute of Neurological disorders and stroke

This brain MRI demonstrates the after-effects of the massive stroke. The photos depict rain that is depleted of nutrients an hour just after system began. The bottom images demonstrate the restoration of blood and nutrient supply following successful usage clot-busting drug.

Diagnosis

In 2011, the American Stroke and Heart Association published a joint factual hypothesis on vascular disease's role in dementia and moderate cognitive impairment (MCI). According to the 2011 statement's clinical diagnosis, the inclusion conditions indicate that the greatest likelihood of dementia or MCI is triggered by vascular changes [88]:

1. Neurocognitive examination confirms the diagnosis of MCI or dementia, which entails many sessions of formal or computerised assessments that assess basic thought abilities such as decision, planning, problem-solving, memory, and reasoning.
2. Brain imaging data, typically MRI, confirms:
    - A current stroke or
    - Other vascular brain alterations whose magnitude and pattern of damaged tissue are consistent with forms of impairment reported in cognitive test tasks.

3. There seems to be no reason to assume that nonvascular causes play a role in cognitive decline.

1.4.3 Frontotemporal (lobe) Dementia (FTD)

FTD is associated with both complex protein bundles and rounded nerve cells in the brain. Except in the case of the previous inception, it occurs in 1 in 5000 individuals. It is responsible for 5% including all dementia cases. The term "Frontotemporal Lobar Degeneration" (FTLD) is a macro-anatomical term that refers to a clinically and pathologically heterogeneous community of disorders. It is defined jointly as gradual atrophy of the temporal and/or frontal lobes.

Numerous diseases may result in frontotemporal degenerations. The two most well-known are 1) a class of brain diseases associated with the protein TDP43; 2) a class of brain diseases associated with the protein tau. For unknown causes, these two classes exhibit a tendency for the temporal and frontal lobes associated with dementia.

Types of FTD

1. FTD formally known as behaviour variant frontotemporal dementia is characterised by significant behavioural and personality changes that typically occur in humans in their 50s or 60s but it can occur as soon as the 20s or as far as the 80s. The neuron cell loss has been most pronounced in parts of the brain that regulate action, reasoning, foresight, and empathy among other skills, in behaviour variable frontotemporal dementia.

2. PPA is the second most common form of frontotemporal degeneration, affecting and writing, verbal abilities, speech, and understanding. PPA usually appears in middle age, long before the age of 65, but it can occur at any age. PPA can be classified into two categories, each with its own set of symptoms:
    - People with semantic PPA lose their capacity to understand and communicate terms in spoken conversations.
    - Individuals with agrammatic/non-fluent variants of PPA talk very slowly, laboriously, or ungrammatically.

3. Motor (muscle or movement) control disorders encompass three subtypes of frontotemporal degeneration that manifest as shifts in motor or muscle function both with and without language (PPA) and behavioural (bvFTD) difficulties:

    - ALS known as Amyotrophic lateral sclerosis is often a disease that results in weakness of muscle. ALS is indeed a motor neuron condition that is also known as Lou Gehrig's disease.
    - Uncoordinated or stiff arms and legs are symptoms of corticobasal syndrome.
    - Progressive supranuclear palsy (PSP), an ailment characterised by muscle weakness, trouble walking, and postural adjustments. Additionally, it has an impact on eye movements. Both PPA and action variant frontotemporal dementia are much less prevalent in adults over the age of 65 than AD. PPA and frontotemporal dementia, on the other hand, are almost as common in the 45–65 age bracket as younger-onset Alzheimer's. Only approximate statistics are valid, but there may be 50,000 to 60,000 people in the US who have behaviour variant PPA and frontotemporal dementia, the largest of which are here between ages of 45 and 65 [89].

Diagnosis

The diagnosis of behaviour variant PPA and frontotemporal dementia is made after a specialist review by a physician experienced with any of these disorders. The nature of the patient's symptoms and the findings of neurological examinations form the basis of the diagnosis. Brain imaging like glucose positron emission tomography (PET) and MRI are extremely beneficial adjunctive examinations, but they should be viewed in conjunction with the patient's history and neurological examination [49,50].

1.4.4 Dementia with Lewy Bodies (DLB)

Diagnosing dementia's signature brain abnormalities started with Frederic Lewy in the first decade of the twentieth century, mostly when he worked with Dr. Alois Alzheimer's research team. Although it seems to be a predominant part of the Lewy body (LB), the protein alpha-synuclein seems to have a rudimentary function. From LB, the second most prevalent type of degenerative dementia, comes the low-to-moderate dementia category. This accounts for 10% to 15% of cases and is characterized by dysregulation and alpha-synuclein accumulation.

Both the clinical forms of LB disease have LB as a common etiology. While DLB is often presents with a combination of cognition issues as well as fluctuating concentration and movement disorders, this is not the case in all patients.

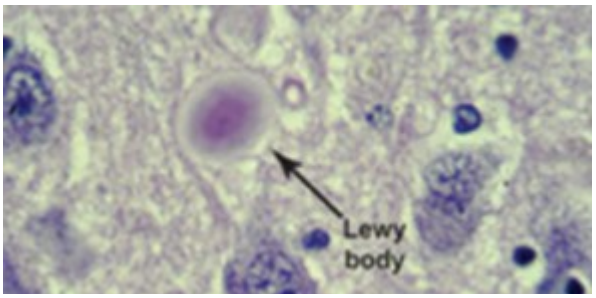


Figure 1.3 Lewy bodies [91]

Lewy bodies are also present in other types of dementia, such as Parkinson's disease and Alzheimer's disease. Many people who have Parkinson's disease gradually develop cognitive and thought difficulties, and many people who have Lewy body dementia exhibit movement symptoms like hunched position, rigid muscles, a juggling walk, and difficulty initiating motion.

Symptoms

Symptoms of LB dementia include the following:

- Cognitive and reasoning changes.
- Alertness and confusion that differs greatly according to the time of day or day of the week.
- Sluggishness, gait mismatch, and other characteristics of parkinsonian movement.
- Visual hallucinations that are well-formed.
- Abnormalities of the so-called "automatic" (autonomic) nervous system.
- Severe but less noticeable memory problems than in Alzheimer's disease.
- Difficulty deciphering visual details.
- Disruptions of sleep.
- Illusions

Diagnosis

Numerous specialists also agree that Parkinson's disease dementia and Lewy body dementia are two distinct manifestations of the very same underlying issue with both the brain's alpha-synuclein synthesis. However, the majority of physicians continue to diagnose Parkinson's disease and Lewy body dementia as distinct diseases.

A person develops Lewy body dementia, when:

- The development of dementia symptoms is associated with Lewy body dementia begins first.
- Parkinson's disease is diagnosed when both mobility and dementia symptoms are present at the time of diagnosis.
- When signs of dementia occur within a year of the onset of movement symptoms.
- When a person is initially diagnosed with Parkinson's disease dependent on movement symptoms but dementia symptoms don't occur for a year or more, the condition is PDD.

1.4.5 Parkinson’s disease

Parkinson’s disease (PD) condition is persistent mostly in nervous system. It is caused by the depletion of the neurotransmitter dopamine within the brain. PD is characterised by tremors, weakness in the joints and limbs, speech difficulties, and difficulties performing body

movements [92]. This disease accounts for about 3% to 4% of all dementia cases. The suggested clinical diagnoses for Parkinson's disease dementia (PDD) involve four domains: 1). those rooted in key features, 2). those associated with similar clinical features, 3). Indefinite diagnoses that have not come true and 4). those that represent the prognosis of PDD. A likely PDD is given if all four conditions are met; a potential PDD if only one of the first four conditions have been met and/or if additional uncertain clinical features are present. The occurrence of dementia is around 4.5 times greater in patients with Parkinson's disease, but the severity of the condition is almost equal to that of 30% in age-matched controls. For patients with PD who are still alive after ten years, collect a minimum of 75% of all of their claimants. It is related to both tardive dyskinesia and parkinsonism, a disorder that causes tardive dyskinesia and Parkinson's, where there is a certain 12-month period requirement for the disease to manifest. The severity of the pathology varies, although the time period between the onset of Parkinson's disease and dementia does not.

Motor Symptoms:

- Substantia nigra pars compacta -~400,000 dopamine neurons.
- Basal ganglia –inputs of Acetylcholine, Norepinephrine, and Dopamine.
- 70% failure with the onset of symptoms.

Memory/Cognitive Symptoms

- Pathology may eventually spread to the parietal/bi-frontal regions and hippocampal circuit.
- Late stages may resemble AD.
- Early Mild Cognitive Impairment.
- Tau -AD-based neurofibrillary tangles.

The primary changes in the brain associated with Parkinson's disease (PD) and Parkinson's disease dementia (PDD) are irregular microscopic substances consisting primarily of alpha-synuclein, a protein contained in abundance throughout the brain via an unknown normal function. The reserves are referred to as "Lewy bodies." PD is often a fairly frequent neurological disorder among older people, affecting about 2% of those over the age of 65.

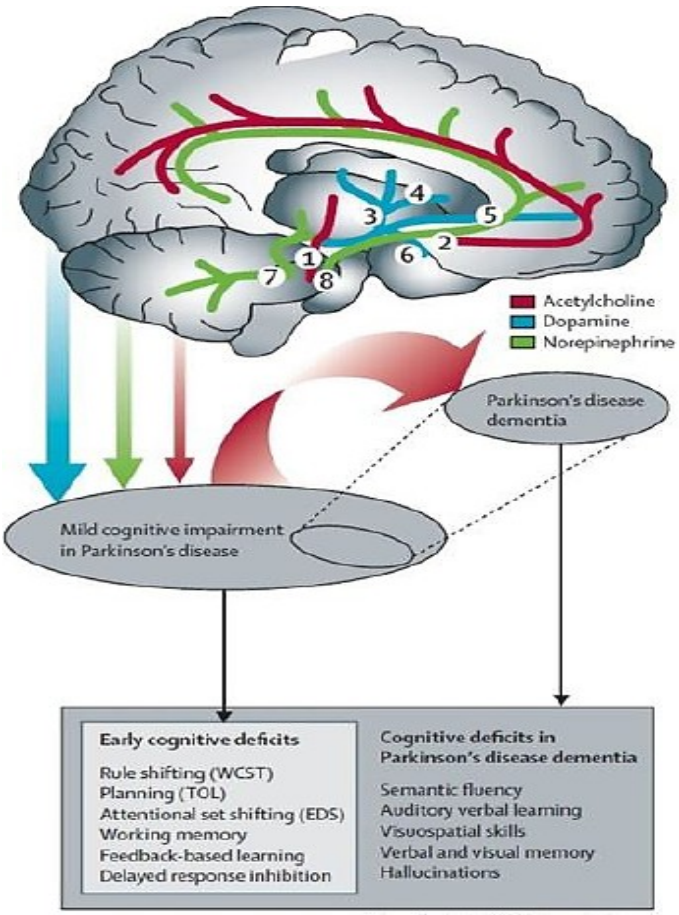


Figure 1.4 Parkinson disease dementia [92]

According to the National Parkinson's Foundation, more than10 million Americans are having PD at present. Current findings of Alzheimer's association reports that between 50% and 80% individuals with Parkinson's may develop dementia. The Weil Institute for Neuroscience gauged that beginning of Parkinson's Disease and getting converted to Dementia takes almost 10 years.

Symptoms

Among the most frequently recorded symptoms are the following:

- Changes in concentration, judgment, and memory.
- Visual knowledge is difficult to understand.
- Visual hallucinations.

- Muffled speech.
- Delusions, particularly paranoid thoughts
- Irritability, anxiety, and depression.
- Rapid eye movement (REM) and Excessive daytime drowsiness sleep disorder are two examples of sleep disturbances.

Diagnosis

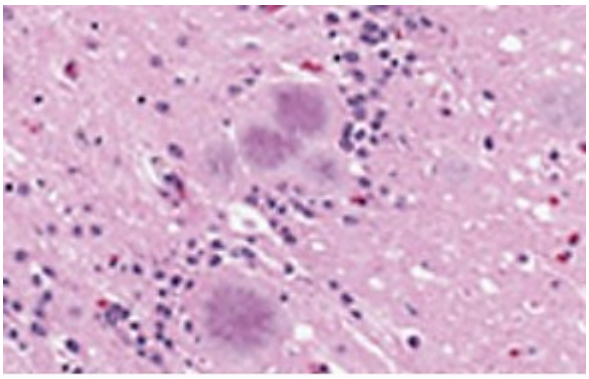
There seems to be no single test or set of tests that can definitively determine whether or not someone has Parkinson's dementia.

- When a person is diagnosed initially with Parkinson's disease-centered on movement-related symptoms and dementia symptoms do not manifest for at least a year, the condition is Parkinson's disease dementia (PDD).
- Neurologist keeps a check on the various parameters of a person and then kept under observation for any signs of Dementia.
- Neuroimaging scans are done to find out occurrence of disease.

1.4.6 Creutzfeldt– Jacob Disease (CJD)

Prion diseases may also cause degenerative dementia. There are uncommon diseases. CJD is often a typical human prion disorder. The myoclonic type of CJD dementia progresses rapidly following its insidious onset. Generally, the course includes a distinct stage during which myoclonic jerks and startle reactions are significant. During certain stages of the disease, highly characteristic intermittent sharp waves are often observed on the EEG. CJD seems to be a culminant condition in which cognition disintegrates over a period of a few days. Additionally, it is clear that the disease is fatal within six months of its onset. Each case presents with a unique profile of cognitive impairment. The Heidenhain version of CJD rapidly impairs vision and can result in cortical blindness as a result of spongiform changes within the visual cortex. The disease progresses at a variable pace. The disparity is partly due to genetic problems, specifically a polymorphism at codon 129. Homozygosity for methionine at codon 129 is a characteristic of patients who develop the standard myoclonic CJD type. However, in contrast to valine–methionine heterozygosity or valine homozygosity is associated with ataxia, a longer period of

symptoms, and a less reliable diagnosis via 14-3-3 or EEG antigen assay. CJD diagnosis is completed mostly when intermittent sharp waves are detected on the EEG of a patient with subacute dementia who also has normal standard CSF and MRI. Brain biopsy procedure can be avoided as it is characterised by a bulge in addition to the loss of nerve cells, an increase in the size of brain cells (astrocytes), and irregular prion protein concentrations amongst nerve cells [19]. Individuals can rapidly progress from symptoms to kinetic mutism, wherein they die within six to eighteen months (Australia, 2009).



Sponge-like lesions in the brain tissue of a CJD patient.

Figure 1.5 CJD Brain MRI [94]

The following major forms of Creutzfeldt-Jakob disease are widely recognised by experts:

- **Familial Creutzfeldt-Jakob disease** is caused by mutations mostly in the chromosome 20 gene that codes for the prion protein's biological blueprint. Individuals that acquire hereditary Creutzfeldt-Jakob disease do so as a result of genetic alterations inherited from a parent. Around 10% to 15% of cases are of familial Creutzfeldt-Jakob disease. It usually manifests earlier than intermittent Creutzfeldt-Jakob disease, with certain genetic variants manifesting as early as the age of 20 to 40 [94].
- **Sporadic Creutzfeldt-Jakob disease** develops naturally and without apparent cause. It is responsible for 85% of incidents. Creutzfeldt-Jakob disease usually manifests itself between the ages of 60 and 65.

- **Acquired Creutzfeldt-Jakob disease** occurs as a result of exposure to an irregular prion protein via an external source. Around 1% of Creutzfeldt-Jakob disease cases are thought to be caused by these causes. The two most often cited external sources are [94]:

    - Medical procedures that use neurosurgical tools, growth hormone, or some transplanted human tissues, such as dura mater (the fibrous membrane coating the spinal and brain cord) and corneas (the eye's transparent outer layer). Additionally, this form of acquiring CJD is referred to as iatrogenic CJD (iCJD). The risk of contracting iCJD during medical interventions has indeed been drastically decreased through enhanced neurosurgical tool sterilisation methods, the development of solitary devices, including the use of dura mater sources and synthetic growth hormone.
    - Meat or other items from cattle contaminated with bovine spongiform encephalopathy (BVE), also known as "crazy cow disease," which was identified as the cause of variant CJD in the mid-1990s (vCJD). The new strain of CJD was linked to the intake of beef from cattle fed processed brain tissue from other species. Since then, approximately 200 reports of vCJD have been diagnosed, mainly in the UK and other EU nations. Variant CJD is more prevalent in children and adolescents than in intermittent or familial types. The risk of developing of vCJD has dramatically decreased, most likely as a result of improvements in animal feeding practises.

Symptoms

Individuals' specific Creutzfeldt-Jakob disease symptoms and the order in which they manifest will vary considerably. Several typical symptoms include the following:

- Mood swings, agitation, and apathy
- Depression.
- Disorientation.
- Rapidly worsening confusion.
- Issues with thinking, memory, judgment, and planning.
- Trouble in walking.

- Muscle toughness, spontaneous irregular actions.
- Vision difficulties, like hallucinations and double vision.

Diagnosis

Rapid illness development of signs is one of Creutzfeldt-Jakob syndrome. As there is no one test that can identify the condition, the findings of this test can help in further evaluation to see whether a patient appears to have Creutzfeldt-Jakob disease.

It is thought that an electroencephalogram can serve as an electrocardiogram (EKG) for the brain's MRI. It is capable of identifying certain neurodegenerative changes in the brain relevant proteins in the spinal fluid which is measured using a lumbar puncture. For a protein misfolding cyclic amplification, or PMCA, the acronym PSA stands for protein. Misfolded protein complexes can frequently be detected using polymerase chain reaction (PMCA)

1.4.7 Mixed Dementia

The most popular example of mixed dementia is vascular dementia, in which irregular deposits of proteins associated with AD co-exist with blood vessel issues due to vascular dementia. Alzheimer's disease-related changes in the brain frequently coexist alongside Lewy bodies. An individual may well have changes in the brain associated with all three disorders-in some cases — Lewy body dementia, Alzheimer's disease and vascular dementia.

While previous researchers do not know how often elderly people diagnosed with a particular form of dementia currently have combined dementia, autopsies have suggested that the disease is substantially more prevalent than previously recognized [95].

Since the majority of dementia-related changes in the brain cannot yet be measured in living people, autopsy studies are critical for focusing attention on mixed dementia. Previous researchers compare each cognitive health of each participant and any diagnosed disorders throughout life with post-mortem brain examination in the most detailed studies.

Symptoms

The symptoms of mixed dementia (MD) [95] differ according to the form of brain regions impacted and the brain changes involved. Symptoms can be identical to that of AD or some other form of dementia in several cases. Occasionally, a set of symptoms can indicate the presence of multiple types of dementia. Previous studies anticipate that a better understanding of MD symptoms as long-term research will shed light on the connection between cognitive performance and specific brain disorders.

Diagnosis

The majority of people whose autopsies reveal mixed dementia were initially diagnosed with a single form of dementia, quite generally AD. For instance, mostly in NIA research, which included long-term cognitive tests accompanied by brain autopsy, 94 percent of responders with dementia were eventually diagnosed with AD. Nonetheless, autopsies of patients diagnosed with AD revealed that 54% had coexisting pathology in addition to the classic Alzheimer's changes in the brain. Coexisting abnormalities most often included previously unknown blood clots or other signs of vascular disease. Lewy bodies has been the second most often occurring coexisting brain abnormality.

1.5 Brain Imaging For AD/DEMENTIA

Brain imaging for detecting dementia has advanced dramatically over the last two decades, owing to a plethora of modern technologies that are remarkably accurate. The Neuroimaging Work Group Report summarises the current state of the field and suggests future paths. Brain imaging techniques may help to coordinate these numerous causes. The marginal diagnostic value provided by the brain imaging method (i.e., increased sensitivity and specificity) can be extended to neuropharmacology clinical studies [68]. When diagnostic homogeneity is improved by brain imaging, medication efficacy and clinical trials become much more insightful.

Additionally, brain imaging is being used to identify AD in a preclinical environment. Neuropsychological, Neuropathologic, and brain imaging evidence cumulatively suggest that AD is preceded by a type of progressive maturity level cognitive decline. Eventually, brain

imaging includes information about fundamental disease pathways, which can aid in the creation of more effective drugs. Although on the one hand, it is hard to diagnose a patient's cognitive condition using neuroimaging since it should be treated clinically[6,57]. However, on the other hand, neuroimaging using MRI or CT is useful in excluding systemic brain lesions in people with dementia, and abscesses. Both techniques are highly effective at identifying brain tumours, strokes, and hematomas. Although mass lesions are common, it is critical to conduct imagery work to assess each dementia person initially.

Although empirical evidence predominantly has emerged from a quantitative study of structural brain MRI. However, the qualitative evaluation of medial temporal atrophy almost always is consistent with quantitative tests. These qualitative estimates also become suitable for medical diagnosis. Brain imaging enables the early detection of Alzheimer's disease. In light of this, the following suggestions have been made:

- The Neurology recommendations are followed by the American Academy; If AD is reported, it obtains brain scans as evidence of the dementia process and amends the AAN guidance to include individuals with amnestic MCI i.e., Mild Cognitive Impairment.
- The effect of widespread white matter infection still is unknown. Consequently, it is critical to support experiments on a wide range of patients with MCI to determine the precise usefulness of imaging in predicting potential "AD diagnosis" and the particular type of MCI which is probably to still be "prodromal AD."
- Coronal brain imaging, if practicable, must be done perpendicular to a hippocampus's long axis and should be incorporated into routine MRI protocols.
- Monitoring imaging parameters to the greatest extent possible by rigid adherence to standard imaging protocols and analysis techniques will lead to potentially effective outcomes. Every health system equipped with brain imaging equipment can customise the imaging series.
- It is important to use a commonly accepted, structured, and approved procedure to understand medial temporal atrophy on MRI clinically. These qualitative tools are becoming increasingly scarce in the modern era. Two scales have been used, and both show (1) intra- and inter-rater reliability, (2) associations including quantitative volumetric and neuropsychological variables, and (3) prospect predictive value. The

Work Group proposes creating and/or validating standard protocols for quantifying, demonstrating, and interpreting the clinical significance of structural reforms detected in brain images.

- Systematic reviews are necessary to determine the effectiveness of MRI in early detection and differential diagnosis. The MRI images have the ability to identify AD and its pathology. Additional research with an emphasis on the qualitative analysis of various types of anatomical brain images from diverse populations is needed to determine the efficacy of this method for diagnosing dementia slightly earlier [51,70].
- If CT imaging is used to treat AD in its initial stages, it is important to focus future studies on those that can undergo MRI classifications.

1.5.1 Brain Imaging

Neuroimaging is often a highly skilled field of study that focuses on the diagnosis and treatment of AD at a preliminary phase [57]. Typically, this approach is used in clinical practise to find out alternative causes of cognitive impairment (e.g., brain tumours) and to recognise large variations consistent with AD, vascular disease, or some other trigger of dementia. The structural brain image reveals the scale, shape, position, and density of brain tissue. Imaging techniques such as MRI and CT are used to acquire structural images. In comparison to CT, when employed in a wide variety of ways, MRI seems to have a better resolution, which enables a more complete analysis of the brain anatomy. According to structural imaging research, people’s brains with AD keep shrinking significantly as the disease progresses. As per the study, shrinkage in specific brain regions, including the hippocampus, is a symptom of early Alzheimer's disease. Specific types of dementia can indeed be distinguished by the patterns of shrinkage in specific brain regions, for example, frontotemporal dementia is primarily caused by volume loss throughout the temporal and/or frontal lobes. Nonetheless, additional work is required to establish standards for brain volume which represent the significance of shrinkage for an individual at a specific moment in time [41].

Functional brain imaging depicts the active use of oxygen or sugar by cells in the brain for the structural purpose. Functional imaging is accomplished by the use of Positron Emission

Tomography (PET) and functional magnetic resonance imaging (fMRI). At the moment, the most commonly used method for detecting dementia is fluorodeoxyglucose (FDG)-PET, which measures the brain's glucose intake. According to FDG-PET analysis, AD is frequently associated with insufficient glucose intake in brain areas critical for memory, learning, and solving problems. The process of impaired glucose metabolism in different areas of the brain is associated with other types of dementia. Relative to the shrinkage detected by structural imaging, additional research is needed to define firm criteria for diagnosing an individual using common patterns of decreased activity.

Molecular brain imaging allows the use of extremely specialized radiotracers to detect changes in the chemical or cellular composition of the brain associated with specific diseases. PET, fMRI, and Single Photon Emission Computed Tomography are all examples of molecular imaging technologies (SPECT). Molecular imaging methods are one of the methodologies that have been extensively studied in attempt to develop novel methods for detecting AD in its earliest stages. These strategies can detect biological indicators of the onset of AD long before it alters the function or structure of the brain or results in permanent memory loss, thought, and reasoning [15]. Additionally, molecular imaging offers a novel method for evaluating the effectiveness of next-generation, disease-modifying therapies.

1.6 Diagnostic Tests for Dementia

Dementia can also be diagnosed using the following protocols [98]:

- **Neuropsychological and cognitive assessments.** These assessments are being used to evaluate solving problems, memory, language ability, math abilities, and other cognitive abilities.
- **Laboratory examinations.** Checking the blood of a person and other bodily fluids, and also the levels of various chemicals, vitamins, and hormones, will assist in determining or excluding possible reasons for symptoms.
- **Scans of the brain.** These methods can reveal strokes, cancers, as well as other conditions associated with dementia. Additionally, scans detect changes in the structure and function of the human brain. The most frequently used scans are [98]:

- Computed tomography (CT) produces brain images and other organs using x-rays.
- Magnetic resonance imaging (MRI) employs radio waves and magnetic fields to create accurate representations of internal body systems such as tissues, muscles, nerves, and bones.
- Positron emission tomography (PET) is a technique that employs radiation to create images of brain function.

- **Evaluation by a psychiatrist.** This assessment will assist in determining whether anxiety or some other mental disorder is leading to or triggering a person's symptoms.
- **Genetic examinations.** Certain types of dementia are triggered by a recognized genetic mutation. In these instances, a genetic test may help individuals determine their likelihood of developing dementia. It is critical to consult a genetic counsellor prior to and after testing, as well as relatives and the doctor.

1.7 Clinical Diagnosis

Diagnosing Alzheimer's disease by various techniques has advanced significantly, but we are also unable to discern who has it and who does not, which makes these tests imprecise. It is important to determine the existence of distinct patterns of cognitive and neuropsychiatric issues when diagnosing dementia. When neuronal observations are not very useful, an alignment in cognitive profiles exists. Often, individuals with AD and FTLD have deficiencies in their executive function and memory.

It is essential to provide a "normal" clinical diagnostic evaluation in order to assess the importance of new diagnostic methods for determining AD. There seems to be currently no widely recognised clinical approach for evaluating dementia patients in actual environments. The procedure varies according to the environment. Numerous approaches exist, for example, amongst primary care physicians, clinical neurosurgeons, and dementia investigators at academic centres. Due to the growth of managed care schemes, more defined criteria will be developed, likely with a greater emphasis on cost containment.

Two diametrically opposed views toward dementia diagnosis are prevalent within the medical community, both of which have negative consequences. One would be that improvements in cognition and behaviour found in older adults are simply a result of the natural ageing process and therefore quickly ignored. Secondly, cognitive loss occurs in older adults as a result of Alzheimer's disease. Alzheimer's disease and Dementia are synonymous phrases. Both of these attitudes can contribute to the catastrophic belief that no attempt should be made to correctly assess dementia.

Clearly, as innovative and specialised therapies become more common, it is necessary to optimize diagnostic accuracy. However, accuracy of diagnosis continues to be a major objective. Perhaps these efforts will contribute significantly to recognising potentially reversible or treatable disorders that contribute to cognitive decline and dementia. Correct diagnosis may provide critical prognostic data to families, allowing them to set appropriate goals and prepare for the patient's future needs.

1.7.1 How is dementia diagnosed?

Primary care's role

The fundamental role in primary care is to rule out treatable disorders and refer those that develop symptoms or patterns of simple (but serious) changes to be seen by a specialist. For example, elevated serum vitamin B12 levels. Both the patient and the caregiver should be given a comprehensive history from the start, but a further examination is required in order to determine if they suffer from neurological difficulties and whether they need assistance. The screen for physical manifestations must be run to rule out any focal medical disorders, vision, and hearing complaints out. An initial medical workup and use of the various diagnostic and assessment devices is essential before making a referral to secondary treatment in primary care, inquiries and brief cognitive testing methods for dementia [41]

1. Blood tests: A complete blood count, electrolytes and urea, an erythrocyte sedimentation rate, vitamin B12, thyroid function, and folate must be requested. Where clinically indicated, a chest radiography, midstream urine specimen, and electrocardiography also may be required.

2. Two brief cognitive testing instruments

- **Assessment of cognition by a general practitioner:** It requires no more than 5 minutes and is divided into two modules: a six-item cognition test administered mostly to patients and an informant questionnaire (if the cognitive test scores is uncertain: 5-8 inclusive). Scores greater than 8 are considered to indicate cognitive disability, whereas scores less than 5 indicate intact cognition. Sensitivity is between 82 and 85 percent; specificity is between 83 and 86 percent.

- **Six-item cognitive disability test:** This test takes about three to four minutes to complete and consists of six questions about memory and orientation. Although the test can be influenced by education and language. Scores between 0 and 7 are often considered average, while 8 indicates cognitive impairment. Sensitivity ranges from 78.5 to 83 percent; specificity ranges from 77 to 100 percent.

- **Mini-cog evaluation instrument:** This device takes approximately 2-4 minutes to finish. It comprises of 2 modules: a three-item recall and a clock drawing test. Individuals with cognitive dysfunction didn't recall any one of the 3 items or can only recollect one or two, resulting in an odd clock. Sensitivity ranges from 76 to 99 percent; specificity ranges from 89 to 96 percent.

- **Memory impairment screen:** This is indeed a four-item memory impairment test with postponed cued recall and free recall which takes around four minutes to complete. A score of 4 suggests the possibility of dementia. Sensitivity ranges from 74 to 86 percent; specificity ranges from 96 to 97 percent.

Role of secondary care

Primary care is playing a part mostly in evaluation and deep care of dementia patients. A multicentre randomized clinical trial discovered no proof that specialist memory clinics were much more successful at delivering post-diagnostic aid than general practice services. Secondary care is critical for identifying the dementia subtype, managing more severe cases, and stratifying

which patients with moderate cognitive impairment. This is because such patients are at more risk of developing dementia and require the maximum follow-up [41].

1.7.2 Diagnostic Criteria

There is no single examination that can definitively decide if someone has Alzheimer's disease. A diagnosis is confirmed based on the occurrence of specific signs and the exclusion of all possible forms of dementia. This requires a comprehensive medical assessment, which includes a detailed health history, mental fitness testing, blood tests, a neuropsychological examination, and brain imaging examinations, such as [96]:

- **Neuroradiology:** MRI (Magnetic Resonance Imaging) uses magnetic waves of energy to produce images of different organs within the body. CT scans of the brain are used to diagnose and locate possible signs of dementia, including a brain tumour, stroke, or bleed on the brain.
- **MRI of the head:** The MRI, using a magnetic field, radio frequency waves, and a monitor, produces very detailed photographs of internal organs, bone, soft tissues, and almost all other body parts. Mild cognitive dysfunction (MCI) may be detected by an MRI scan that shows brain anomalies consistent with MCI and that could indicate which patients with MCI will go on to develop Alzheimer's disease in the future. Alzheimer's disease does, in fact, appear on an MRI scan in the primary stages of the disease. MRI will show that different brain areas have been reduced in size (affecting the parietal and temporal lobes).
- **PET and PET/CT scans of the head:** PET, or positron emission tomography, is a diagnostic process that uses small amounts of radioactive material (known as a radiotracer) to diagnose and measure the severity of a variety of disorders.

Detailed anatomy and physiology can be obtained from PET/enhanced CT imaging (from PET scan). A PET/CT scan can assist in distinguishing AD from other forms of dementia. This imaging technique is also known as single-photon emission tomography. However, owing to new tracers, which can be injected into humans, scientists have been able to identify beta-amyloid plaques in the human brain for quite some time now, so far only through [utilizing] the C-11 PIB and PET scans. It is becoming difficult to avoid comparable radiotracers in clinical

practice. During the psychiatric work-ups, an emotional and physical assessment is conducted, along with a neurological review to help with cognitive performance testing. Additionally, they seem to be tests for behaviour and caregiver fatigue as well. Global Deterioration of academics, including the Clinical Dementia Rating Scale, was widely used.

Disease-out medical disorders that could result in dementia was discovered by way of a laboratory examination. Plasma Amyloid and cerebrospinal fluid testing are not typically used to diagnose bipolar disorder. In addition to that, urine-based assays for Amyloidosis protein and other neurotransmitters have also not been considered to be diagnostic. While certain nonconforming signs are noted, the diagnosis is confirmed only when memory loss and related functional areas, such as orientation and expression, is symptom, or pathology. It varies in onset and begins with sensory and motor function deprivation, and progresses over time. Alterations of long-term memory and remote memory loss of capability have been recorded in almost all cases to occur during the disease's stage of disease [17].

1.8 Motivation

As discussed in the above sections that AD is the most important form of dementia. An estimated 5.5 million people over the age of 65 are affected by AD, It is also the top cause of mortality in the globe. Treating AD has a huge financial, personal, and social impact on the country's health care system[65]. AD has long term, organic cognitive impairment due to no established pathophysiological treatment[43]. There have been significant endeavours made to develop early diagnostic methods, especially at the stages prior to the onset of disease[59]. Cognitive neuroscience studies and all have also tried to use sophisticated approaches like MRI and PET to map out the molecular and cellular aspects of both AD and structural/structural biomarkers[70]. Prominent, large- scale, multimodal advances in neuroimaging research have made the synthesis of many small- scale neuroimaging data more difficult. The incorporation of machine learning techniques has created an appetite for innovation as well. These well-established pattern analysis techniques, including LPBM, LDA, SVM, SVM-RFE, and LR, all look to be effective at the earlier stages of AD progression [54].

1.9 Organization of Thesis

Chapter 1: This chapter serves as an introduction to the review, providing an overview of Dementia/AD and the different deep learning technologies used to detect Dementia/AD.

Chapter 2: It presents the literature review of the proposed with the study of papers in brief. It targets the literature analysis as well as the inferences drawn from the review.

Chapter 3: It describes the Proposed approach based on machine learning approach, proposed work, parameters.

Chapter 4: It describes the Proposed approach based on Deep learning approach, proposed work, parameters.

Chapter-5: In this chapter a comparison of optimized feature optimized approach with existing approaches has been discussed. It entails analysing outcomes based on the optimised approach's performance.

Chapter-6: This chapter demonstrates the comparison of CNAT-TRXG (Proposed-2) approach with existing approaches. It involves the analysis of results based on the performance of the existing and the proposed approach.

Chapter-7: Here in this chapter, the conclusion drawn from the present research and the future scope in terms of the proposed and the existing approaches for the analysis of dementia is discussed. The chapter's last section closes with a number of findings that point to the optimal approach being used.

CHAPTER 2
LITERATURE SURVEY

The literature survey section is one of the significant parts of a thesis. It focuses on comprehensive material collected from numerous books, research articles or essays, journals, and research papers published at national and global levels. Literature survey generates methods that aid in determining the grounds for the technology.

2.1 Literature Analysis

Small, G. W. (2002) found that recognizing dementia is extremely hard in its initial stages, when members of the family and doctors sometimes mistake the patient's symptoms for normal ageing (1,2). According to the research, the prevalence of unrecognized memory failure beyond that associated with normal ageing or a dementia diagnosis can vary from 50% to 90% of cases.

Choi et al. (2003) investigated the GDS and CDR scales, which are widely used to assess dementia occurrence. However, there are no clear guidelines for converting CDR to GDS scores and vice-versa. Two auditors separately scored GDS and CDR in 78 dementia patients and 34 controls and use a semi-structured questionnaire. GDS and CDR have a curvilinear relation, according to regression analysis. This curve could provide a guideline for combining CDR and GDS scores (or CDR based Sum of Boxes).

Petrella et al. (2003) investigated how the research relates to magnetic resonance imaging (MRI) tests, which are increasingly being used to track treatment outcomes in clinical studies of antidementia agents and cognitive enhancers. Single photon emission CT and PET are useful in distinguishing Alzheimer's disease from many other subcortical and cortical dementias and they may also have prognostic value. Furthermore, PET tests have shown that slight abnormalities can be seen in the prodromal stages of Alzheimer and in people who bear susceptibility genes.

PET ligands for detecting amyloid plaques are nearing completion, and human trials have already started. Memory test tests related to the functional MR are also being created.

Noe et al. (2004) Dementia with Lewy bodies (DLB) was linked to AD and Parkinson's disease with dementia (PDd) in terms of neuropsychological and clinical patterns. Sixteen DLB cases were linked to two groups of patients with PDd (n = 15) and AD (n = 16) who were matched for the dementia stage. In the AD (93.8 percent) and DLB (31.3 percent) classes, isolated cognitive dysfunction was perhaps the most usual form of presentation, whereas parkinsonism was observed in 100% of PDd subjects. DLB patients (31.3 percent) had more psychoses linked to cognitive dysfunction at the start of the disorder than AD (6.3 percent) or PDd (0 percent) patients.

Svansdottir and Snædal (2006). Trained music therapists conducted this case-control study consisting of two psychogeriatric wards and two nursing homes. The respondents were 38 AD patients who were assigned randomly to one of two groups: the control group and the music therapy group. During a 6-week cycle, the music therapy community demonstrated a substantial decrease in activity disruptions as calculated by the Behaviour Pathology in AD Rating Scale (BEHAVE-AD). The number of behaviour disruptions, aggressive behaviour, and depression scores also decreased significantly. Many symptoms, as measured by BEHAVE-AD subscales, won't improve substantially. After four weeks, the adverse effects were mostly gone.

Hinton and Salakhutdinov (2006) established a strategy for initialising weights that allows deep autoencoder network to learn low-dimensional codes that surpass principal component analysis as a data dimensionality reduction approach.

Lynch et al. (2006) suggest that instead of the CDR total global ranking, find the CDR number of the utility of the box scores. The goal of the work was to discover whether the CDR total number of scores can be used to detect ICD-10 dementia in cognitively-impaired individuals. To complete the study, they researched the clinic's hospital database for all patients seen for six years. They found 272 primary care records of patients having CDR global rating of 0. The researchers used logistic regression to study the link between CDR sum scores and the consensus

diagnosis of dementia. The study observed a strong correlation between ICD-10 CDR scale scores and being diagnosed with dementia (p 0.001). -1. With each increase in the CDR cumulative score, the likelihood of being diagnosed with the condition went up by around 95 percent.

Bouchard (2007). To increase the validity of clinical trials and thereby lead to the improvement of more effective treatments, the authors updated the current criteria for a diagnosis and made suggestions for improvements in the sense of the 2nd Canadian Conference on the Development of Antidementia Therapies, conducted in 2004, and updated in light of the recent evidence as of early 2006. It is anticipated that such dementia clinical study eligibility requirements will need to be updated mostly in near future that included various subtypes of dementia as well as structural, functional, and biomarkers imaging.

Swanson and Carnahan (2007). This article discusses the diagnosis and treatment of common forms of dementia and associated conditions. Clinically, dementias are distinguished based on their history, symptom appearance, and exclusion of other potential causes via lab and imaging tests. Although cholinesterase inhibitors are beneficial, they are not appropriate for all forms of dementia and offer only limited advantages. Some clinical comorbidities can raise one's risk of developing dementia, while genetics also play a role in the disease's aetiology. Psychiatric comorbidities of dementia involve delirium, that is typically handled by treating specific medical problems; however, antipsychotics can be beneficial for symptom control and patient safety. Other psychological comorbidities are treated first with nonpharmacologic therapies, while drug therapy can be helpful at times. The treatment of dementia patients presents numerous challenges and will tend to do so until significant disease-modifying agents are created.

Pimentel et al. (2009) elucidate the function of neuropsychology in order to diagnose dementia and differentiate AD from VaD. The following section provides a summary of the most commonly used tools for assessing cognitive function in dementia, and also the cognitive changes observed in VaD and AD. The claim made was that while there is some variation in cognitive changes in between two forms of dementia, every form has distinct features that are

recognizable and measurable on neuropsychological tests and serve as a framework for differential diagnosis.

Salmon and Bondi (2009) demonstrate that AD related cognitive deficits are distinct from age-related cognitive loss. There are qualitative and quantitative differences across such a variety of cognitive domains, but they are particularly evident in episodic memory (especially delayed recall), semantic knowledge, and certain dimensions of executive functions. In very elderly AD patients, the qualitatively different pattern of deficiencies is less noticeable than in young AD patients. While a loss in episodic memory is typically the first cognitive shift seen prior to the onset of the AD dementia syndrome, asymmetry in cognitive skills can also occur during this "preclinical" stage of the disease and signal impending dementia. Cognitive defects manifest in distinct trends in AD and other neuropathologically distinct age-related neurodegenerative disorders. These distinctions aid in clinically differentiating between numerous causes of dementia as well as provide valuable models for comprehending the brain-behaviour associations that facilitate the cognitive abilities impacted by numerous neurodegenerative diseases.

Vincent et al. (2010) proposes a novel technique for deep network construction based on layering denoising autoencoders that are locally trained to denoise corrupted versions of their inputs. The resulting algorithm is indeed a straightforward variant of autoencoder stacking. However, it is demonstrated on a benchmark set of classification problems that it produces substantially lower classification error, trying to bridge the performance gap with deep belief networks (DBN), and in certain cases exceeding it. Additionally, the higher degree representation learned in this solely unsupervised fashion aid in the improving performance of corresponding SVM classifiers. Contrary to conventional autoencoders, qualitative analyses showed that denoising autoencoders can train Gabor-like edge detectors from larger stroke detectors from digit images and natural image patches.

Krizhevsky and Hinton (2011) demonstrate how to learn multiple layers of feature information from colour images, which we then use to initialize deep autoencoders. The autoencoders are then used to convert the images to short binary codes. By utilizing semantic hashing, 28-bit codes can be used to quickly extract features that are identical to a query image regardless of the size

of the database. This lightning-fast retrieval enables searching using a variety of different transforms of the test image. 256-bit binary codes enable significantly more precise matching which can be used to refine the collection of images discovered utilizing 28-bit codes.

Belmokhtar and Benamrane (2012) defined an automated system for identifying MCI, AD, and healthy controls using three dimensional MRI sets of data. The built classification system is based on SVM binary modelling and utilizes data analysed to use a combination of neuropsychological and VBM tests to categorize the three classes of subjects. The researchers have used JADE multi-agent framework to reduce the total processing time. The results obtained were extremely satisfying in terms of computational speed and accuracy of the system.

Farabet et al. (2012) suggest a methodology for automatically selecting the optimal collection of segmentation parameters that better describe the scenario from a pool of segmentation parameters; such elements may be random, for instance, they may be drawn from some family of over segmentations or from a segmentation tree. The device achieves record accuracy mostly on a "SIFT Flow dataset (33 classes) and Barcelona dataset (170 classes)", as well as "near-record accuracy on the Stanford history dataset (eight classes)", while "running orders of magnitude faster than competing approaches, labelling a 320240 image in less than a second", including extracting features.

Li et al. (2014) created a multi-modal imaging data analytics models using deep learning The design consists of CNNs that are used as both output and data. The method is made up of several different training examples that show how various input and output modalities relate to one another. After extensive testing, the device can predict the type of media to which the subject will react with a high degree of accuracy. the technique was evaluated on the ADNI, which uses PET and MRI scans as output and original scans as input. The system worked dramatically better than earlier methods, as shown by the findings.

Suk et al.(2014) The paper proposes an interesting new way to describe latent and shared aspects of imaging modalities using deep learning. The researchers use a deep network with a restricted Boltzmann as a building block, followed by a Deep Boltzmann (DBM) to create a function

representation from multi-modal MRI and PET patches They used the study strategy's success in the ADNI dataset and compared it with cutting-edge methods.

Li et al.(2014) present a comprehensive DL method for detecting various stages of Alzheimer's disease development in AD patients employing MRI and PET scans. The researchers used the dropout method to analyse classic DL via avoiding weight co-adaptation, a common source of overfitting in deep learning. Additionally, they built a deep learning system that incorporates an adaptive learning element, a multi-task learning strategy, and stability selection. The researchers validated the proposed approach using the ADNI set of data and conducted experiments for the diagnosis of MCI and AD conversion. The experimental results indicate that the dropout strategy is extremely successful at diagnosing AD, enhancing accuracies based on classification by an average of 6.2 percent as compared to the conventional deep learning techniques.

T O'Brien and Thomas (2015). This article discusses most of the key areas and concerns, summarizes current treatment studies, and provides recommendations about progress required to enhance the understanding of pathogenesis. It also recommends increasing potential for the creation of new and successful management practices.

Aggarwal et al. (2015) summarizes the current findings and novel therapeutic methods for AD's amyloid and tau pathologies, as well as the pharmaceutical and biomarkers therapies available and in progress for each AD process.

Suk et al. (2015) suggests a stacked auto-encoder-based DL-based latent feature representation. The researchers assume that latent complex non-linear patterns exist in low-level features like relationships between features. Mixing latent data with actual features enables the creation of a comprehensive approach for AD/MCI identification with a high diagnostic accuracy.

LeCun et al. (2015) describe how deep learning enables computational models consisting of various processing layers to train data representations at multiple abstraction levels. The researchers discuss several techniques which “have significantly enhanced the state-of-the-art in visual object recognition, speech recognition, object detection, and a variety of other domain

names like genomics and drug discovery". Deep learning uncovers intricate structures in large amounts of data using the algorithm of backpropagation to show why a machine's internal parameters must be changed in order to calculate the representation for each layer from the prior layer's representation.

Makhzani and Frey (2015) suggested the k-sparse autoencoder, a quite fast sparse coding method that ensures identical sparsity mostly in the hidden layer. The paper's primary message is that one can use the resultant representation to achieve state-of-the-art classifier performance solely by implementing sparsity in the secret units and without relying on any additional regularization or nonlinearity. Additionally, the study explores how well the k-sparse auto encoder can be used to pre-train deep and shallow supervised structures using the k-sparse auto encoder.

Herr Schmidhuber (2015). This historical review condenses pertinent work, the majority of which dates from the prior millennium. The distinction between deep and shallow learners is in the breadth of their credit task routes, that represent the chains of potentially learnable causal ties between behaviour and consequences. The authors discuss deep supervised learning (including a brief overview of backpropagation), reinforcement learning, evolutionary computation, and unsupervised learning, as well as the indirect quest for short programs encoding wide and deep systems.

Russakovsky et al. (2015) discuss the process of creating this data set and the advancements in object recognition that have resulted. The research highlighted the challenges of accumulating large-scale ground truth annotation, demonstrated major advances in classification object recognition, conducted a comprehensive study of the state - of -art in massive object detection and image classification, and compared state-of-the-art vision - based accuracy to human precision. They give an overview of the knowledge gained over the course of the challenge's five years and make recommendations for possible directions and changes.

Payan and Montana (2015) developed an algorithm that can determine a patient's disease activity centred on an MRI scan of a brain using deep learning methods, specifically 3D CNNs

and sparse autoencoders. The analyst's study on experiments involving 2,265 historic scans using the ADNI data collection. They show that 3D CNNs outperform many other published classifiers and deliver state-of-the-art results.

Khan and Usman (2015) present a study, interpretation, and critical appraisal of recent studies on the early detection of Alzheimer's disease using machine learning methods. Various techniques demonstrated encouraging predictive accuracy; though, they were tested on disparate pathologically unverified sets of data from disparate imaging modalities, rendering reasonable comparisons difficult. Additionally, several other variables like pre-processing, the number of major attributes for selecting features, and class imbalance all have a noticeable effect on the prediction accuracy evaluation. To address these difficulties, an association rule mining framework is designed that consists of a basic pre-processing phase is followed by imperative attribute classification and selection. Additionally, this proposed model-based methodology points the way forward for early-stage AD research and has the ability to differentiate AD from safe controls.

Ritchie, et al. (2015) give a critical analysis of contemporary dementia research and explore possible explanations why development in the field has not been as fast as it is in other disciplines. The developers give a wider approach in maintaining with the topic's breadth. They address the complexities involved in researching dementia at all levels of study, from 'bench' to the 'bedside' to the 'community'. Additionally, they make specific reference to concerns surrounding the operational definition of the dementia condition and the changing view of dementia mostly as testing 'outcome.' The researchers debate current 'critical issues' in dementia research methods, with a particular emphasis on models of dementia, states of pre-dementia, and biomarkers. Realizing the importance of large-scale clinical trials and prospective epidemiological cohorts, they place a premium on such methods and the difficulties inherent in generating outcomes with 'real world' outer validity. They conclude with suggestions for future dementia studies based on the thoughts. The analysis is intended to be critical but still not excessively so. There are reasons to be cautiously optimistic in the field of dementia studies.

Andrieu, et al. (2015). In recent decades, randomized controlled trials have examined both pharmacological and lifestyle approaches for the mitigation of cognitive impairment or dementia in individuals predominantly aged 50–55 years even without risk factors for AD. Numerous studies examining the impact of physical exercise, cognitive stimulation, and antihypertensive treatments demonstrated some effectiveness on a primary cognitive endpoint. However, the majority of these trials had limited follow-up times, and further research is required to validate the efficacy and to determine the optimal design or dosage of treatments, as well as the optimal target populations. The introduction of multidomain approaches and the use of genetic inclusion or biomarker criteria are significant developments in ongoing trials. The use of appropriate trial designs, the creation of structured, responsive assessment tools, and the requirement for treatments which can be incorporated in resource-limited settings are all challenges.

Cooper, et al. (2015). The research will examine public health strategies promoting early support seeking that has resulted in a rise in the diagnosis of mild cognitive impairment (MCI) in Western countries. It will also look into ways to cure dementia and how to forecast how people with the disease would fare. The researchers combed through electronic databases and references for longitudinal data on potentially modifiable risk variables for incident dementia after MCI. Two reviewers assessed the study's consistency separately using only a checklist. Three or more reports is combined in meta-analyses. There had been 76 papers that qualified. Prediabetes and diabetes raised the likelihood of transformation from amnestic MCI to AD; however, one study found that the risk was lower in treated than untreated diabetes. Diabetes was however linked with an increased incidence of transformation from any-type or non-amnestic MCI to dementia due to any cause. Individuals with amnestic and any-type MCI, respectively, metabolic syndrome and prediabetes expected all-cause dementia. The Mediterranean diet has been shown to lower the risk of Dementia. Conversion from any form of MCI to all-cause dementia was predicted by neuropsychiatric indications or lower serum folate levels, but not by a lack of formal education. Depressive symptoms documented transition from every type of MCI to all-cause dementia in epidemiological but not clinical investigations.

De Strooper and Karran (2016). To examine the efficacy of sparsity on its own, the researchers propose the "k- sparse autoencoder," which would be a linear activation function

autoencoder with secret layers that retain just the k highest operations. When applied to the NORB and MNIST datasets, the designers find that this approach outperforms de-noising autoencoders, RBMs, and dropout networks. Since k-sparse autoencoders are easy to train and have a quick encoding level, they are very well for large problem sizes where traditional algorithms based on sparse coding are ineffective.

Sarraf, et al. (2016). It illustrates deep learning's leading-edge pipelines for segmenting human brain MRIs and functional MRI images in the same classification group. These pipelines were applied rigorously and meticulously using a GPU-based system. Following that, only invariant (or high level) features were retained from the examples were employed in the CNN The functional MRI data is now used in the deep learning approaches for medical image recognition and for the diagnosis of Alzheimer's disease for the first time. For the MRI and fMRI pipelines, the researcher achieved expected and implemented these regulated and measurable accuracy values, respectively: 98.84% and 99.9%.

Tsai and Boxer (2016). This study will describe the presently offered treatments for FTD and associated conditions, as well as the scientific evidence supporting them. Additionally, it addressed recent advances in FTD pathophysiology, medication progress, and biomarker discovery, and also their relation to recently concluded or continuing clinical testing, as well as their possible consequences.

Dubois, et al. (2016) conducted a systematic review of the literature, utilising both meeting abstracts and standards (PubMed). Over the last decade, there has been a philosophical change in the field of Alzheimer's disease (AD) toward seeing the disorder as a “continuum”. Amplification of meanings and lexicon, historical background, and development markers is required at this asymptomatic level. This review provides answers to every one of these points by presenting a comprehensive review of the study.

Islam and Zhang (2017) Using brain MRI data, the researchers introduce a novel deep learning approach for multi-class detection and classification of AD. They build a quite deep convolutional framework and evaluate its output on the OASIS repository.

Cheng and Liu (2017) suggest employing PET and MRI images to create "multi-level CNNs to gradually learn and integrate multi-modality characteristics for the classification of AD". To begin, deep 3D-CNNs are built to compress the statistics from the entire brain into portable features (high-order) for each kind of modality. Then, a cascade of two-dimensional CNNs is used to combine the image classification's high-level features. The current technique will automatically extract common characteristics for the classification of AD from PET and MRI imaging data. The brain images are not subjected to strict image segmentation or registration. The suggested approach is tested using baseline PET and MRI images from the AD Neuroimaging Initiative repository on 193 subjects, comprising 93 individuals with AD and 100 individuals with normal controls (NC). The results obtained and comparison display that this approach achieves an accuracy of 89.64 percent for NC vs. AD classification, indicating a successful classification efficiency.

Cheng et al. (2017) reported that it is preferable to study the deep 3D features from various regions of the brain, and then use these learned features to diagnose Alzheimer's disease. Their study demonstrated that first, various local images from the brain image collection are used to train a 3D-CNN for portability Then, the upper convolution and connected convolutional layers are crafted to work with several 3D CNNs. The method used in this research derived a class-agnostic features from an imaging database. The treatment was assessed on a sample of 429 individuals from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database, which included typical controls and those with "mild", "moderate", and "severe cases of the disease". The finding of this research show that the recommended approach reaches a precision of 87.15% and an AUC of 92.26%, with promising results.

Elahi et al. (2017) provide an insight into various dementia subtypes - vascular dementia, Alzheimer disease, frontotemporal dementia, Lewy body dementias, and associated syndromes, and prion diseases - emphasizing specific epidemiology, neuropathology, signature signs, risk factors, and symptoms.

Tible et al. (2017) seek to create an individualized care plan through the use of a clinical decision tree that is modified according to the individual's and environment's risk profile. Nonetheless, recovery can be complex and taxing. Clinical empiricism also intervenes when controlled trials have inconclusive evidence. Psychosocial recovery methods are critical to the success of BPSD treatment. Sometimes, opioid therapy is preceded by a mixture of several non-pharmacological approaches. Constant evaluations of the care plan and any prescribed medications are essential to identify symptoms of relapse and to discontinue any medications that have become ineffective. Even with optimum management, BPSD does not always resolve fully and will continue to pose difficulties for all parties involved. This review is indeed a narrative study that is heavily influenced by the Swiss interprofessional therapies for the management of BPSD. To develop the guidelines, a comprehensive review of the literature was conducted.

Korolev et al. (2017) demonstrate how the plain and residual 3D CNN architectures can obtain comparable performance without these extracting features steps. On the ADNI database of three-dimensional MRI brain scans, the researches show the efficiency of the suggested method for AD classification versus moderate normal controls and cognitive impairment controls.

Vu et al. (2017) suggest a framework for deep learning multimodality fusion. In depth, our approach involves training and testing a CNN and a sparse autoencoder (SAE) on mixed MRI-PET data in order to diagnose a patient's disease status. The researchers emphasize the benefits of multimodality in terms of having additional data rather than just one, which results in increased classification accuracy. They led trials on a database of 1272 scans from ADNI study and discovered that the suggested technique can obtain an accuracy rate of 90% amongst AD patients and controls, a substantial increase over using a single modality.

Rathore et al. (2017) conducted a study of research using neuroimaging to classify Alzheimer's disease. The authors discussed structural MRI, functional DTI, MRI, FDG-PET, amyloid-PET, and multimodality imaging. Cross-validation was used to verify the published studies. They classified the analyses according to the methodology used for extracting features. The researchers addressed the difficulties, inconsistencies in test conditions, and possible future strategies.

Hanson et al. (2017) evaluated the goals of care (GOC) decision-making process, as well as the effectiveness of an initiative to enhance palliative care and communication quality for nursing homes with severe dementia. He did that on “a single-blind cluster randomised clinical trial was conducted in 22 care homes with 302 residents with severe dementia and their family’s decision makers”. A GOC video decision help in combination with a formal dialogue with care home healthcare professionals; attention management with the use of an educational video and routine care planning. Further evaluation lead to that “at three months, the key results were communication quality, a questionnaire scoring 0-10 with better ratings suggesting higher quality”, “family report of agreement with clinicians” mostly on the main objective of care (promoting the very same goal as its "best keeper to guide care and medical treatment" and physicians' "highest priority for medicine and healthcare treatment"), and “therapy aligned with priorities (score of Advance Care Planning Problem)”. When evaluated for longer time “at nine months, secondary results included family scores of symptom control and care”, “inclusion of palliative care realms in care plans”, “fulfilment of Medical Orders for Scope of Treatment (MOST)”, and “hospital transitions”. The primary unit of research was resident-family dyads, and all studies were conducted using an intention-to-treat strategy.

Liu et al. (2017) suggest a new classification scheme, built upon the application of CNNs and RNNs, that decomposes a 3D model into 2D slices and sequences and reclassifies the results inter-to-intra. The CNNs [2D CNNs] are used to isolate image attributes, while the RNNs (GRUs) are stacked to represent inter-to-class relationships. Visualizations that do not use of PET, does not employ segmentation or registration. People in the ADNI database include the control subjects, and 93 individuals with AD, and 100 minor cognitive impairments from an average participant are used to derive a 'baseline' value (MCI). A proposed model achieves an AUC of 95.3 for NC vs. AD vs. MCI classification, showing promising results.

Schelke et al. (2018). In relation to AD, six pathways are possible targets for risk reduction: inflammation, dysregulation of glucose metabolism, oxidative stress, and cytotoxicity, both of amyl-protein build-up, and toxicity caused by high calcium levels could be involved.

Furthermore, the analysts have a holistic approach to dealing with AD in the pre-prevention stage. Often targeting the causes of pathologies will lead to AD being entirely reversible.

Thakur et al. (2018). This study included an overview of Alzheimer's disease as well as the cure and pathology. Three major databases (Science direct, PubMed, and Google Scholar) were used to carry out the analysis. AD dementia is often characterized by rapid neuronal and synaptic destruction that happens in distinct areas, producing distinct clinical signs. The pathology of Alzheimer's is due to various factors, including amyloid and tau toxicity, as well as mitochondrial oxidative stress. Herbal treatments, besides the multitude of biomarkers, therapeutic targets, and to a lesser degree, currently known secondary metabolites, are also being considered as new therapy options for AD. If we want to clarify the mode of action of herbal remedies, non-pharmacological therapies, and their secondary metabolites in the conduct of AD, more study is essential.

Grilli et al. (2018) stated that emotionally and cognitively stable older adults carry the most common gene risk factor for late-onset Alzheimer's patients is "the ε4 allele". The researchers introduced three bases of processing—a baseline challenge, a semantic elaboration project, and an imagining project—and asked participants to use each of different age groups to tell emotional and personal stories to themselves in order to see what or autobiographical memories came to their mind. Self-related processing led to greater memory recognition memory for narrative content, but not to an increased level of ambiguity. However, carriers of the elderly allele did not demonstrate a positive emotional response, while the noncarriers did. These findings suggest that while self-referencing abilities do not seem to be impaired in healthy elderly adults with normal cognitive function, impairment in emotional memory may be an early warning sign of later development

Islam and Zhang (2018). According to this study, another frequent hereditary Alzheimer's marker, apolipoprotein E4, is tested as to see whether carriers show the same degree of cognitive benefits vis-a-vis non-APOE carriers that exhibit genetic predisposition for late-onset AD. The emotional and non-emotional explanations were recorded for the baseline procedure. Content-oriented memorization and semantically or on the student's ability to project and analyse. Though

semantic memory seemed to be reduced in 4 status, self-referential memory was better among the elderly subjects. However, in comparison, noncarriers showed little effect on mental well-being, although carrier status did not manifest itself until adulthood. The results show that while ε4 carriers do not seem to suffer from an age-related loss in self-identification, their semantic memories degrade over time.

Gangisetty et al. (2018) examined the different epigenetic pathways that regulate gene expression. He stated that "each epigenetic alteration involved in the ageing process and its function in normal age neurodegenerative disorders were covered in detail". The function of epigenetic factors as stated are "mostly in the body during the process of aging and age-related neurodegenerative diseases". Such findings shed new light on how epigenetic-based treatment is gaining traction as a treatment option for neuropsychiatric disorders. The present understanding of epigenetic changes that take place during ageing and age-related disabilities is critical, and epigenetic-based rehabilitations must be established soon.

Midtbust et al. (2018) examined health practitioners' perspectives on possible challenges and facilitators in delivering palliative care in deep care facilities for people with serious dementia. It was a comprehensive qualitative analysis. Twenty-person in-depth interactions and four focus groups with health care providers from four Norwegian care homes provided the results. According to Clarke and Braun, the data were analysed using thematic textual analysis. The main results indicate that the biggest obstacle to promoting palliative care is a lack of continuity among healthcare professionals. The poorest and housebound dementia residents are particularly affected by increased productivity requirements and time pressure. Healthcare workers are torn between having to devote more time to each particular resident and feeling obligated to assist everyone. Despite the fact that resources are limited, healthcare professionals often prioritize dying residents, either by adding additional staff or reorganizing tasks that allows someone to remain mostly with the terminal resident.

Lu et al. (2018) identified persons at the likelihood of developing AD using a novel deep NN. The analysts' multi-modal and multi-scale deep-NN was considered to integrate data from multiple modalities and scales from different areas in the grey brain matter (FDG-PET and T1-

MRI). To begin, the designers illustrated the suggested MMDNN approach's discriminant capacity by contrasting it to state-of-the-art approaches mostly on the duty of distinguishing among persons with pMCI vs. sMCI. After which they taught the classifier to discriminate between subjects on a path toward a medical diagnosis of probable AD and those who were not (i.e, the pMCI, pNC subjects). They discovered that MMDNN classifiers constructed using a structural MRI image and a mixture of FDG-PET performed better than any of those constructed using only FDG-PET or structural MRI neuroimaging scans. Additionally, the classifier trained on a composite trial of pMCI, sAD, and pNC was shown to have the maximum overall "accuracy of 82.4 percent" in classifying people with MCI who would move to AD three years preceding to converting (86.4 percent composite accuracy for change across 1–3 years), as well as a 94.23 percent sensitivity in classifying. These findings indicate that DNN classifiers could be a valuable tool for establishing a medical assessment or diagnosis of probable AD.

Lalzi et al. (2018) differentiated AD patients using CAD. It is defined as follows: It is said to be: reconstructing of estimated grey matter, white matter, and cerebral spinal fluid concentrations from noisy MRI and PET scans Any of the PET and MRI data that this research uses is obtained from the ADNI database (http://adni.edu/projects/database). Clustering is said to exist on three levels: anticipation, understanding, and implementation. First, a fuzzy initial centroid is determined using the FCM i.e., FCM initial classification. Fuzzy results of the PCM algorithm are applied to a partition to obtain a probabilistic C-means (FCM) cluster as the last step. After this, the last partitioning method, the final classification is used to separate the structures of the brain. Classification may be carried out using a support vector machine (SVM) in combination with various kernel functions. CAD seems to be more sensitive, more precise, and accurate as compared to PCM, VAF, and FC PET and MRI scans on 55- to 60-year-olds (Voxels-As-Features). With respect to PET, compared to other methods, the accuracy ratings for noisy images were at 20% (73% accurate) versus 68.5% (median, 68%) versus 70% (extremal, 64.7%); with respect to MRI, they were 74% (68.5% vs. 71%) versus 70% (low, 67.6%) versus 66.3% (high, 64.7%)

Ahmed et al. (2018) presents a systematic review of recent publications on automated dementia diagnosis methods based on machine learning algorithms and medical image processing.

Following analysis of the current literature, the researchers discovered that, while the majority of studies concentrate on AD, new studies have shown good success in identifying other forms of dementia. Multimodal imaging research and deep learning methods have demonstrated promise in diagnosing these additional forms of dementia. The following are the primary highlights of this research article. 1) This article addresses neuroimaging techniques for dementia diagnosis based on a comprehensive review of the current literature. 2) It provides a systematic explanation among the most recent machine learning methods, especially deep learning strategies for dementia early diagnosis.

Li (2018) analysed that neuropsychological and neuroimaging statistics, demographic data, as well as large quantities of data in clinical science are also considered to be sources of valuable information. With this diversity of data, they will develop computer-based methods that help clinicians to find hidden patterns. Data mining and deep learning algorithms are also used in computers that can be used as a clinical design and diagnosis tools. These pages review existing "state-of-the-art techniques" and "models in the field", and then briefly cover some new methods being developed.

Veitch et al. (2018) deepened the interpretation of late-onset AD and published in 2016. The amyl hypothesis provides a linear, step-by-by-step progression model for the course of AD illness, while other methods, such as data-driven models, depict a more complex picture of the disease with many interactions. Functional changes in the high metabolic demand areas such as the PCC centre can disrupt the brain's blood-brain barrier and contribute to poor BBB clearance, leading to deficits. These recent studies show A having the ability to work at different levels of the DMN as well as depositing, suggesting that it is able to reach more distant locations when loaded with metabolic burden This cerebral sinus fractal deposition early on allows FTD to form within the brain, which causes atrophy, neuronal death, and cognitive dysfunction. Anatomical and functional networks disconnection are believed to occur during the disease process. Cognitive deficiency is detectable prior to visible brain atrophy, but has not yet been researched, or fully studied.

Hachinski et al. (2019). This research implied that whatever factors are causing these trends can be modifiable. Globally, neurological disabilities account for the greatest proportions of disability-adjusted years of life (10%). Dementia (10%) and Stroke (42%) are the most prevalent neurological diseases. Dementia and Stroke are risk factors for one another and share several risky and curing factors that are essentially configurable. In theory, 35% of dementias, and 90 percent of strokes are curable. Since a stroke doubles the risk of dementia and stroke is much more prevalent than dementia, stroke prevention may avoid more than a triple of dementias. Pathophysiological, pathological and clinical developments in totality lead to new interesting directions.

Rasmussen and Langerman (2019) provide a summary of the problems that must be addressed prior to a person meeting the requirements for Alzheimer's dementia. It discusses how and when to increase AD diagnosis levels, the consequences of early detection for the person, career, and community, and the critical role of reducing risk in preventing or delaying progression. While no disease-modifying agents capable of preventing the early pathological changes are currently active, adjusting susceptibility to common causes may be necessary to avoid or postpone the progression of dementia in a subset of the population. In many other individuals, early detection of the disease or risk of infection is also beneficial because it gives the person and their career time to make decisions and plan for the long term, as well as provides access to medications which can help control symptoms.

Orlandoni et al. (2019) evaluate the adverse effects of domestic enteral nutrition prescribed through percutaneous endoscopic gastrostomy and nasogastric tube in patients with advanced dementia in terms of gastrointestinal, mechanical, and metabolic risks, evaluate survival, investigate survival potential risks, and monitor trends of individuals with dementia to those of patients lacking dementia

DeTure et al. (2019) outlined the pathologic characteristics of AD that are etiologically related, and those that are unavoidable but uncertainly significant, including such Hirano bodies and granulovacuolar degeneration. Other disease mechanisms that are common but not unavoidable, such as pathologic processes that really can clinically resemble AD, are also addressed. Lewy

body disease, Cerebrovascular disease, argyrophilic grain disease, and TDP-43 proteinopathies are only a few of them. The goal of this review is to give a general idea of AD pathology, including pathologic substrate definitions and associated pathologies that can influence diagnosis and treatment.

Arvanitakis et al. (2019) examined that dementia is often linked with several neuropathological areas, most commonly AD and cerebrovascular pathology. Dementia is diagnosed by a history of cognitive loss and impairment in everyday activities, corroborated by a household member or nearby friend, in addition to a rigorous mental status test by a clinician to delineate impairments in memory, vocabulary, attention, visuospatial cognition like executive function, spatial orientation, and behaviour. Concise questionnaires for cognitive disability screening may aid in initiating and planning the cognitive evaluation. Even so, if the evaluation is inconclusive (for example, symptoms exist but evaluation results are normal), neuropsychological evaluation may assist in determining the presence of dementia. A physical examination can aid in determining the cause of dementia. Nonpharmacologic recovery options include cognitively stimulating behaviours like reading, physical activity such as socialization, and walking, such as social events. Pharmacologic interventions may provide some symptomatic relief. This includes an acetylcholinesterase receptor like donepezil for moderate to severe dementia and memantine (alone or in combination with other medications) for mild to moderate dementia in AD. Rivastigmine can then be used to cure Parkinson disease dementia (PDD) that is symptomatic.

Gkioka et al. (2020) attempted to validate the Dementia Knowledge Assessment Instrument 2, Dementia Attitudes-based Scale, and the Trust in Dementia Scale in the Greek language edition. For validation, a quantitative cross-sectional strategy was used. This survey adhered to the STROBE guideline for qualitative studies. The construct validity (PCA), convergent validity, and internal constancy (Cronbach's alpha) of the instrument were evaluated. Internal reliability for the Trust in Dementia Scale was reported to be significantly high (0.85), sufficient for the Dementia Knowledge Analysis Tool 2 (0.68), and satisfactory for the Dementia Attitudes Scale (0.74). The construct validity of the Dementia Attitudes Scale was sufficient (two factors: knowledge and social comfort). This examination demonstrates convergent validity. Each of the

three instruments is accurate and relevant for assessing awareness, trust, and attitude towards dementia in the context of Greek study.

Chandra et al. (2020) provides an overview of the key economic issues posed by AD. Although there is some overlap with the economics of ageing, the 'economics of Alzheimer's Disease' is defined by a focus on cognitive impairment, patient preference, and a variety of issues where complex agreements between caregivers and patients are difficult to implement. Economists have a tremendous opportunity to add to our knowledge of AD-related problems, such as drug growth, effective patient care, competitive contracting within families and with healthcare professionals, long-term care risk, public services, and financial decision-making for AD.

Houben et al. (2020) provide the findings of a field study in which they examined the responses of 19 individuals with dementia to a range of different sounds heard in a care home, and also the role of such reactions in the medical facility. Vita, a 'pillow-like' media player, was put to the test for four weeks at two dementia care centres, with statistics taken. After that, they conducted interviews with caregivers who had utilised Vita in their everyday care routines. The findings demonstrate how Vita's daily sounds sparked meaningful dialogue, playfulness, and interaction between caregivers and residents. Additionally, they discuss design consequences for incorporating common sounds into dementia treatment.

Cao et al. (2020). The analyses in these studies were segmented according to age, gender, and geographic area. Meta-regression was used to determine if there were statistically relevant variations between classes. These researchers analysed 47 reports. The pooled occurrence of all-cause dementia, AD, and VaD was 697 (CI95 percent: 546–864) per 10,000 individuals, 324 (CI95 percent: 228–460) per 10,000 individuals, and 116 (CI95 percent: 86–157) per 10,000 individuals, respectively, amongst individuals aged 50 and over in the group. According to our research, the occurrence of all kinds of dementia is 244 times higher in individuals aged 100 years and older (6,592 per 10,000 cases) than in those aged between 50–59. (27 per 10,000 cases). Every 5 years, the percentage of patients with dementia significantly increases. All in all, women have the highest prevalence than men (788 case per 10,000 persons versus 561 cases per 10,000 persons).

Wendrich-van Dael et al. (2020). One reviewer extracted data, which was then verified by a second. The authors independently evaluated the methodological consistency using the Joanna Briggs Institute and AMSTAR-2 instruments. To determine efficacy, results were classified and computed. Thematic synthesis has been used to analyse qualitative data. The researchers included 19 reports (163 specific investigations) and 11 primary papers that used a variety of care planning concepts and were of varying quality. Care plan planning was linked to a reduction in hospitalizations, an improvement in concordance among care received and previous wishes, and an improvement in the completion of advance care papers, but the main research quality was uncertain. The perspectives on ACP for dementia patients can be summarized as follows: 1) tailoring and timing, 2) willingness to participate, 3) roles and obligations of healthcare professionals, 4) relations, 5) preparation, and 6) services required. The progressive deterioration of decision-making ability is a critical overarching function.

Brzezińska et al. (2020) suggests that MDD, i.e., Major Depressive Disorder may be a risky factor for dementia and it may eventually lead to cognitive impairment both in advanced and early onset variants, according to new research. Anxiety, on the other hand, may not have been a trigger, but instead an effect: this may be a reaction to cognitive impairment or change the threshold where the cognitive impairment manifests or is identified. Another possibility would be that depression is often a part of a prodrome for AD, implying a neurobiological connection rather than a psychological one. Individual physical and cognitive reserves, and also medical records and personal vulnerability, can clarify a few of the variances in common phenomenology among diagnoses. When symptoms appear comorbidly, the sequence in which they have been diagnosed may focus on local physical and cognitive reserves, and also the medical records and individual susceptibility. This theory is biologically valid, but it has yet to be thoroughly tested. The present study emphasizes how genetic differences play a role in the development of both MDD and AD, and the hazard posed by such variations on the co-occurrence of these two disorders is a significant factor for potential pathoetiological pathways research and study test stratification in randomized trials.

Kozlova et al. (2020). In this study, while using titrating task and free recall requirements to reach equilibrium baseline output across patients, temporary memory binding has indeed been

demonstrated to be directly affected by AD. On the TMB, people with PD were classified into those with having a cognitive disability and those that do not have this disability and compared to those with AD and amnestic moderate cognitive impairment (aMCI). The findings indicate that only patients with Alzheimer's disease have reduced TMB efficiency. TMB has a high specificity and sensitivity for AD and aMCI as compared to PD groups and safe controls, as determined by receiver operating curve tests.

McKeith et al. (2020) offer operationalized diagnoses that are ready for preliminary verification in the LBs to be included in a clinical environment as far as the prodromal memory syndrome is concerned, they are in agreement with the diagnosis criteria for certain neurodegenerative disorders, like Alzheimer's and Parkinson's. Since there is inadequate data to recommend the development of specific guidelines for DLB (delirium with dementia), the designers advocate for the construction of certain criteria for DLB manifestations and improving diagnostic awareness.

Kim et al. (2021) analysed data on 84,144 adults aged over 60 years in Gangwon province between Jan 1, 2009, and Dec 31, 2009, utilizing data from the (Korean) National Health Insurance Service. After an eight-year hiatus, the researchers returned in 2017 to examine the connection between dementia and metabolic syndrome. They categorized dementia either as AD or VD. AD and VD were specified using the Clinical Modification codes from the International Classification of Diseases (10th Revision). Multiple logistic regression studies were conducted to govern the relationships amid metabolic syndrome or its five elements and dementia. Age, smoking, sex, physical inactivity, alcohol, prior heart disease, and prior stroke were all included in the studies.

Dashwood M et. al. (2021) examined that for the most part, dementia may be detected with paper and pencil cognitive tests, but they are cumbersome and do not pick up on early-stage signs of the disease. Dementia may be detected in its early stages using specialised brain scans and body fluid biomarkers, but these methods are either too intrusive or too costly for general usage. The use of Artificial Intelligence (AI) in early-stage dementia diagnosis is showing promising

outcomes as technology advances. Existing AI-assisted techniques are examined, as well as possible future research paths.

Shimoda A (2021) investigated that more than 16 million unpaid carers are thought to be caring for people with Alzheimer's and Dementia in the United States. Unpaid carers contributed $244 billion in 2016 by providing 18.6 billion hours of care for no pay A person with Alzheimer's disease has unique care needs, and those needs will only grow as the illness advances. More severe health issues often develop as the illness progresses. Financial and income security is often threatened, leaving many family carers feeling overwhelmed and depressed Because of the lack of training and knowledge needed for Alzheimer's and Dementia care, direct care (paid) professionals, such as nursing assistants, have a tough time in their jobs.

Kim J. & Lim J. (2021) provided their insight that to make things worse, just 7,293 trained geriatricians were available in the United States as of 2016. In other words, there is one geriatrician for every 1,924 people over the age of 65 who need medical attention. According to the American Geriatrics Society, an extra 23,750 geriatricians would be required by 2030 to handle the burgeoning elderly population. For the first time in 2017, Medicare began paying medical providers for complete Dementia care plans, which include outpatient visits to address gaps in treatment. Dementia care management relies heavily on comprehensive care planning, and it may lead to the delivery of services that improve the quality of life for persons with dementia and their careers.

Solje E et.al. (2021). This study examined that Alzheimer's patients and their families bear the brunt of the economic and financial consequences. In 2019, the cost of caring for a single person was projected at $357,297 [14]. As the most expensive illness, Alzheimer's and Dementia will cost approximately $290 billion in 2020 in health and long-term care [10]. AD is likely to cost 4.6 trillion dollars by the year 2050, based on the present global Alzheimer's disease population of 5.8 million people and the anticipated future global Alzheimer's disease population of 88 million. It's anticipated that there will be many more instances in the future, as well as higher healthcare expenditures due to the ageing population.

Doborjeh M. et.al. (2021). In this study, the researchers analysed that Dementia or Alzheimer's disease may have devastating effects on a person's quality of life, but there is no treatment at this time and much more research is needed. Only five medicines have been authorised by the FDA so far, and none of them have demonstrated any convincing evidence of reducing or remitting the symptoms of Alzheimer's disease permanently. Instead, these drugs' sole real accomplishments are in managing and slowing the symptoms of neurocognitive decline associated with diseases like Alzheimer's and dementia. It would be an understatement to say that pharmaceutical research has been sluggish, since there are no medicines available to prevent or postpone the onset of the illness. For the time being, the FDA has only authorised a mixture of two older Alzheimer's disease medicines from 23 and 16 years ago as a treatment forAD. There are development attempts being made.

2.2 Inferences drawn from literature survey

S. No.	Author's Name	Tool/Method Used	Paper Title	Application Domain	Inferences
1.	**Choi, et al. (2003)**	GDR and CDR	*Use an equaliser (an algorithm) to adjust the ratings on the clinical dementia rating scale and the global decline scale.*	To ascertain the degree of dementia.	CDR and GDS had a curvilinear relationship according to regression analysis.
2.	**Svansdottir and Snædal (2006)**	pathological behaviour in AD's rating scale (BEHAVE-AD).	*An analysis of cases and controls from a case-control*	To quantify serious or mild dementia	During a six-week cycle, the music therapy community

			review examining the efficacy of music therapy in patients with mild and serious dementia of Alzheimer's type		demonstrated a substantial decrease in behavior disruptions as assessed by the BEHAVE-AD.
3.	**Lynch, et al. (2006)**	Clinical information that has been stored in our Memory Clinic database	*mild dementia's clinical dementia ranking box score.*	The main goal of this research is to discover whether the CDR sum of box scores is useful in identifying a diagnosis of dementia in patients with mild cognitive impairment.	The researchers discovered that an increased CDR amount of box score was significantly correlated with a greater likelihood of receiving an ICD-10 dementia diagnosis ($p < 0.001$).
4.	**Swanson and Carnahan (2007)**	Cholinesterase inhibitors	*The diagnosis and treatment of dementia and comorbidities is covered here*	To provide an overview of the diagnosis and treatment of various forms of dementia and associated conditions.	Nonpharmacologic therapies are recommended as first-line treatment for other psychological comorbidities,

					whereas medication therapy can be helpful at times.
5.	**Pimentel (2009)**	Diagnosis of AD vs. VaD	*Role of neuropsychological assessment in the differential diagnosis of Alzheimer's disease and vascular dementia.*	Differential diagnosis of AD and VaD	There is some variation in cognitive changes between such two forms of dementia.
6.	**Salmon and Bondi (2009)**	Qualitative and Quantitative differences	*Neuropsychological assessment of dementia.*	Cognitive impairments associated with AD	Understanding these distinctions enables clinicians to make clinical distinctions between different causes of dementia.
7.	**Vincent, et al. (2010)**	Deep networks constructed by stacking denoising autoencoders	*Stacked denoising autoencoders: Learning useful representations in a deep network with a*	Investigate a novel technique for constructing dense networks focused on the stacking of layers of	Autoencoders for denoising are capable of learning Gabor-like edge detectors from regular image patches and larger

			local denoising criterion.	denoising autoencoders.	stroke detectors via digit images.
8.	**Belmokhtaand Benamrane (2012).**	VBM methodology and neuropsychological examinations	*Classification of Alzheimer's disease from 3d structural MRI data*	An automated methodology for classification of MCI and AD.	The obtained results were extremely satisfying in terms of computational speed and accuracy.
9.	**Li, et al. (2014)**	Alzheimer's Disease Neuroimaging Initiative (ADNI)	*Robust deep learning for improved classification of AD/MCI patients.*	A system focused on deep learning for analysing multi-modality imaging data.	The system greatly surpassed prior approaches, as shown by the results.
10.	**Aggarwal, et al. (2015)**	Novel therapeutic strategies for AD that address both tau and amyloid pathology	*Alzheimer's disease: Unique markers for diagnosis & new treatment modalities.*	Disseminate information about pharmaceutical and biomarkers interventions.	To describe the evidences that are currently available.
11.	**LeCun, et al. (2015)**	Deep learning methodology	*Deep learning*	The analysts place a premium on areas such as visual object recognition, object detection, and speech recognition.	Signify how well a machine's internal parameters that are used to evaluate the interpretation for each layer must be

					modified in comparison to previous layer's representation.
12.	**Schmidhuber (2015).**	Deep learning methodology	*Deep learning in neural networks: An overview.*	Historical survey	The authors discuss deep supervised and unsupervised learning, as well as evolutionary computation and reinforcement learning.
13.	**Payan and Montana, (2015)**	3D CNNs and Sparse autoencoders	*a neuroimaging research conducted using 3D convolutional neural networks in order to predict Alzheimer's disease*	Deep learning	The results of this analysis show that three-dimensional CNNs outperform most other classifiers.
14.	**Ritchie, et al. (2015)**	Contemporary dementia research	*The trials of dementia and the tribulations that face dementia*	Dementia tribulations and dementia trials	The researchers debate current 'hot topics' in dementia research methods, with a

			researchers both have scientific and theoretical issues.		particular emphasis on pre-dementia states, dementia models, and biomarkers.
15.	**Andrieu, S., et al. (2015)**	Sporadic AD	*Current and future directions for the fight against sporadic Alzheimer's disease.*	The advancement of cross-domain strategies and the use of the genetic inclusion or biomarker criteria.	Among the difficulties are the use of adaptive potential meanings and the creation of systematic and sensitive outcome measures.
16.	**Cooper, et al. (2015)**	Mild cognitive impairment (MCI)	*This systematic review and meta-analysis evaluates modifiable predictors of dementia in mild cognitive impairment.*	To forecast or treat the result of dementia in dementia patients.	Depressive symptoms predicted the transition from every type MCI to all-cause dementia in epidemiological studies but not clinical trials.
17.	**Sarraf, et al. (2016)**	Alzheimer's MRI and fMRI	*DeepAD: A new method of classifying Alzheimer's disease, one*	ADs classification via deep CNNs	The pipelines implemented and built demonstrate a significant improvement in

			that incorporates MRI and fMRI with deep neural networks.		classification efficiency as compared with previous reports.
18.	**Dubois, et al. (2016)**	Traditional (PubMed) sources	*Preclinical Alzheimer's disease: definition, natural history, and diagnostic criteria*	Study of preclinical AD	This article will answer each of these points by presenting an updated review of the study.
19.	**Cheng and Liu, (2017)**	Multi-level CNNs	*CNNs based multi-modality classification for AD diagnosis.*	AD classification using PET and MRI images.	The experimental data and comparison show that this approach achieved an accuracy of 89.64 percent for AD vs. NC classification, indicating a positive classification efficiency.
20.	**Vu, et al. (2017)**	Sparse Autoencoder (SAE) and CNN	*Using convolutional neural networks and Sparse*	To suggest a framework for deep learning multimodality fusion.	Between AD patients and safe monitors, the proposed approach has a

			Autoencoders, the learner learns multimodal information.		classification accuracy of 90%.
21.	**Liu, et al. (2017)**	CNN and RNNs	*Founded on a mixture of convolutional and recurrent neural networks, the classification of Alzheimer's disease is performed using FDG-PET videos.*	Alzheimer's Disease Neuroimaging Initiative	The proposed approach produces a region under the receiver operating characteristic curve (AUC) of 95.3 percent for NC vs AD classification and 83.9 percent for MCI vs. NC classification, according to experimental results.
22.	**Schelke, et al. (2018)**	Dysregulation of glucose metabolism, inflammation, oxidative stress, trophic factor release, amyloid burden, and calcium	*In the clinical practise of Alzheimer's disease prevention, risk control mechanisms are at work.*	AD prevention.	In some cases, targeted risk reduction directed at specific pathological factors may turn AD into a completely

		toxicity— involved in AD pathogenesis			avoidable disorder.
23.	**Islam and Zhang (2018)**	Alzheimer's Disease diagnosis using CNN	*A neuroimaging research used deep learning models to identify early-stage Alzheimer's disease.*	AD diagnosis using brain MRI data analysis	The suggested method has a high probability of being used to extend CNN to other domains with a small dataset.
24.	**Lu, et al. (2018)**	Multi-scale and multi-modal deep neural network (MMDNN)	*A multimodal and multiscale deep neural network that incorporates structural MRI and FDG-PET scans for the early detection of Alzheimer's disease*	To integrate various scales of information from multiple regions of the brain's grey matter derived from multiple modalities.	The findings indicate that deep NN classifiers may well be valuable as a potential method for establishing a clinical diagnosis of probable AD.
25.	**Lalzi, et al. (2018)**	Fuzzy c-means (FCM) and possibilistic C-means (PCM) algorithm, SVM for classification stage	*system for diagnosing Alzheimer's disease aided by computers Using Fuzzy-Possibility*	CAD scheme for discriminating patients suffering from AD.	PET photographs of 45 AD and 50 normal brains from subjects aged 55 to 90 years demonstrate increased

			Classification and SVM Tissue Segmentation for Segmentation and Classification.		sensitivity, precision, and accuracy.
26.	**Aryanitakis, et al. (2019)**	Alzheimer disease with cerebrovascular pathology	*Diagnosis and management of dementia*	Diagnosis and management	The study reveals that the neuropsychological testing and pharmacologic approaches can provide modest symptomatic relief
27.	**Houben, et al. (2020)**	Vita, a 'pillow-like' sound player	*The role of everyday sounds in advanced dementia care*	Advanced dementia care	The findings demonstrate how Vita's daily sounds sparked meaningful dialogue, playfulness, and interaction between caregivers and residents.

2.3 Gap Analysis

- Researchers have previously ignored the dimensions reduction challenge in their past work.
- Previously published studies classified dementia stages using two categories, which did not diagnose early detection of the disease.
- The previous studies have not been able to provide efficient results in an increase of the non-linearity of features.
- In prior researches, it was discovered that not selecting the most efficient features and learning all features at the same weight increased feature overlapping.
- The previously conducted study did not optimize features or place a premium on segmented features.

2.4 Research Objectives

1. Objective 1: -To collect dataset from various sources and apply pre-processing techniques in dataset.

2. Objective 2: -To extract features from unstructured data set.

3. Objective 3: -To propose a Model for detection of dementia using deep neural network.

4. Objective 4: -To analyse the accuracy of the model.

CHAPTER 3

Grey Wolf Based Features Optimization approach

3.1 Introduction

The 2021 World Alzheimer Report emphasises the devastating effects of dementia on the global population. The report reveals that “dementia is the 7th leading cause of mortality globally”. According to this report, “Dementia is one of those with the highest cost of society”. It calls on governments globally to get grip on dementia to “enable better planning, treatment, care and support”. Dementia is known to be of progressive, which declines the logical or perceptive sense of a person. Issues with logical or perception is not the only symptom of having dementia. Dementia is a combination of various diseases.

The previous chapters provided insight into the various types of dementia, and how those types could significantly be the reason for dementia. The previous chapters also discussed the stigmas people having symptoms of dementia face as they avoid consulting the physician with the anxiety of being dependent on others.

In this chapter, Machine learning classifiers like Support vector machine (SVM), Random Forest (RF), Decision Tree will be discussed. Using those classifiers and grey wolf optimization technique, a methodology will be formulated to classify dementia.

a) Clinical diagnostic

If you've established the patient has an illness, the next step is surgical imaging of the whole body. Thus, in cognitive dysfunction, if the next move for the clinician is a brain scan to uncover the source of the issue, he or she must be creative to seek out the best treatment, such as nursing, traditional, imaginal, interpretive, and behavioural.

In an MRI, the image is generated using magnetism waves of magnets. According to this MRI, it is possible to look at multiple ailments of the brain, including dementia This scan depicts the interconnectivity of the brain regions of those having Alzheimer's disease clearly. Instead of developing images using standard injections, the patient is injected with positron-emission

tracers which enable visualization of these three ways: oxygen, glucose, and blood flow in the brain. In addition, this will show the operation of the brain. In SPECT nuclear imaging, one single photon is sent into the brain. It helps to measure the brain's activity and how well different parts of the brain are connected with each other by using blood flow. As we know dementia is a neurodegenerative condition that influences both the cognitive capacities of the patient and the person's daily life, it is very important to treat it with appropriate medication. There will be a strong influence in the future on the clinical diagnosis and care of dementia because of machine learning. The use of emerging technology for the study of dementia diagnosis also drives progress. Since dementia has no available cure or medication till date, it is more inspiration for mankind to try and discover how to understand and deal with the illness rather than to simply support dementia patients. It is of interest to patients, their families, and society as well. We have agreed on a study action plan as part of the G8 Summit

3.2 GLCM algorithm

One of the image features for grey-level co-occurrence is the GLC and texture calculations. A tabulation of many different intensities is found in a picture is best known for texture analysis and dappled (light/grey/mottled) quilting. A picture is made up of pixel intensity combinations; GLC is a tabulation of the various pixel intensities in that image or segment. As skin-texture function measurement results are performed at the pixel of interest, it uses the contents of the GLC to provide a measure of strength variance.

Properties of GLCM

- **SQUARE MATRIX**- Same number of rows and columns as quantization level of image (image should be resampled to not more than 4 bit).
- It can be viewed from any direction and with any offset.
- Symmetrical on both sides of the diagonal.
- Symmetry is accomplished by counting each pair of pixels twice, once backward, and once forward.

North and South: Vertical Matrix

East and West: Horizontal Matrix

3.3 SVM classification algorithm

A support vector machine (SVM) is a machine learning classification/regression technique that does unsupervised learning in parallel with multiple layers Under supervision, machine learning and artificial intelligence, the device receives all data (target input) and labels (output). A supervised machine learning technique that can be used for both classification and regression purposes, the SVM can be employed. However, in the vast majority of classification questions, it is used.

To generate the best judgment boundary in n-dimensional space that allows us to isolate and classify new points, the SVM algorithm searches for separating factors. The searching factors groups all the current data points in the n-dimensional space into the different classes. One of the most effective ways to divide space is a hyperplane.

The SVM computes the extreme or high-dimensional points or vectors that contribute to the development of the hyperplane. In these extreme instances, an algorithm is referred to as a help machine. Consider the diagram below, which employs a decision boundary or hyperplane for breaking up differentiating the two different categories:

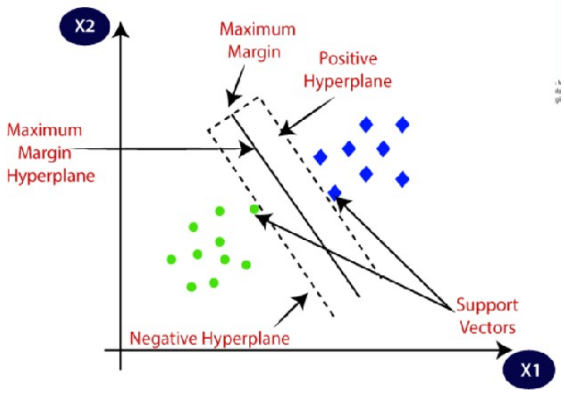


Figure 3.1: SVM Base Hyper plane [7]

For linearly separable form of data, the linear SVM can be employed, which indicates that a dataset can be classified into two separate categories that used a solid line.

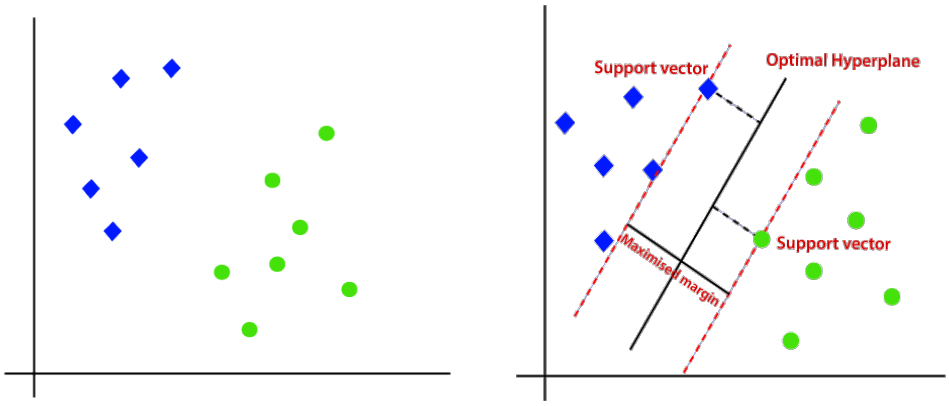


Figure3.2: Instances of classification and Hype plane

Support Vector Machine algorithm locates the most closely associated points from both groups. The hyperplane's difference between the vectors and the margin is called size. The main purpose of SVM is to increase the efficiency of this gain. The best-fitting hyperplane has the greatest total amount of margin.

Non-linear SVM: For non-linear and non-early data, non-separated SVM is utilised, which indicates that a database can indeed be recognized by a straight path.

For non-linear results, we cannot draw a straight line. Now think about the below picture:

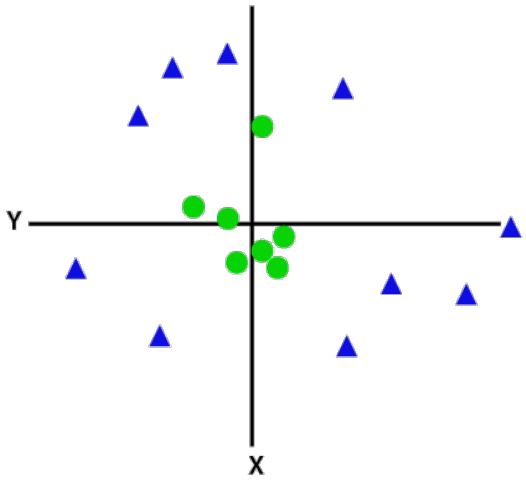


Figure 3.3: Linearly arranged data

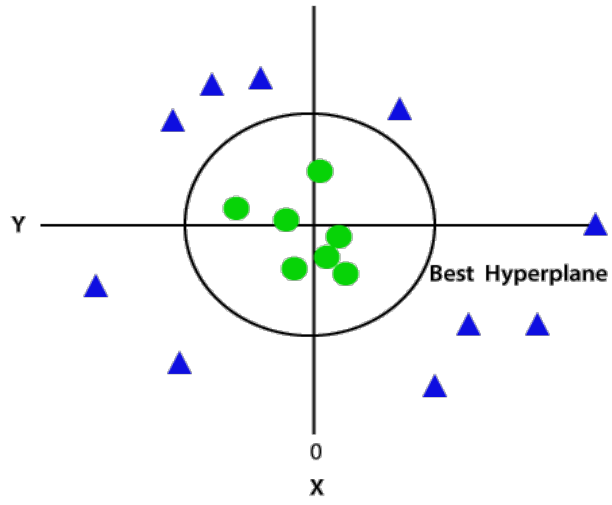


Figure 3.4: Classified data

3.4 Random Forest

The randomized forest classifier can be used for classification and regression. However, most of the time, it is applied for classifying problems. Trees make a forest, but more robust forests equal more trees. Random forest generates random decision trees on the samples, and chooses the most accurate outcome based on a polling procedure. Instead of a single decision tree, which overfits easily, and average the results, it is recommended to use ensembles which better balance the data.

3.4.1 Working of Random Forest Algorithm

- These steps will enable one to understand the workings of the Random Forest algorithm.
- Start by randomly selecting samples from a dataset.
- Next, an algorithmic decision tree will be built for any sample.
- Then any forecast will be right.
- When you have completed the process outlined in Phase 3, we will count and tabulate the votes for any prediction.
- Lastly, pick the prediction that garnered the most votes as the final prediction. The following diagram will demonstrate the process

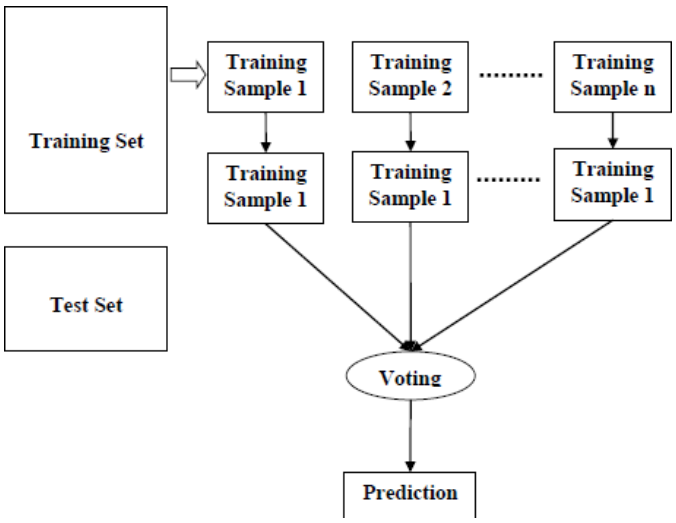


Figure 3.5: Ensemble classifier voting based

Decision tree algorithm

Decision tree learning is supervised. Both regression and classification can be addressed by using them. Each node in a leaf of the tree represents a class has decision attributes.

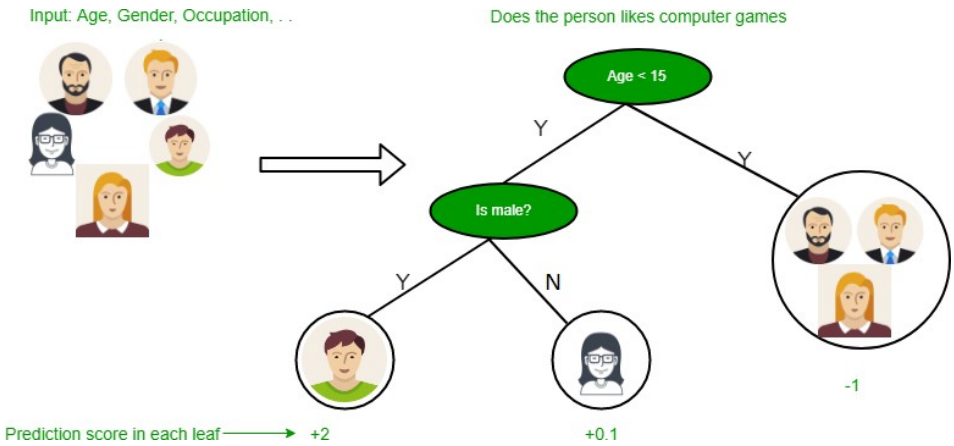


Figure 3.6: An example of a Decision Tree

Below are some assumptions that made while using the decision tree:

- First, start with the entire training set (class as a whole).

- Categorical qualities are favoured to construct the model, then begin by turning continuous values into discrete values.
- Often attribute values are referenced on the descendant nodes in a node
- Ordinal approaches are used for ordering attributes at the base or in the interior of the data tree.

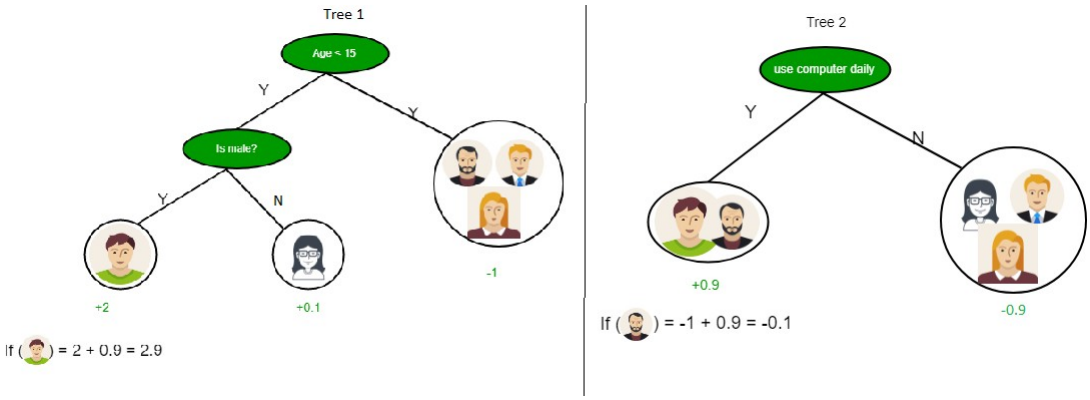


Figure 3.7: Numerous examples of decision trees

The identification of attribute for root node in every level is indeed a major difficulty in Decision Tree. Attribute selection is the term for this procedure.

Ensemble methods

Some of these approaches result in the simultaneous modeling of several models to give better outcomes. Bagging can be defined as a process to enhance the working of prediction model. It works to overcome overfitting in the working of model. Boosting as the word signifies, helps in improving the prediction model. In it many learning methods work in collaboration with each other to overcome weak points to reach an enhanced results. In our experience, using multiple models to make predictions seems to have more reliable results than a mere one model. In a number of AI contests, the winning methods have used multiple ensemble methods.

Figure 3.8: Ensembled Decision tree example

3.5 Research Methodology

(Grey Wolf Based Features Optimization Approach (Feature Optimize-RF))

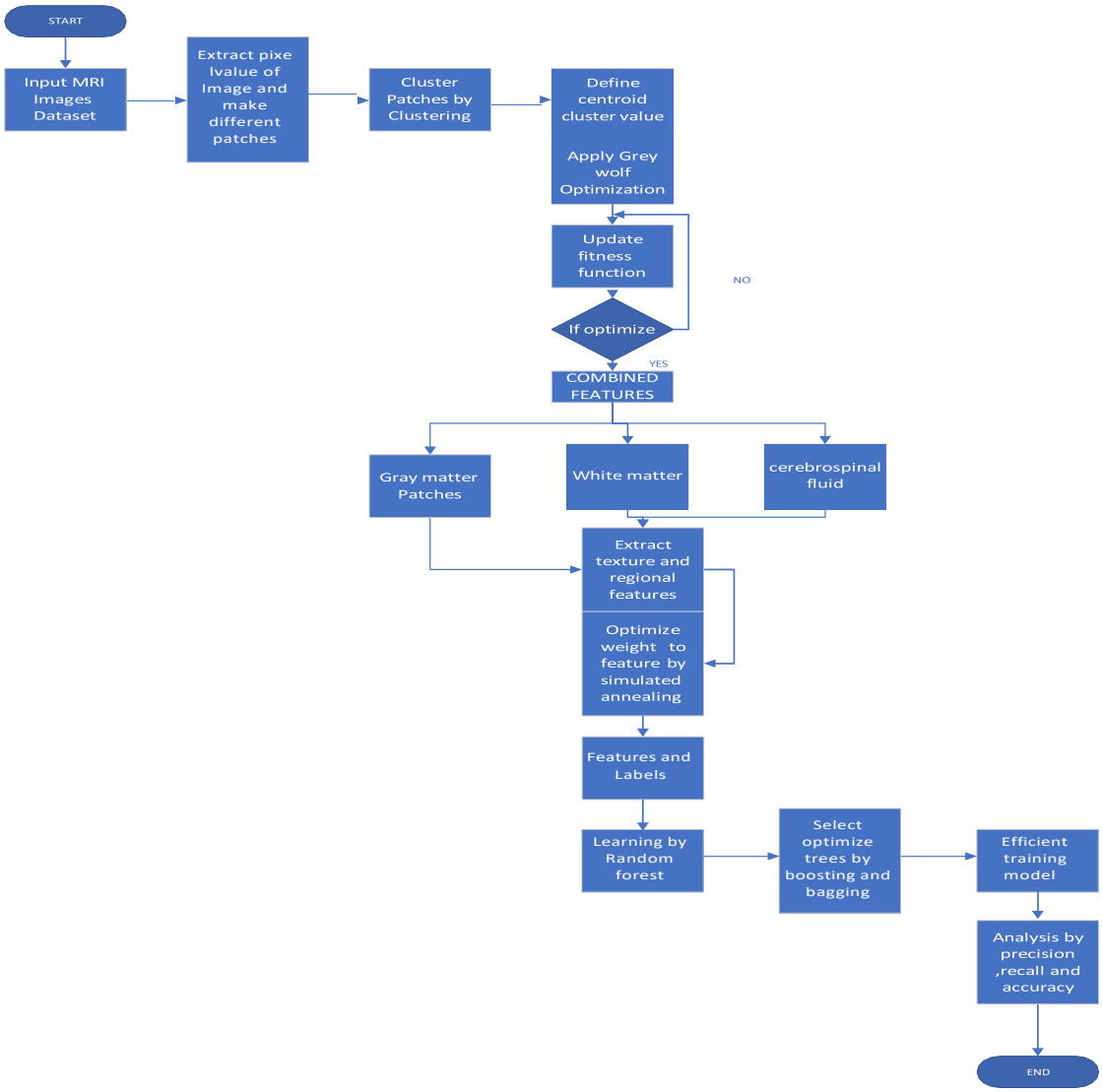


Figure: 3.9 Flowchart of Grey Wolf Based Features Optimization approach (Feature Optimize-RF)

3.5.1 Methodology steps

This entails a number of steps, which are outlined below:

Step-1: Upload the MRI image and fine-tune the Gaussian distribution. This Gaussian distribution enhances the image's pixels by normalising their values and reducing noise.

Step 2: After optimising the pictures, the next task is to optimise the feature selection by finding the specific region on the picture that contains the greatest number of disease possibilities. Both areas were segmented using a clustering technique and the clustering was enhanced using GWO. Specifically, the optimization of grey wolves

The conventional GWO algorithm must constantly update its hunters' knowledge of prey based on the alpha, beta, and delta wolves. Nonetheless, due to the wolves' insufficient diversity in certain instances, the GWO populace remains susceptible to stagnation at the local extremum, and immature convergence issues persist. DE will assist GWO in determining the most cost-effective way to address the aforementioned issues on a global scale. By employing this concept, one can guarantee that GWO performs global searches more proficiently. The fit setting function is being used to enhance clustering's benefits. Individual wolves' fitness is determined using the fitness function, which would be a criterion provided by the analysis procedure. The better it looks to be, the less the individual appears to be, but the worse it seems to be, the bigger the individual seems to be. The following is a description of GWO's fitness function based on clustering and the GWO algorithm:

$$= \begin{cases} \dfrac{1}{\sum_{j=1}^{c}\left(\frac{d_{ik}}{d_{jk}}\right)^{2/(m-1)}}, & d_{jk} \\ 1, & d_{jk} = 0, j = k \\ 0, & d_{jk} = 0, j \neq k, \end{cases} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$v_i = \frac{\sum_{k=1}^{n}(\mu_{ik})^2 x_k}{\sum_{k=1}^{n}(\mu_{ik})^m}, \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

The more clustering there is, the smaller the C-GWO score. By iterating the algorithm's positions, the fitness function can be represented and denoted as the as one centre.

$$\left\{X_i(0)\middle| x_{i,j}^{L} \leq x_{i,j}(0) \leq \middle| x_{i,j}^{U}; i = 1,2, \ldots\ldots, N.P; j = 1,2, \ldots\ldots, D\right\} \ldots\ldots (3),$$

$$x_{i,j}(0) = x_{i,j}^{L} + rand\ (0,1)\left(x_{i,j}^{U} - x_{i,j}^{L}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Population initialization- Population initialization- As is common for swarm intelligence algorithms, standardized masks are implemented to determine the edges in order to make sure that populace inside the algorithm is randomized and different. A spatial filtering masking is a mn-dimensional w matrix. Suppose that n=2+1 and m=2+1 are positive integers greater than zero. As a result, the mask's smallest size is 33. These mask coefficients represent a configuration of coordinates. For edge detection, the image area underneath the mask is shown in Figure 1.b.

Step3: After clustering, simple segmentation extracts different features; segmented patch extraction extracts white matter, grey matter, and cerebrospinal fluid textural features; algorithm 3 optimises these features employing simulated annealing. The optimizer assigns weights to features in order to increase the classifier's domain.

Step4: Following that, features are selected using four classes. SVM and RF are used to accomplish learning in different courses, and accuracy, recall, and precision are used to perform analysis.

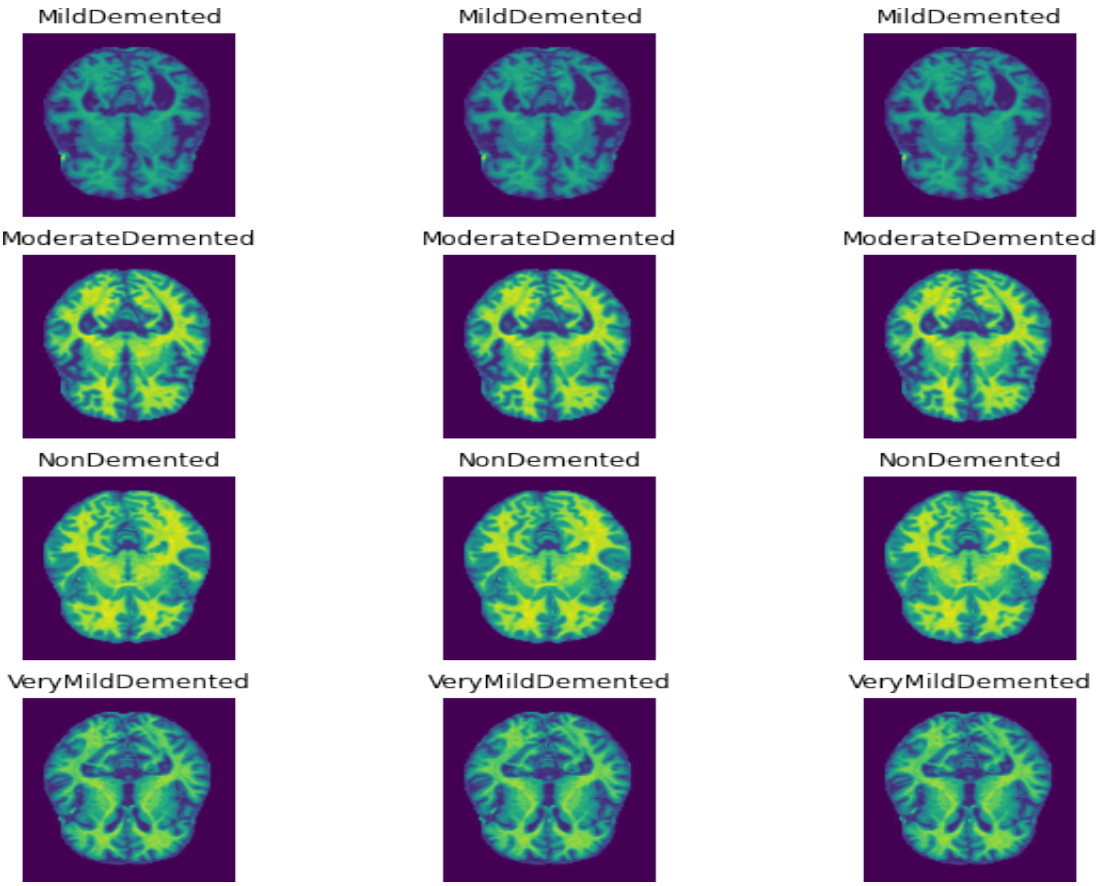


Figure 3.10: Diverse classes during the segmentation phase

3.5.2 Proposed methodology Algorithm

Algorithm 1: Segmentation (Image)

Input: Input Images

Output: Segmented Images

Begin

N← no. of Images

P←i x j Pixels

Define centroid $\{X_1, X_2, \ldots\ldots\ldots\ldots, X_n\}$

While (Centroid >0)

Start

Define the population of grey wolves

GW←Centroid

G_α← G(P)

G_β← N

G_δ← P

Update weights

$$w^{n+1} = \frac{w_0\, G_\alpha + \sum GW}{G_\alpha + G_\beta + G_\delta} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (5)$$

End

Algorithm 2: Features Extraction

Input: Segmented Images

Output: Texture features

Begin

While (pixel >0)

Start

Image divided into (128x128)

generate Gray matrix, white matter matrix and cs fluid

flattened matrix

End

Apply Simulated annealing (flattened matrix)

Weighted features

Finish

Algorithm 3: Classification(image)

Input: Images
Output: Classified dementia or not Dementia
N←number of images
While (N>0)
Start
Pre-process (N_i)
Start
Pre-process (N_i)
Segmentation (N_i)
Features (N_s)
N_s←(Features, label)
LBP (N_s)
Texture (N_s)
Finish
Feature←$\{x_1, x_2, \ldots\ldots\ldots, x_n\}$
Label←$\{l_1, l_2, \ldots\ldots\ldots, l_n\}$
T_s←(Features, label)
Train← Random Forest (T_s)
Test← Train (T_s)
Analyze Precision, Recall and Accuracy
End

3.6 Dataset used for Research

Table 3.1 Experiment Setup

Parameters	Values
Dataset	ADNI
Classes	4
Optimizer	GWO and simulated annealing
Features	Texture
Classifier	Random forest and SVM
Metrics	Precision, recall, accuracy and F-score

3.6.1 Dataset: Using data from the Alzheimer's Disease Neuroimaging Initiative (ADNI), which is freely available on the internet (http://adni.loni.usc.edu/). The ADNI's mission is to create more responsive and effective methods for diagnosing Alzheimer's disease earlier in the disease's course, as well as to show the progression of AD using biomarkers. A total of 694 structural MRI scans were used in this study, with subjects initially classified as AD (n=198), NC (n=230), pMCI (n=166), and sMCI (n=101). At baseline, Te 166 pMCI subjects were diagnosed with MCI, but conversion to AD occurred within a 36-month follow-up span. The subjects ranged in age from 55 to 90 years, and the MMSE scores for each group ranged from 20–26 (AD), 24–30 (MCI), and 24–30 (MCI) (NC).

3.6.2 Summary

This chapter discussed the use of a Grey Wolf-based optimization approach to the optimization of image features. As discussed in the current chapter SVM and RF were used to accomplish learning of the model. For performance analysis of the model, the following were used:1) accuracy, 2) recall, and 3) precision has been used in the current research work**.** Additionally, it encompasses the research process and the application of proposed algorithms to the study objective.

CHAPTER 4

Designing a Hybrid CNN-based Approach for Dementia Early Detection (CNAT-TRXG)

4.1 Introduction

Dementia has a huge impact on older people and their families. It is becoming major health issues for adults fall in the age category (50-70). The World Health Organization (WHO) report examined that dementia is not an inevitable consequence of ageing. This report further addressed that "currently more than 55 million people live with dementia worldwide, and there are nearly 10 million new cases every year. By the year 2050, there will be about 120 million people with dementia and 75 million people with Alzheimer's'". Our inequalities would nearly vanish if everyone got a fair shot. Dementia is a neurological illness that affects normal functioning and eventually kills people by affecting their hearts and lungs. Dementia is classified as neurodegenerative or non-neurodegenerative [18]. Table 4.1 lists types of Dementia.

Table 4.1: Types of Dementia [18]

Neurodegenerative	**Non-neurodegenerative**
Alzheimer's disease	Vascular dementia
Frontotemporal dementia	Normal pressure hydrocephalus
Dementia with lewy bodies	Autoimmune causes
Multiple system atrophy	Infectious causes
Alcoholic cognitive impairment	Toxic causes
Huntington disease	Vitamin deficiency

The following methods were used to diagnose and treat dementia when it first emerged in the public eye:

a) Personal history involving a neurologist interview

b) Mental state focusing on neurological tests

c) Blood testing

d) Brain scan to diagnosis.

All of these stages remained the same for diagnosing dementia.

Alzheimer's disease represent the most usual kind of dementia. This condition has become increasingly frequent in the elderly (65+) and is called late onset Alzheimer's disease (Load). This illness has exploded in recent years all across the world.

This chapter provides insights into the deep learning technique. It discusses the following deep learning techniques:

1). Convolutional neural network (CNN), 2). CNN-attention layer, and 3). CNN-transfer layer. Using the above-mentioned techniques, a hybrid CNN-based approach will be designed for detection of dementia.

4.2 Convolutional Neural Networks (CNN)

Convolutional Neural Networks (CNN) were introduced by Yann LeCun in 1998 for Optical Character Recognition (OCR), whereby they worked well. Signals and speech recognition, video, volumetric imagery, and sound spectrograms are all common uses for CNNs.

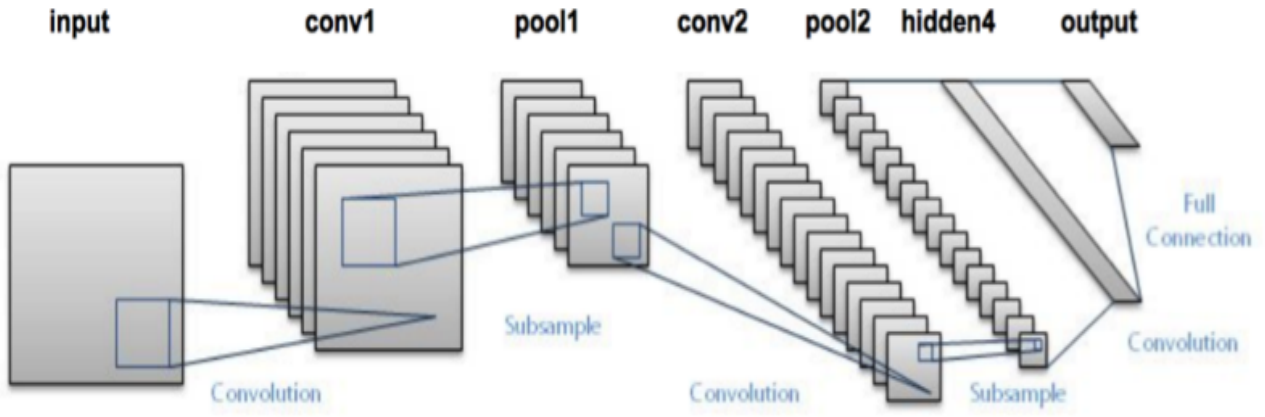


Figure 4.1: CNN's multi-layered architecture.

The following is a list of the layers that are used to construct CNN topologies.

- Convolutional Layer
- Pooling Layer
- Activation Layer

A densely connected layer, as opposed to a completely connected layer, is defined in greater detail in section 3.

Prior to the development of Convolutional Neural Networks (CNN) in 1998, Yann LeCun introduced a CNN to perform Optical Character Recognition (OCR) that yielded effective results. The use of CNN does not only include image-based work, but is often employed for text analysis, audio, film, and 3D imagery.

Convolution layer

Convolution Layer performs a convolution operation where a 2-D or 3-D filter scrolls across the image and adds filters to every visual depth. Convnets are a specialised type of Multi-Layer Perceptron (MLP) that is more suited to 2D/3D input than to 1D input. Convolutional layers were built on the notion of detecting fundamental features such as boundaries, edges, and endings and combining them with several layers to create higher features which can adequately reflect an entity. Additionally, this framework is optimised for extracting high-level features from the image anywhere at specific layer to characterise an item such as a face, chair, or car. Additionally, convolution offers a vital and significant feature called shift invariance. That is, if first layer's input is displaced, the first layer's output is also moved by same degree. Convolution has two primary factors that affect its behaviour: padding and stride.

The convolution layer's output is determined using the following equation.

$$W_{n\#\$} = \frac{(W_{O*} + F_{-i*/0}123)}{5} + 1 \quad \ldots\ldots(1)$$

F_{width}: When applying the appropriate formula, specify the size of the kernel or filter in terms of the height and width constraints.

P: Padding

S: Convolutional stride window size

W_{new}: New width of the output image

W_{old}: The input image's previous width feature map.

As the feature's actual location is immaterial, just its placement in respect to other features matters, notably for classification.

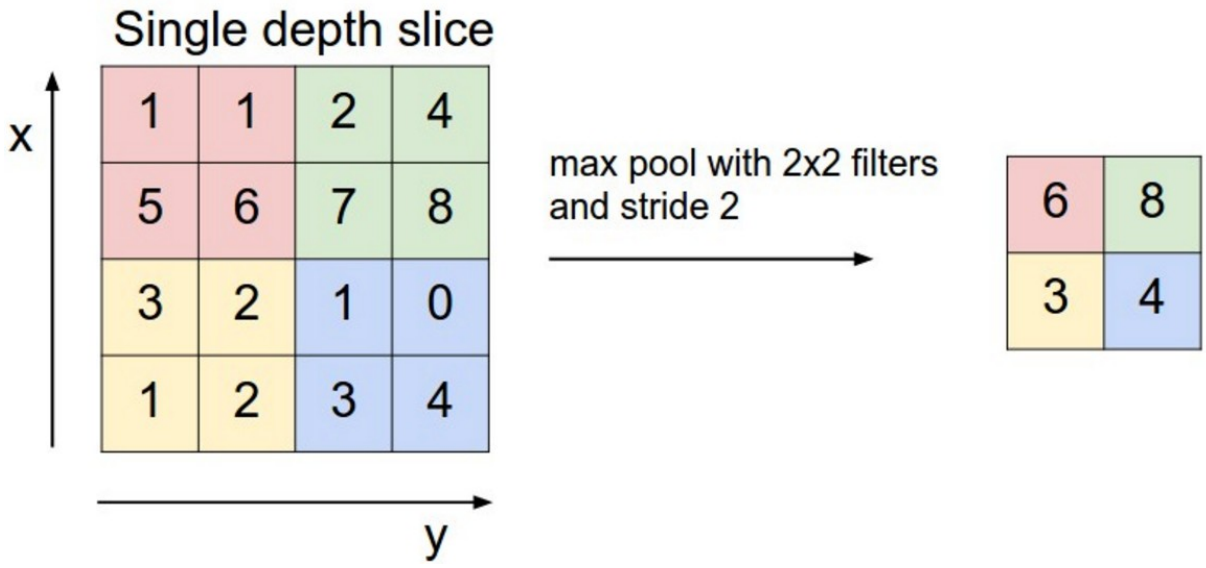


Figure 4.2: Max Pooling

The output of the pooling layer is determined using the relation below.

$$W_{n\#\$} = \frac{(W()^{*}+F)}{5} + 1 \quad \ldots\ldots(4.2)$$

$W_{n\#\$}$: The output image's new width.

$W_{9:\varsigma}$: Width of the image input

F: Size of Filter Width

S: Stride size

This equation is often used to compute the width of an output picture from the pooling layer, and it can also be used to compute the height of an output image from pooling layer by swapping the width and height parameters.

4.2.1 Fully Connected Layer

The dense layer seems to be fully connected layer, whereby every neuron inside one layer is coupled to every neuron in the subsequent one. This works on the same premise as the standard multi-layer perceptron NN model. In the entire CNN model, the fully-connected layers are known to as the final layers. The fully-connected layers work as an MLP, called as Multi-Layer Perceptron with 2 or 3 hidden units and one classifying layer in most cases. The MLP's features make it an exceptional function for approximations. This can-do approximation at any function only with two hidden layers assuming that has enough hidden neural layers. The quantity of neurons in each hidden layer is relatively stable in deep networks with wide input images, with 4096 becoming a prevalent number.

The fully linked layer can indeed be compressed and linked to an output layer, reducing the size of a layer for image categorization. Whereas if input comes from a max pool layer or convolution layer with a size of XxYxZ, one can set the amount nodes that need inside the fully-connected flattened layer only at fully-connected layers. The number of sensor nodes could be XxYxZ or (X*Y*Z)/2, and the output will be decreased before being fed to a output classification stage.

4.2.2 Activation Function

In the complex and sophisticated deep-neural network, the activation function plays a critical role. They provide neural networks the ability to be nonlinear. Activation functions are used to turn an input signal into an output signal. This is utilised for abstract depiction of action-based potential triggering the node in each and every node of the deep-NN. When no activation function is given, the output-based mapping function would be a linear combination by default. When learning complex function limitations (boundary lines) of input data, linearity is much less efficient. In the section below, we'll go through certain activation functions in further detail.

4.2.3 Strides

Stride is a notion that governs how the kernel moves across an image during max pooling and convolution operations. The kernel runs over image by default by moving one place vertically or horizontally at a moment. Starting at (0,0) inside the image, but if the stride is 1x1, this would

travel 1 both in vertical and horizontal directions. Stride is specified as [1,2,2,1], indicating that every component in the array is specified as [batch; vertical shift; horizontal shift; channels] correspondingly.

Take, for instance,

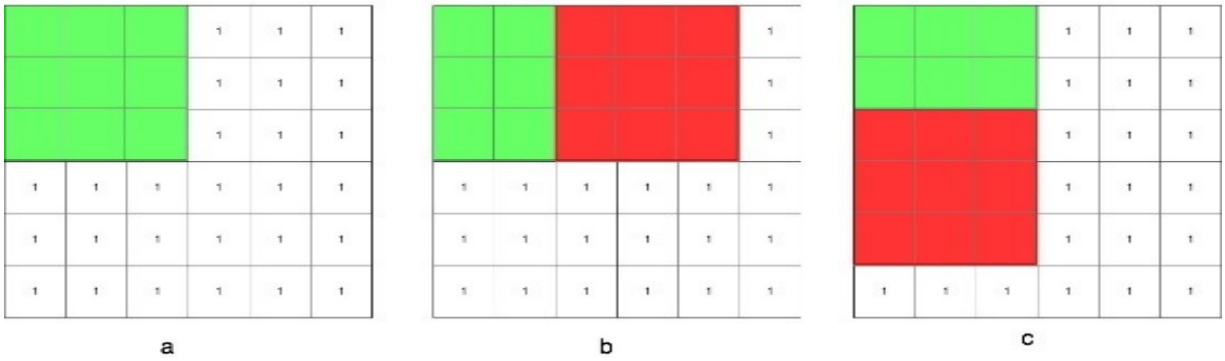


Figure 4.3: On a 6x6 image, a 2x2 stride is employed for the kernel in the convolution process.

The stride is 2x2 in the preceding convolution; in figure 13b, the kernel would be moved by two places in the horizontal plane, as indicated by the red colour; and in figure 13c, the kernel is moved by two places in the vertical position.

Resnet

1.It is an artificial neural network that has residual block piled over each other to form a connection.
2.It was introduced by Kaiming He, Xiangyu Zhang, Shaoqing Ren and Jian Sun in 2015.
3.Keeping in view the performance benefits of Resnet, it is used in the current thesis.
4.It helps in decreasing the training errors and training loss, thus improving in the working of the model.

4.3 Research Methodology

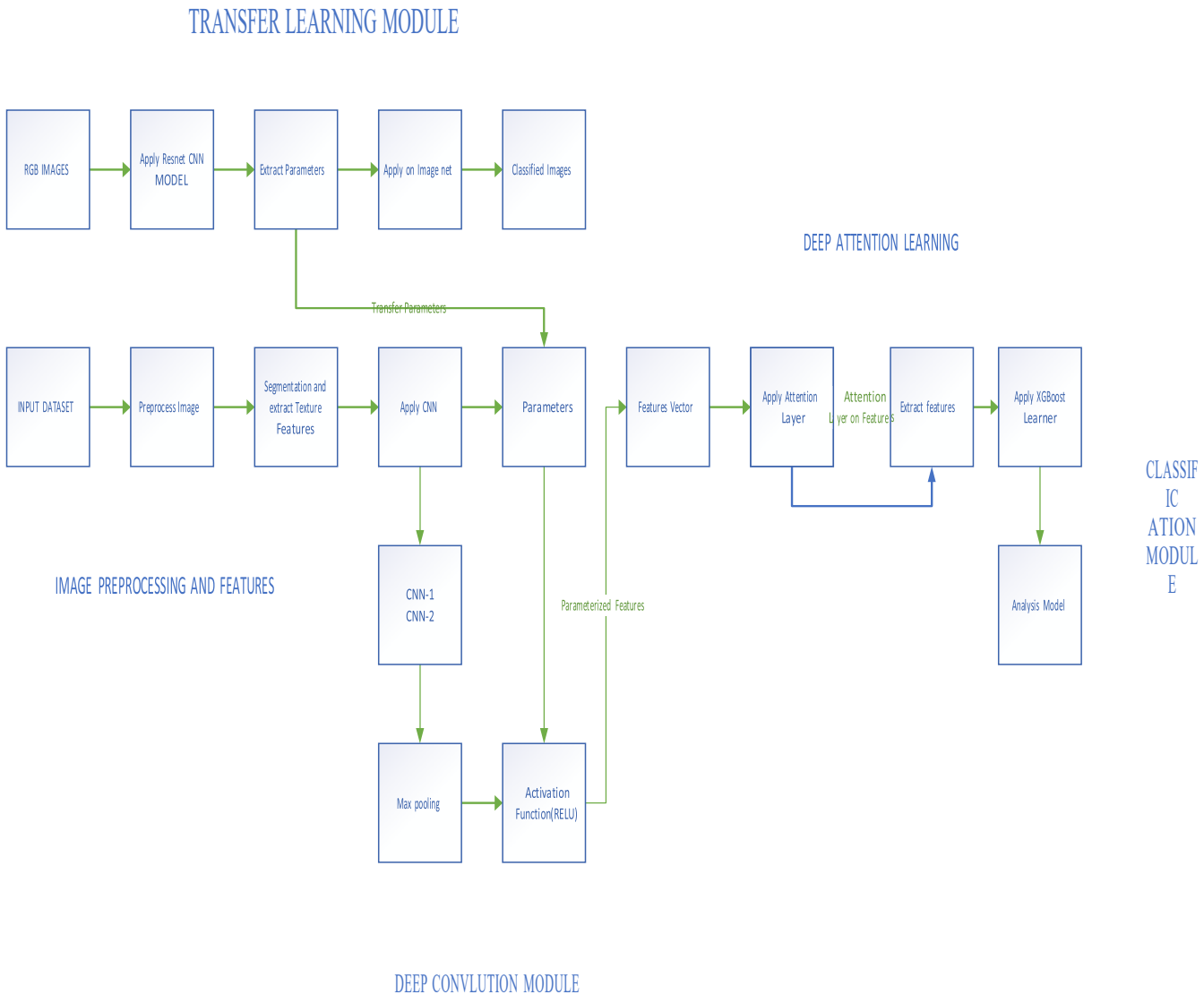


Figure 4.4: Hybrid CNN Based Approach for Dementia Disease Detection (CNAT-TRXG) Workflow chart

Algorithm 5: classification(image)

Input: Images

Output: Classified Dementia

N←number of images

While (N>0)

Start

Pre-process (N_i)

Start

Pre-process (N_i)

Segmentation (N_i)

Features (N_s)

N_s←(features, label)

LBP (N_s)

Texture (N_s)

Finish

Feature←$\{x_1, x_2, \ldots\ldots\ldots, x_n\}$

Label←$\{l_1, l_2, \ldots\ldots\ldots, l_n\}$

T_s←(features, label)

Theta<-Apply Transfer learning(RGB)

F <-CNN(theta,T_s)

A_F <-Attention(F)

Train← Xgboost (A_F)

Test← Train (T_s)

Analyze Precision, Recall, and Accuracy

End

4.3.1 Transfer Learning

Now the CNN extraction process is used, as it is seen in Figure 2 for CNN function discovery and transition learning. According to CNN, the results of the model are the parameters of a natural ImageNet image package. Low-level characteristics are extracted from the obtained mammogram images. Transfer learning was implemented with four convolutional layers and a ReLU activation functions, as seen in Table 4. Using transfer learning, the pre-trained model was fine-tuned and

mass classification feature vectors were developed. It has high-level features from the pre-trained CNN model

Table 4.2 CNN Model for Transfer Learning

Input - Image		
RESnet	Conv Block 1 (4*48*64) Pooling (2*24*64)	Conv + ReLU
		Patch 7*7
		Max Pool_3*3
	Conv Block 2 (2*24*64)	Conv + ReLU 1*1(64)
		Conv +ReLU 3*3 (256)
		Conv +ReLU 1*1 (512)
	Conv Block 3 (2*24*64)	Conv + ReLU 1*1 (128)
		Conv +ReLU 3*3 (128)
		Conv +ReLU 1*1 (512)
	Conv Block 4 (2*24*64)	Conv + ReLU 1*1 (256)
		Conv +ReLU 3*3 (256)
		Conv +ReLU1*1 (1024)
	Conv Block 5 (2*24*64)	Conv + ReLU 1*1 (512)
		Conv +ReLU 3*3 (512)
		Conv +ReLU1*1 (2048)
FC + ReLU (Dropout= 0.5)		
Output (Sigmoid)-[0,1]		

4.3.2 Convolution with Attention Layer

The characteristics of CNN and attention modelling are brought together in this process. Both images are applied simultaneously to separate the mammographic characteristics from the input data. CNN incorporated features, which were assembled on a large sheet of CNN. Additional or sustained focus is key to the improved collection. The mechanism accommodates varying

document size by selecting text features according to scale so that the document can suit the scale. as it calculates the array balance of focus, it checks the distribution of weight. X_i

$$S_l^{\rangle} = FL_{ensm}\mathrm{E}X_l^{\rangle}\mathrm{G} \quad \text{.....(1)}$$

$$X_{atten}^{\rangle} = \mathbf{K}^{L}_{\mathbf{j}\mathrm{O}^{\rangle}} \alpha_L^{\rangle} X_L^{\rangle} \quad \text{.....(2)}$$

Classifier Model

$$\partial^L_{\rangle} = Softmax\,\mathrm{X}MLP\mathrm{E}X^{\rangle}_{atten}\mathrm{G}[\quad \text{.....(3)}$$

4.3.3 CNN Model

The related features have been found in the M feature set are identified by the CNN model. The CNN is explained in Figure 4.5. There are four convolution layers, with two max pooling and one attached for good measure. It contains a lot of neurons. Neurons in this network are linked with each other and make use of interconnections. This layer incorporates convolution into the feature map. However, the kernel sequence of input patterns is converted to the input matrix.

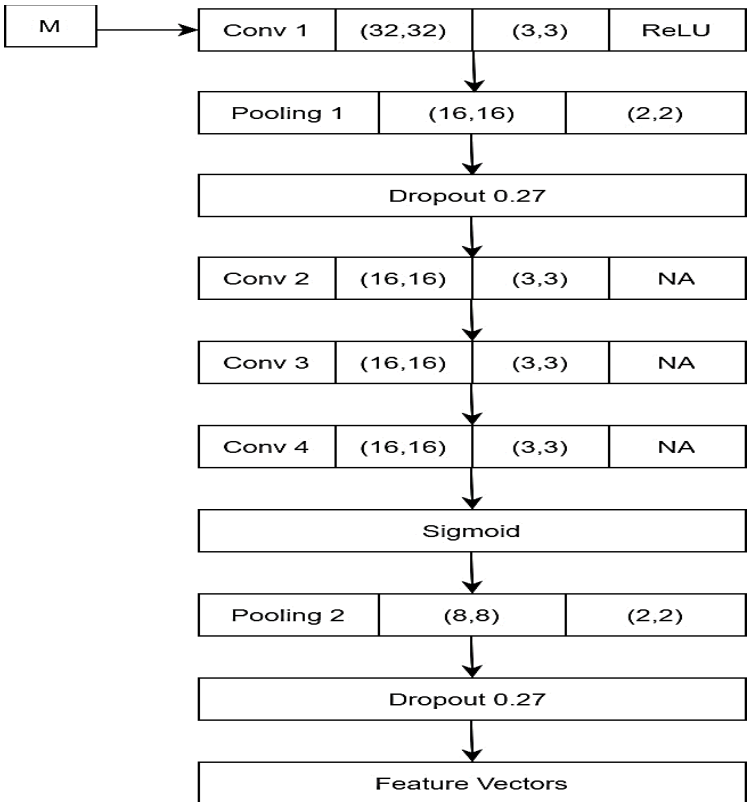


Figure 4.5: Proposed CNN Architecture

4.3.4 Ensemble Learning Model for Classification

With ensemble learning, (which is an enhanced gradient boosting strategy), Intense Gradient Boosting gets underway. The Xg-boost in the proposed scheme is used to generate the function vectors with different regression tree values as well as to choose different labels for each. It can not make the final statement about the various tree configurations. Hence, then as in the checking process, the C approach takes as the threshold values. A F is better used if it has a zero-one scaling; in contrast, less value is created when the following objective functions are used: Zero to one or Gain.

$$F = \sum_{x\mathrm{Og}}^{n} l\mathrm{E}A_x, A_x\mathrm{G} + (\gamma T - (1-\gamma)T) + {}^{\mathrm{g}}\frac{\lambda}{2}\sum_{y\mathrm{Og}}^{T} w_y^2 \quad (6)$$

4.4 Summary

This chapter includes the formation of a Hybrid CNN-based technique for the early detection of dementia Convolution neural network with attention layer-Transfer learning and XG boost (CNAT-TRXG). It entails research using the CNN model, CNN-attention layer and CNN-transfer learning process. All these techniques lead to the formation of a CNAT-TRXG.

CHAPTER 5

Comparison of Grey Wolf Based Features Optimization approach with Existing Approaches

5.1 Result Analysis

In this chapter the comparative analysis of methodology-1(Grey Wolf Based Optimization approach) with the existing approaches will be discussed. This research work has used ADNI's four-class dataset. Feature extraction and weighting by an optimizer has been included in the methodology-1. Grey wolf-based features optimization technique(methodology-1) will be compared with support vector machine (SVM), Random Forest (RF).

Analysis Model for performance of the proposed-1 with other approaches will be discussed approach wise.

Following analysis is the result of methodology-1 which has been achieved using Google Colab platform. For proposed methodology-1, please refer to chapter 3. Now using the metrics (accuracy, recall, precision and F-score) results of the comparison will beshown in tabular as well as graphical form in the current Chapter.

5.1.1 Comparison of Grey wolf-based feature optimize-random forest and support vector machine (SVM)

In Table 5.1, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the features optimized-SVM classifier, the features optimize-RF (proposed-1) classifier acquired fairly better values for all parameters.

Table 5.1 Comparison of Feature optimize random forest and SVM

Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (methodology-1)	**72.33**	**72.45**	**71.22**	**72**
Features optimize-SVM	**69.12**	**70.45**	**68.34**	**66.23**

The graphical comparison of methodology-1 and feature optimize-SVM is shown in figure 5.1. The grey wolf-based feature optimize-RF technique(methodology-1) has shown higher values in the graph than the support vector machine.

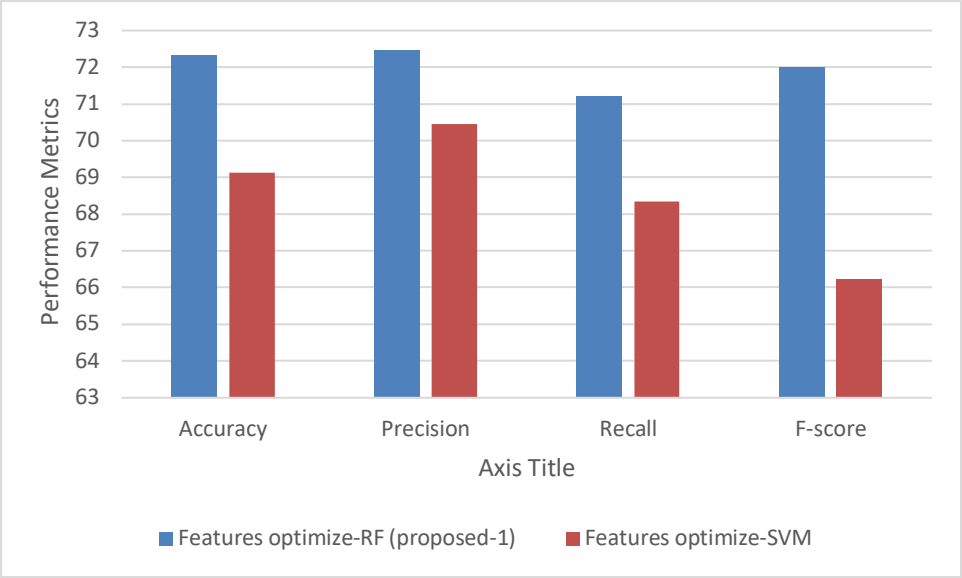


Figure 5.1: Comparison of Feature optimize random forest and SVM

5.1.2 Comparison of Grey wolf-based feature optimize-random forest and random forest (RF)

In Table 5.2, two different types of classifiers are analysed, on the basis of four parameters: accuracy, precision, recall, and F-score values. In comparison to the RF classifier, the features optimize-RF (proposed-1) classifier acquired considerably better values for all parameters.

Table 5.2 Comparison of Feature optimize random forest and without optimize Random Forest

Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (methodology-1)	72.33	72.45	71.22	72
Random forest	60	50.34	58.34	55

Graphical comparative analysis of methodology-1 and random forest is shown in figure 5.2. The grey wolf-based feature optimize-RF technique(methodology-1) has shown higher values in graph than random forest classifier of machine learning technique.

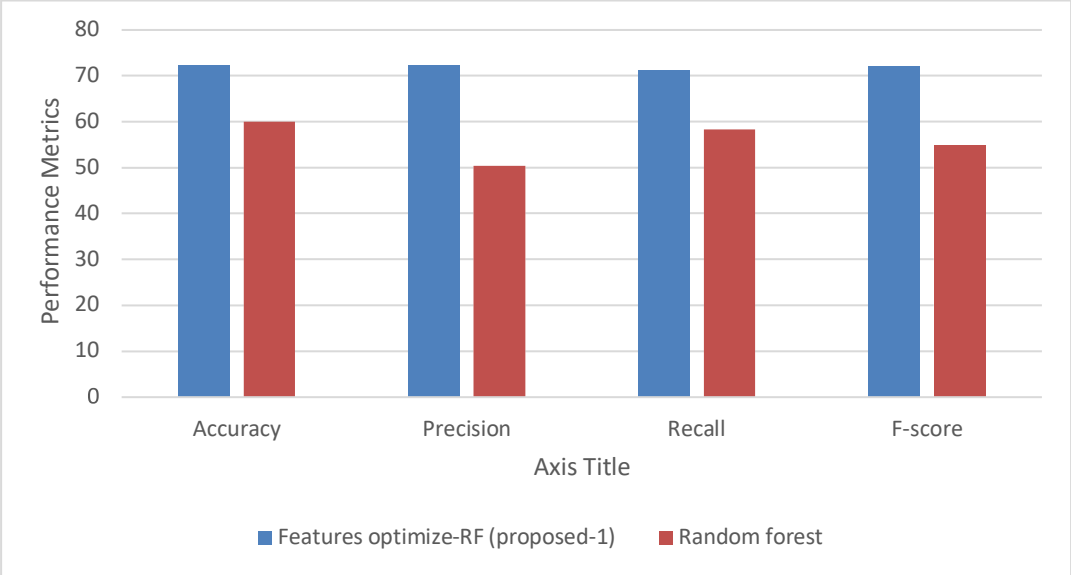


Figure 5.2: Comparison of Feature optimize random forest and without optimize Random Forest

5.1.3 Comparison of Grey wolf-based feature optimize-random forest and support vector machine (SVM)-Linear

In Table 5.3, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the SVM-Linear classifier, the features optimize-RF (proposed-1) classifier acquired somewhat better values for all parameters.

Table 5.3 Comparison of Feature optimize random forest and SVM-linear

Table 5.3Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (methodology-1)	72.33	72.45	71.22	72
SVM-Linear	59	34.12	58	48

Graphical comparative analysis of methodology-1 and the random forest is shown in figure 5.3 on the basis of accuracy, recall, precision and F-score. The grey wolf based feature optimize-RF technique(methodology-1) has shown higher values in the graph than the support vector machine(linear) classifier of the machine learning technique .

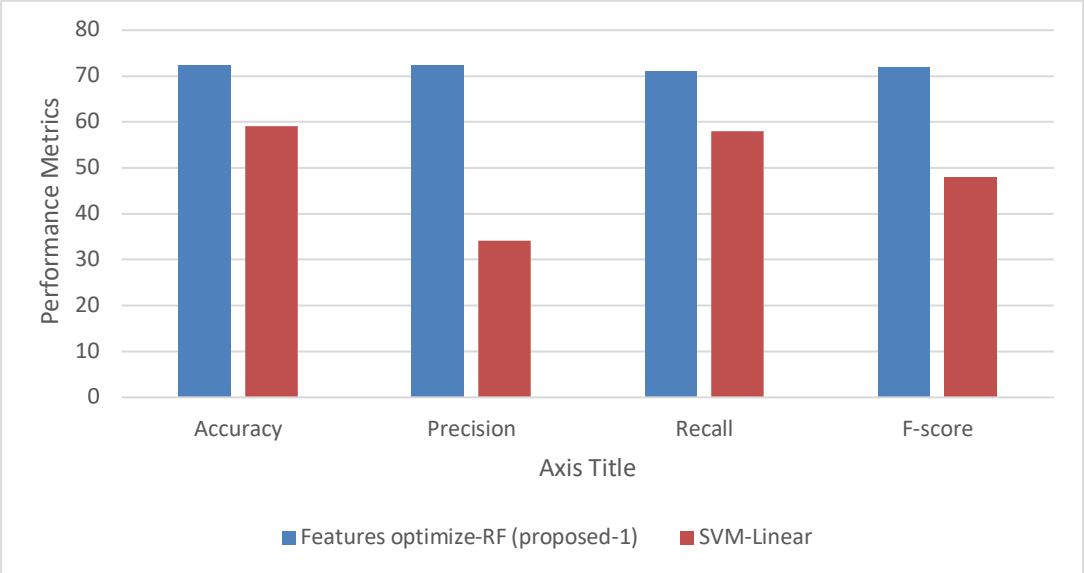


Figure 5.3: Comparison of Feature optimize random forest and SVM-linear

5.1.4 Comparison of Grey wolf-based feature optimize-random forest and SVM-RBF

In Table 5.4, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the SVM-RBF classifier, the features optimize-RF (proposed-1) classifier acquired good values for all parameters.

Table 5.4 Comparison of Feature optimize random forest and SVM-RBF

Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (methodology-1)	72.33	72.45	71.22	72
SVM-RBF	58.23	48.12	57.34	52.13

Graphical comparative analysis of methodology-1 and the random forest is shown in figure 5.4 on the basis of accuracy, recall, precision and F-score. The grey wolf based feature optimize-RF technique(methodology-1) has shown higher values in the graph than the support vector machine-Random forest (SVM-RBF) classifier of machine learning technique .

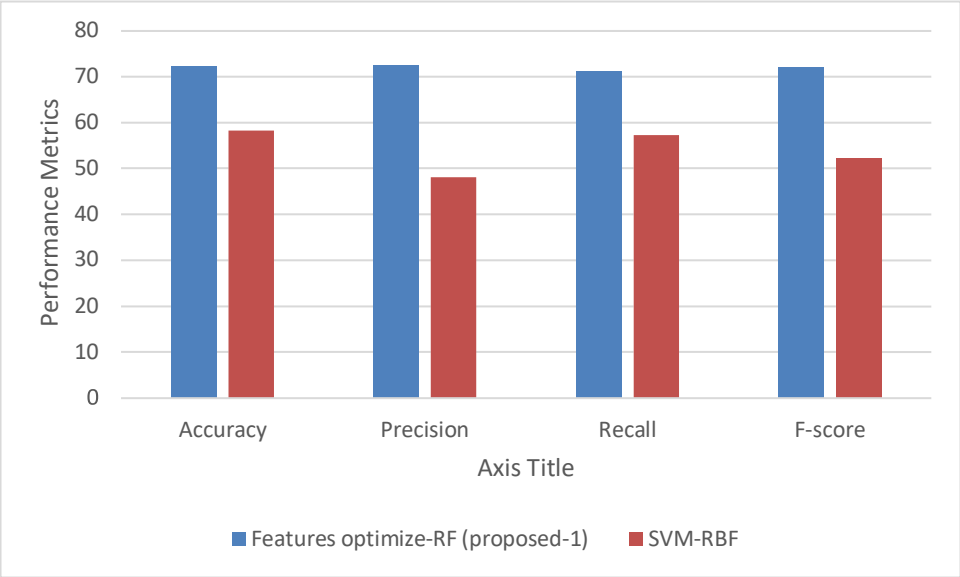


Figure 5.4: Comparison of Feature optimize random forest and Without optimize SVM-RBF

5.2 Summary

To conduct the experiment, the current research used the ADNI's four-class dataset. Feature extraction and weighting by an optimizer are included in the proposed model, which is based on a classifier trained using machine learning. Four methods are used in the analysis: SVM, Random Forest, SVM-Linear and SVM-RBF (without optimize).

The grey wolf-based optimization approach has comparatively shown better results than support vector machine (SVM), random forest (RF). These results of grey wolf based optimization technique will be further enhanced in Hybrid CNN-based technique (methodology-2) as discussed in the next chapter.

CHAPTER 6

Comparison of Hybrid-CNN (CNAT-TRXG) (proposed-2) Approach with existing Approaches

6.1 Result Analysis

In this chapter the comparative analysis of methodology-2(CNAT-TRXG) with the existing approaches will be discussed. As discussed in chapter 4, this research work has used ADNI's four-class dataset on which deep learning techniques were applied and a new technique was formulated named hybrid CNN/convolutional neural network with attention layer-transfer and XG boost (CNAT-TRXG).

In this chapter, Convolutional Neural Networks (CNN), CNN with attention layer and CNN with transfer layer will be compared with (Convolutional neural attention-transfer XG boost) CNAT-TRXG (methodology-2) using Google Colab platform.

6.1.1 Comparison of Hybrid CNN with CNN

In Table 6.1, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the CNN classifier, the CNAT-TRXG (proposed-2) classifier acquired good values for all parameters. In the case of accuracy, CNAT-TRXG has scored 92.34% in comparison to the convolutional neural network.

Table 6.1 Comparison of Proposed and CNN

Classifier	Accuracy	Precision	Recall	F-score
CNAT-TRXG (methodology-2)	**92.34**	**91.23**	**94.23**	**96.23**
CNN	**84.13**	**84.7**	**83**	**85**

Graphical comparative analysis of methodology-2 and convolutional neural network (CNN) is shown in figure 6.1 on the basis of accuracy, recall, precision and F-score. CNAT-TRXG (methodology-2) has shown higher values in the graph than Convolutional neural network.

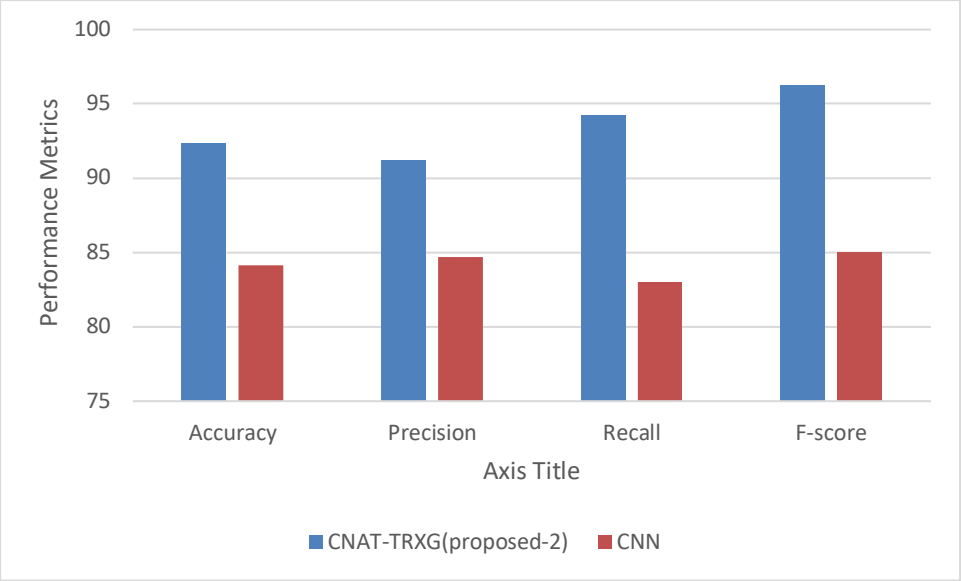


Figure 6.1: Comparison of Proposed and CNN

6.1.2 Comparison of Hybrid CNN with CNN-Attention

In Table 6.2, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the CNN-Attention classifier, the CNAT-TRXG (proposed-2) classifier has slightly more accurate values for all parameters.

Table 6.2 Comparison of Proposed and CNN-Attention

Classifier	Accuracy	Precision	Recall	F-score
CNAT-TRXG (methodology-2)	**92.34**	**91.23**	**94.23**	**96.23**
CNN-Attention	**90.12**	**90.23**	**84.12**	**94.23**

Graphical comparative analysis of methodology-2 and convolutional neural network (CNN)-Attention is shown in figure 6.1 on the basis of accuracy, recall, precision and F-score. CNAT-TRXG (methodology-2) has shown higher values in graph, when compared with Convolutional neural network along with attention layers.

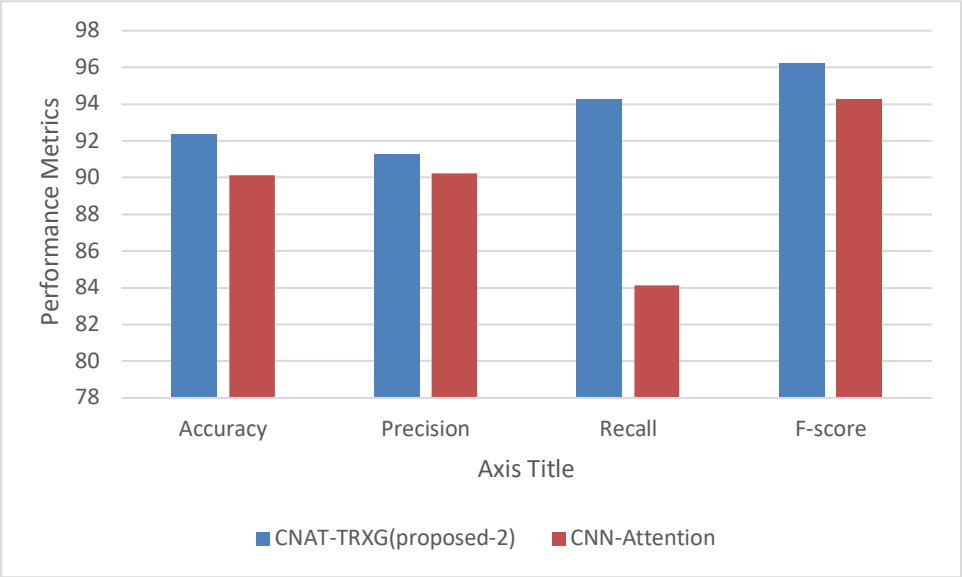


Figure 6.2: Comparison of Proposed and CNN-Attention

6.1.3 Comparison of Hybrid CNN with CNN-Transfer

In Table 6.3, two different types of classifiers are illustrated, each with four parameters: accuracy, precision, recall, and F-score values. In comparison to the CNN-Transfer classifier, the CNAT-TRXG (proposed-2) classifier has more accurate values for all parameters.

Table 6.3 Comparison of Proposed and CNN-Transfer

Classifier	Accuracy	Precision	Recall	F-score
CNAT-TRXG (Methodology-2)	**92.34**	**91.23**	**94.23**	**96.23**
CNN-Transfer	**89.23**	**88.12**	**89.45**	**93.11**

Graphical comparative analysis of methodology-2 and convolutional neural network (CNN)-transfer is shown in figure 6.1 on the basis of accuracy, recall, precision and F-score. CNAT-TRXG (methodology-2) has shown escalated values in the graph, when compared with the Convolutional neural network along with the transfer layer.

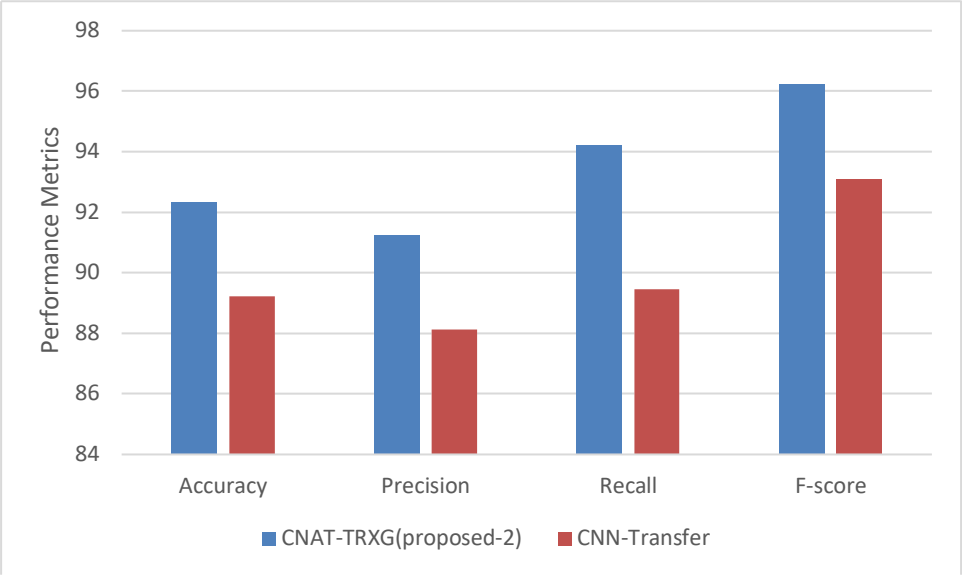


Figure 6.3: Comparison of Proposed and CNN-Transfer

6.2 Summary

- In the current work, ADNI's four-class dataset has been used. Deep learning and transfer learning techniques are used in the current work.
- CNAT-TRXG is the present research work model which has shown much better performance than convolutional neural network (CNN), CNN-attention layer and CNN-transfer.
- Accuracy of the current technique of this thesis has achieved an accuracy of 92.34%.
- Feature mapping on nonlinear space and parameter adjustment via transfer learning are the reasons for improved performance.
- Transfer and attention layer when used with convolutional neural network has brought a surge in the values of the current research work.

CHAPTER 7

Conclusion and Future Scope

7.1 Introduction

The present thesis examined the capacity of widely used machine learning algorithms to distinguish between MRI representations of stable brains, mildly cognitively impaired brains, and brains afflicted by Alzheimer's Disease. Classic machine learning algorithms (i.e., decision trees and rule-based structures), and neural networks, were applied to the standardized ADNI magnetic resonance imaging dataset.

7.2 Comparative Analysis of Both Approaches

Table 7.1 Comparison of Proposed and other approaches

Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (proposed-1)	**72.33**	**72.45**	**71.22**	**72**
Features optimize-SVM	**69.12**	**70.45**	**68.34**	**66.23**
Rm forest	**60**	**50.34**	**58.34**	**55**
SVM-Linear	**59**	**34.12**	**58**	**48**
SVM-RBF	**58.23**	**48.12**	**57.34**	**52.13**
CNN	**84.13**	**84.7**	**83**	**85**
CNN-Attention	**90.12**	**90.23**	**84.12**	**94.23**
CNN-Transfer	**89.23**	**88.12**	**89.45**	**93.11**
CNAT-TRXG (proposed-2)	**92.34**	**91.23**	**94.23**	**96.23**

The technique applied in this thesis is exploratory and experimental, with machine learning results mixed with a number of different dimensional reduction techniques and a variety of diagnostic classes compared (using different merging schemes). Similar issues have been solved successfully by random forests, SVMs, and more recently deep neural networks. In the present study, a categorization system for brain illness based on MRI is proposed. To improve prediction patterns, attention-based transfer learning was utilized, and ultimately, features were learned and used to categorize fMRI data. The present study used boost hyper-parameters to classify dementia risk trends. Gradient boosting is often used to separate dependent and independent variables, resulting in derived variables. The system's MRI is from ADNI. Using the function

extractor method, most characteristics are extracted rapidly. The experimental results showed that the suggested approach can classify performance correctly.

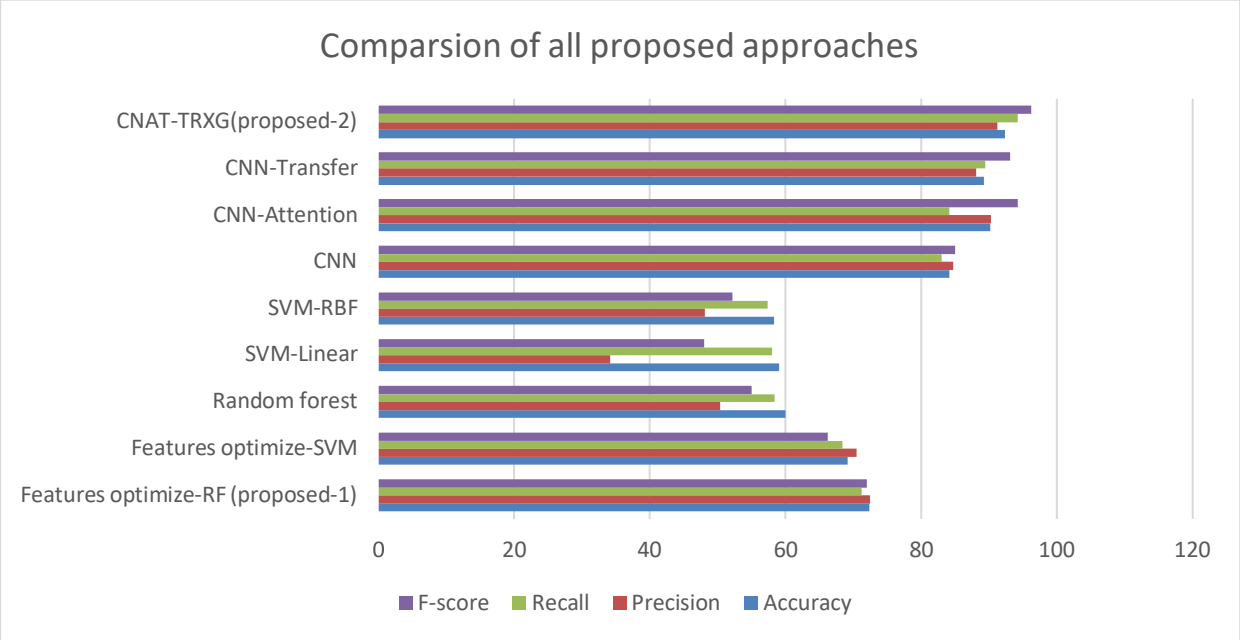


Figure 7.1: Comparison of both methodologies and other approaches

Figure 7.1 exhibits the results achieved in proposed-1 of this research work and proposed 2.The above graphical representation proclaims the movement of this research work from machine learning(ML) to deep neural networks(DNN).The movement of ML to DNN has given much better results.

1st Methodology

Table 7.2 Comparison of Methodology-1 and other approaches

Classifier	Accuracy	Precision	Recall	F-score
Features optimize-RF (proposed-1)	**72.33**	**72.45**	**71.22**	**72**
Features optimize-SVM	**69.12**	**70.45**	**68.34**	**66.23**
Random forest	**60**	**50.34**	**58.34**	**55**
SVM-Linear	**59**	**34.12**	**58**	**48**
SVM-RBF	**58.23**	**48.12**	**57.34**	**52.13**

The method will lead to a 4.2 percent increase in precision and accuracy while retaining a 94.6 percent recall.

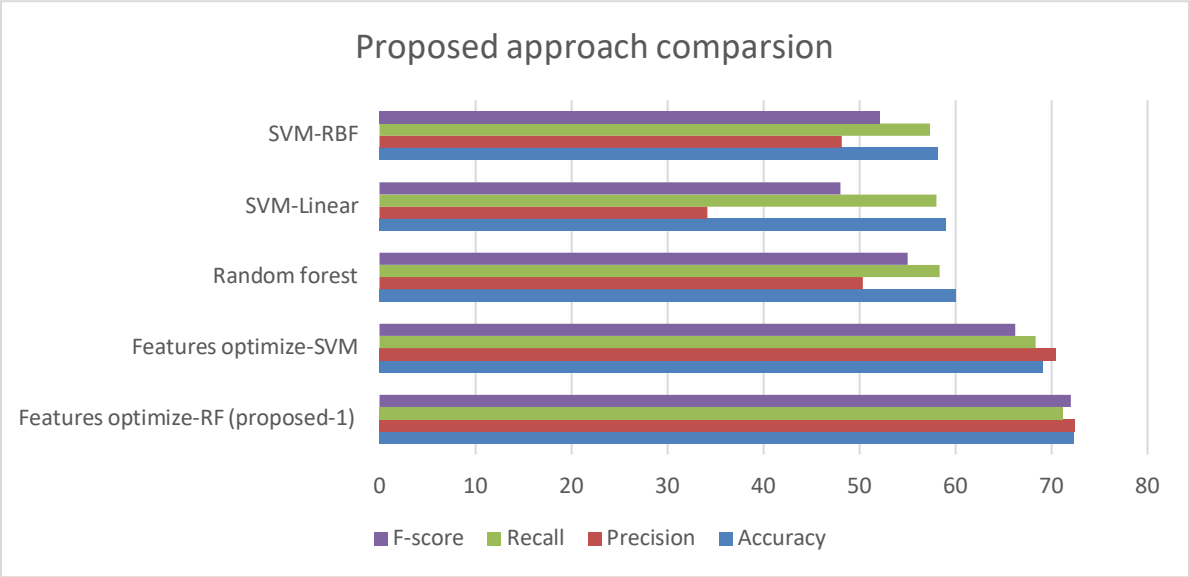


Figure 7.2: Comparison of Proposed-1 and other approaches

This thesis investigates Alzheimer's disease phases using deep learning and multi-class categorization in both the approaches.

2ND Methodology

Table 7.3 Comparison of Proposed-2 and other approaches

Classifier	Accuracy	Precision	Recall	F-score
CNN	**84.13**	**84.7**	**83**	**85**
CNN-Attention	**90.12**	**90.23**	**84.12**	**94.23**
CNN-Transfer	**89.23**	**88.12**	**89.45**	**93.11**
CNAT-TRXG (proposed-2)	**92.34**	**91.23**	**94.23**	**96.23**

The present thesis proposed a CNN-to-transfer attention map. Mild dementia (MD), No dementia (ND), moderate dementia (MMD), and very severe dementia (VSD) are the four MRI classifications suggested by the present work. Tests are run to see how model regularization and overfitting impact current application's overall performance.

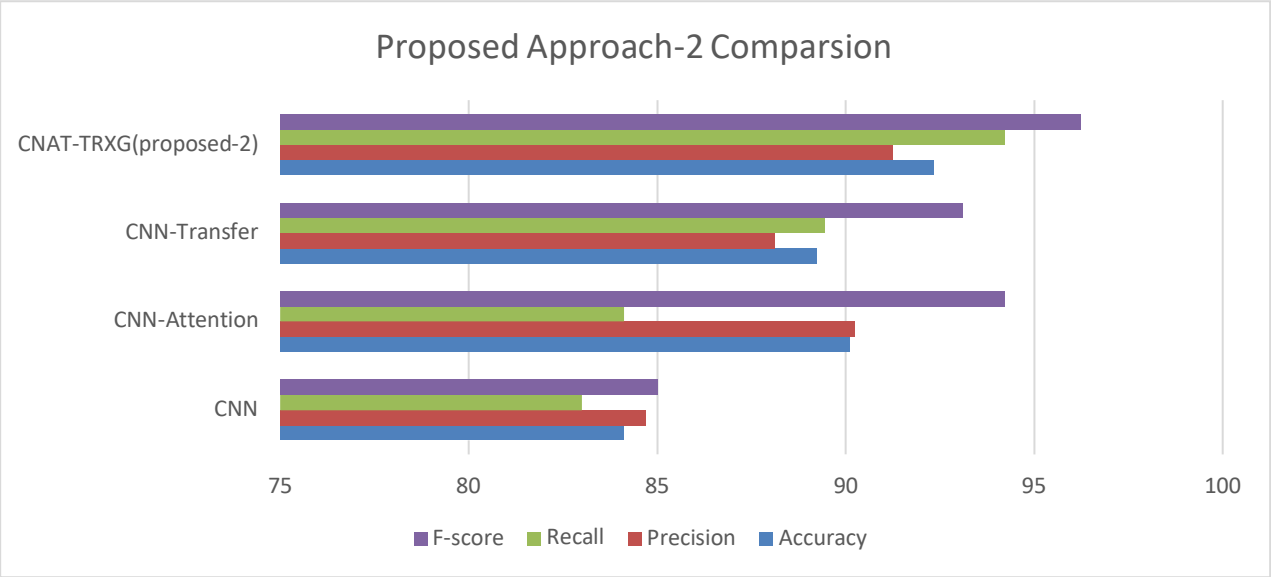


Figure 7.3: Comparison of Proposed-2 and other approaches

The gradient Boost technique uses optimization for pre-processing, allowing weak classifier models to learn progressively. The classifier is built using residual classification and gradient descent. Dementia Elderly individuals have a lower death rate than those in other age groups, particularly those above the age of seventy. Precision will improve by 2-3%, while recall will improve by increasing recall and memory efficiency by 5-6%.

7.3 Future Scope

The dataset's sample size must be increased to boost the model's accuracy. Each sample is assigned a single slice image, which diversifies the dataset and thus improves the model's robustness. To improve efficiency, the researcher will continue to fine-tune the network structure and create new algorithms. Current feature selection approaches are optimized for single-time-point images and are not easily adaptable to multiple-time-point images. Additionally, alternative methods for combining cross-sectional and longitudinal data that are more complicated than the straightforward concatenation approach used in this work should be discussed. When cross-sectional data are combined with longitudinal data, this technique should remove redundant information and can boost classification performance.

The model can be further developed to make it capable of dealing with various stages of other Brain related disorders. The dataset can be used to develop model using various upcoming machine learning technique in the future.

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