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A MULTIMODAL DETECTION AND PREDICTIVE OF THE PROGRESSION OF ALZHEIMER'S DISEASE WITH AI TECHNIQUES

Shams Abdulrahman Shukur ALQAYSI

Master's Thesis

Supervisor

Asst Prof. Dr. Ayça KURNAZ TÜRKBEN

İstanbul, 2023

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The thesis titled A MULTIMODAL DETECTION AND PREDICTIVE OF THE PROGRESSION OF ALZHEIMER’S DISEASE WITH AI TECHNIQUES prepared by SHAMS ABDULRAHMAN SHUKUR and submitted on 21/12/2023 has been **accepted unanimously** for the degree of Master of Science in Electrical and Computer Engineering.

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I hereby declare that this thesis meets all format and submission requirements of a Master’s thesis.

I hereby declare that all information data presented in this graduation project has been obtained in full accordance with academic rules and ethical conduct. I also declare all unoriginal materials and conclusions have been cited in the text and all references mentioned in the Reference List have been cited in the text, and vice versa as required by the abovementioned rules and conduct.

Shams Abdulrahman Shukur ALQAYSI

Signature

DEDICATION

I'd want to start by praising and thanking Allah, the Almighty, for giving me the knowledge, abilities, and opportunity to carry out and successfully complete my research. To my parents, I sincerely apologize. Everything wonderful that has happened to me has been a direct result of them, and everything is built on their love. The right time is now for me to express my gratitude to my sister and brother for their support and love.

PREFACE

I am incredibly appreciative to my advisor, Asst. Prof. Dr. Ayça Kurnaz TÜRKBEN, for providing me with the direction, oversight, inspiration, and assistance I need to complete my studies. My understanding and confidence have much improved as a result of his persistence, willingness to work with me, constructive criticism, and helpful recommendations. He took the time to check my work and point out my errors, which I appreciate. I'd want to thank everyone for their support, prayers, and/or insightful advice last but not least.

ABSTRACT

A MULTIMODAL DETECTION AND PREDICTIVE OF THE PROGRESSION OF ALZHEIMER’S DISEASE WITH AI TECHNIQUES

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Alzheimer's disease is one of the few sicknesses that can have its accurate diagnosis confirmed through the histopathological analysis obtained by brain harvesting or necropsy, which is only feasible after the patient has passed away. Necropsy is a procedure in which the brain is removed and examined under a microscope. This work is justified and conforms to its methodology, which aims at establishing an accurate assessment of the disease in order to enhance the quality of life of patients and the relations of those patients. The goal of this work is to improve the quality of life of patients and the relatives of patients. The relevance of this work can be easily seen when one considers how significant this subject is as well as how closely it adheres to the prevalent trend in research. In light of what was covered previously, the aim of this work is to develop an intelligent system that is predicated on machine learning algorithms and is intended to provide medical practitioners with assistance in making an accurate diagnostic of Alzheimer's disease by utilizing magnetic resonance imaging.

Keywords: ML, DL, AI, CNN, AD.

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ABBREVIATIONS

AD	:	Alzheimer's Disease
PET	:	Positron Emission Tomography
MRI	:	Magnetic Resonance Imaging
MCI	:	Mild Cognitive Impairment
HC	:	Healthy Control
DNNs	:	Deep Neural Networks
GMM	:	Gaussian Mixed Model's
ASR	:	Automated Speech Recognition
FMRI	:	Functional Magnetic Resonance Imaging
CCE	:	Cambridge Cognitive Examination

1. INTRODUCTION

This chapter deals with the main motivations for the development of this work, presenting the problem of Alzheimer's Disease and how it affects people's lives, as well as the importance of accurate diagnosis together with a brief explanation about magnetic resonance images in the identification of pathologies at the end of this chapter we will explain artificial intelligence and machine learning and how to choose a correct model.

1.1 MOTIVATION

As a result of an increase in the population's average life expectancy, dementia has become one of the most feared threats to society and has surfaced as a public health problem of immediate and preeminent concern. Before the middle of the 1960s, Alzheimer's disease (AD) was believed to be a less frequent form of pre-senile dementia than senile dementia, which was thought to be a more common condition [1]. This was in opposition to the belief that senile dementia was a more common form of dementia. It was feasible to establish similarities between senile dementia and the pronounced neuropathological characteristics of Alzheimer's disease (AD) based on works that were published at the time, and not only that, but it was recognized that there was a resemblance in the clinical picture between the pathologies [2]. As a consequence of this, in the year 1976, it was decided to consolidate the two ideas into a single one, and the name senile dementia of the Alzheimer type was selected to symbolize this combined idea. (Figure 1.1).

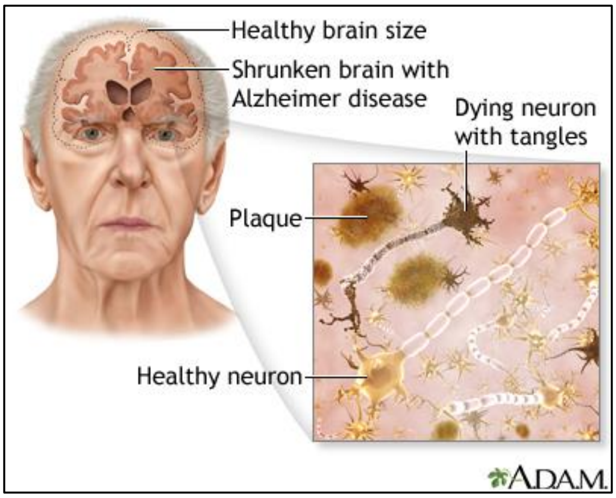

Figure 1.1: Senile Dementia of the Alzheimer Type [2].

Then, Alzheimer's disease went from a circumstance in which it was considered exceptional to the other extreme, in which it has become practically a pandemic today, claiming for itself almost all conditions that match a progressive description of brain tissue deterioration. Today, Alzheimer's disease has become practically a pandemic, claiming for itself almost all conditions that match a progressive description of brain tissue deterioration. In today's world, Alzheimer's disease has almost reached epidemic proportions, encompassing almost all conditions that fit a progressive description of brain tissue deterioration and laying claim to them as its own. This shift occurred as a consequence of Alzheimer's disease moving from a situation in which it was thought to be uncommon to the other extreme, in which it has almost reached the level of a pandemic. Specifically, the illness moved from a situation in which it was thought to be uncommon to a situation in which it has almost reached the level of a pandemic. [3]. The idea that someone could suffer from Alzheimer's disease arose over the course of time, and this idea continues to develop right up until the current day. This is due to the fact that new discoveries are made in the field of neuroscience on a consistent basis; these discoveries have an influence on and change the perspective of how diagnostic and therapeutic procedures are carried out. Since the beginning of the 21st century, there has been a growing interest in the development of more reliable procedures for the identification of Alzheimer's disease. This interest has been spurred on by the increasing prevalence of the illness. (AD). This is due to the fact that there has been a progressive increase in the prevalence of dementia in general and Alzheimer's disease in particular, which has produced difficulties in areas that deal with non-communicable illnesses. not only the sociopolitical and economic ones, but also the ones pertaining to industry and medicine. From certain vantage locations, it is possible to see both the accurate evaluation as well as the moment when it was discovered while it was still in its early phases. For some, this opinion may not have much practical sense since it would not be necessary to anticipate the diagnosis of a disease that has no cure; for another group, it could simply mean a profit opportunity for the pharmaceutical industry, since the advance of the diagnosis of AD would stimulate the consumption of medicines even earlier, increasing the demand. On the other hand, a projection that is founded on scientific evidence actually opens up the opportunity for appropriate therapeutic measures to be put into place in advance, regardless of whether or not these measures require the consumption of pharmaceuticals. This is true irrespective of whether or not the measures in question involve the consumption of pharmaceuticals. In addition to this, it enables patients and family members to better coordinate their time, which not only enables them to be prepared to deal with the impending situation, but it also enables them to search for the resources that will be required in the future. In this context, the utilization of positron emission tomography (PET), which is better suited to recognizing pharmacological changes in the brain, and magnetic resonance imaging (MRI), which is better suited to visualizing changes in brain structure, stand out as particularly helpful imaging techniques.

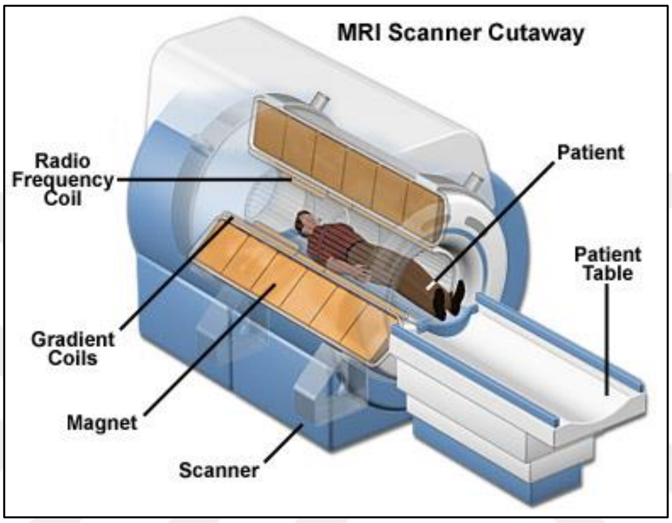

Figure 1.2: Magnetic Resonance Imaging (MRI) of the Brain.

The images that are acquired through magnetic resonance are produced through the use of a method that is not intrusive and does not involve the exposure of the patient to radiation. Due to the contrast that is provided by magnetic resonance imaging, this provides a significant advantage over other imaging tests that utilize simpler technology, such as radiography, for example. As a result of this characteristic, it is possible to differentiate the tissues and identify the structures of the tissues, which is beneficial in identifying pathologies. Moreover, the structures of the tissues can be identified. As was mentioned earlier, magnetic resonance imaging (MRI) does not use radiation; rather, the technology behind it is based on the intrinsic magnetization of the atoms in the body, specifically hydrogen atoms. This allows MRI to produce clear images without exposing the patient to any harmful particles. This investigation generates volumetric photographs in all three planes of the body (transverse, coronal, and sagittal), which indicates that it permits incisions and subsequent volumetric measurements in each of these three planes of the body. When it comes to the number of pictures of people's heads, and with the help of the findings from this investigation. Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Australian Imaging, Biomarker & Lifestyle Flagship Study of Aging (AIBL) are just two examples of global initiatives for the development of biomarkers in response to the growing impact of the disease, particularly in more developed countries with a higher average age of population. Other examples include the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Australian Imaging, Biomarker & Lifestyle Flagship Study of Aging (AIBL). The Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Australian Imaging, Biomarker, and Lifestyle Flagship Study of Aging (AIBL) are two such instances. Researchers employing methods for machine learning would benefit greatly from the wealth of longitudinal data supplied by these initiatives, which contained information on clinical and epidemiological issues. These researchers would be able to use this data to their advantage in a number of different ways. These data could be utilized to explore a broad variety of aspects, some of which include, but are not limited to, socioeconomic standing, racial or ethnic background, age, and gender, to name just a few. Work involving the identification of patterns is where machine learning is most frequently put to use. These patterns need to be discovered within the given accumulation of data, which may include photographs, writings, or quantitative data, for example. The data may also include other types of information. In order for an algorithm to be regarded as having learning capabilities, it must be able to fulfill the following requirements: 1. Recognize and gain an understanding of patterns after having a particular collection of facts displayed to them. 2. After being shown new data and having new information displayed to it, classify the new information while simultaneously preserving the knowledge it acquired from the prior collection of data, from which it identified patterns. In a nutshell, it is the responsibility of the algorithms to carry out the training process within the databases in order to identify patterns and acquire the ability to learn from them, with the ultimate aim of identifying these patterns within new data. This is done in order to achieve the objective of recognizing these patterns within new data. [4]

1.2 PROBLEM STATEMENT

Alzheimer's disease is one of the few sicknesses that can have its accurate diagnosis confirmed through the histopathological analysis obtained by brain harvesting or necropsy, which is only feasible after the patient has passed away [5]. Necropsy is a procedure in which the brain is removed and examined under a microscope. This work is justified and conforms to its methodology, which aims at establishing an accurate assessment of the disease in order to enhance the quality of life of patients and the relations of those patients. The goal of this work is to improve the quality of life of patients and the relatives of patients. The relevance of this work can be easily seen when one considers how significant this subject is as well as how closely it adheres to the prevalent trend in research [6].

1.3 OBJECTIVES

In light of what was covered previously, the aim of this work is to develop an intelligent system that is predicated on machine learning algorithms and is intended to provide medical practitioners with assistance in making an accurate diagnostic of Alzheimer's disease by utilizing magnetic resonance imaging.

As specific objectives or goals, there are:

a. Review of anatomical and physiological concepts associated to Alzheimer's disease, as well as review artificial artificial neural networks, learning machines and deep networks;
b. Develop a system for indicating slices extracted from characteristic magnetic resonance images;
c. Build a learning machine for classifying magnetic resonance images, with the ability to detect impaired regions and classify between with and without Alzheimer's disease, or more classes if they exist;
d. Develop a solution for examining and supporting the diagnosis of Alzheimer's disease.

1.4 THESIS ORGANIZATION

This work is organized in the following manner: in the section that is designated "Related Works," publications that are pertinent to the subject, tools, and strategy that was selected are presented, along with a brief description of each one. This section is located at the end of the document. Following that, the "Theoretical foundations" section presents the theoretical ideas that are necessary for developing an in-depth understanding of this work and explains how they came to be. In addition to an overview of CNN and deep networks, these theoretical concepts include a discussion of the anatomical and physiological theoretical reasons underlying Alzheimer's disease and other neurodegenerative illnesses. The proposition for this body of work is going to be presented in the following chapter. It involves constructing and validating an intelligent system that is built on learning algorithms and makes use of characteristics collected from cross-sectional portions of magnetic resonance images. This proposition is discussed in the chapter that follows the one in question. The discoveries that were obtained through the experiments will be analyzed in both a qualitative and quantifiable manner and displayed in the following chapter, which is labeled "Results." In addition to that, the outcomes will be presented. An evaluation of the scientific contribution will be presented in the very last segment, which is labeled "Conclusion;" this will be followed by a discussion of potential future research avenues.

2. RELATED WORK

2.1 INTRODUCTION

Alzheimer's disease (AD) is the most frequent form of dementia, which is the most noticeable symptom of neurodegeneration, which is the most common disease that affects older individuals. Neurodegeneration is also the most common disorder that causes cognitive decline. The current Alzheimer's disease incidence has shown a clear upward tendency in recent years, and it is projected that the number of sufferers will reach 152 million by the year 2050 [1]. This will have a significant impact on the health of the general population and will place a significant financial load on home care services and social security. Unfortunately, there is not a therapeutic option that is both effective and realistic that can be chosen at this moment. It has been demonstrated that patients can benefit in many ways from early assessment and screening for cognitive impairment, including the preservation of healthy brain activity, the postponement of irreversible brain decline, the slowdown of the development of illness, and the expansion of life expectancy [2]. In this particular setting, postponing the development of cognitive decline requires making an early assessment of mild cognitive impairment (MCI), which is the first stage of Alzheimer's disease. MCI is an abbreviation for the term "mild cognitive impairment." Research on cerebrospinal fluid, brain MRI measurements, and other techniques, along with the use of scales, are currently recognized to be conventional therapeutic approaches for the identification of Alzheimer's disease (AD). These techniques are not desirable due to the fact that not only are they time and labor demanding, but they are also expensive and insensitive to the experiences of the people being researched. When taken together, all of these limiting variables make the techniques challenging to use. The conventional techniques for identifying Alzheimer's disease (AD), such as magnetic resonance imaging (MRI), positron emission tomography (PET), and research on cerebrospinal fluid (CSF) [3,] are not suitable for comprehensive, countrywide early Alzheimer's disease screening. [Citation needed] As a consequence of this, research projects are currently being carried out in order to produce a method of identifying Alzheimer's disease that is not only less expensive but also simpler to acquire.

2.2 LITERATURE REVIEW

According to research conducted in this field, linguistic difficulties appear early on in the development of Alzheimer's disease (AD), and it has been demonstrated that capturing a subject's morphological and acoustic characteristics using automatic speech recognition technology can assist in the diagnosis of the disease [4,5,6]. The findings of research that compared individuals with Alzheimer's disease (AD) to healthy control groups (HC) have produced some very interesting conclusions. Patients with Alzheimer's disease communicate more slowly and pause more frequently in the middle of a sentence as they try to locate the appropriate word [7]. In addition to this, these patients have trouble locating and retrieving the appropriate sentence [6, 8, 9]. Numerous studies on the topic of identifying Alzheimer's disease (AD) have investigated speech-based techniques. These studies have been conducted over and over again. According to a number of studies, a substantial relationship exists between auditory measures and abnormal linguistic characteristics. Voice irregularities detected by automatic language processing have been found to be helpful in the diagnosis of Alzheimer's disease [10, 11]. Previous studies in the field of speech pathology have suggested that dementia is also associated with grammatical symptoms such as breaks in speech, sentences that have no meaning, restarts, repetitions, and unfinished statements. Using the method of logistic regression classification, Fraser, K.C. et al. [4] were successful in recovering linguistic characteristics such as meaning, nomenclature, and information. Additionally, they obtained a success rate of 91% in the AD identification test. After selecting and incorporating temporal features, auditory features, and grammatical features in addition to the AD detection, Liu, Z. et al. ultimately achieved an accuracy of 81.9% for the AD detection. This was made possible through the application of the methodology of logistic regression categorization [12], which was founded on. In addition, Sat, A., and colleagues utilized audio while participants were involved in cognitive activities in order to infer pertinent auditory characteristics. In the categorization between AD and control, they were able to acquire an accuracy of 87% [5]. Deep learning has gained widespread popularity in recent years, which has contributed to significant advancements made by neural networks in their ability to simulate human sounds. Deep neural networks (DNNs) were adapted by Hinton, G., et al. [13] in order to make them suitable for auditory modeling applications. It was necessary to take these steps in order to make the Gaussian Mixed Model's (GMM) findings more accurate. As a result of this, experts in the field of Alzheimer's disease (AD) identification through speaking have begun experimenting with a variety of different techniques to deep learning. With the assistance of a three-layer neural network and some characteristics derived from the target language, D.S. Rosas et al. [14] were able to accomplish an extraordinary success rate of 78.3% when it came to the binary categorization of data. This was an extremely impressive achievement. However, there is a significant dearth of speaking data for individuals who have Alzheimer's disease, and the implementation of neural networks only provides a marginal improvement in the accuracy of categorization. In recent studies, it has been shown that pre-trained models such as BERT [15] can incorporate a wide range of language facts such as lexical knowledge, pronunciation, grammar, semantics, and pragmatics without requiring a significant quantity of data, and generate encouraging outcomes on a variety of standard tasks. This was shown by the fact that these models achieved successful outcomes in a variety of different endeavors, which acted as a demonstration. In order to improve the level of automation achieved by analysis, a pre-trained automated speech recognition (ASR) model has the capability of producing aural embeddings in addition to obtaining a textual representation of spoken words. Because of this, the model is able to comprehend spoken language more effectively. Toth, L. and associates [16] were able to partition the incoming signal and recognize it phonetically by using an ASR model that was based on a one-of-a-kind convolutional deep neural network. This allowed the researchers to accomplish their goal. The researchers were able to isolate auditory characteristics like speaking rate, latency, and hesitation rate as a result of this, which they then used. According to the findings of some recent studies, the technique known as "deep learning" is currently the one that is utilized the most frequently in the diagnosis of Alzheimer's disease. There have also been some review articles written on AD detection that have been published. One example is the in-depth investigation that Inés Vigo et al. [17] conducted on speech-based AD detection and categorization. In spite of the fact that deep learning strategies have shown extraordinary success in AD detection, the vast majority of categorization strategies continue to rely on more conventional machine learning approaches, which are less effective. This is the case despite the fact that these techniques have demonstrated success. Kraepelin described a subgroup of cases in the ninth edition of Clinical Psychiatry: A Textbook for Students and Physicians, which was released in 1910. These cases were defined by the most severe form of starvation. The presence of an abnormally high number of plaques, the death of nearly one-third of the cerebral cortex, and the replacement of these areas with distinct bursts of colored neurofibrils were the defining characteristics of these instances. Kraepelin was the one who first referred to the ailment as "Alzheimer's disease," and he did so during a time when the clinical description of Alzheimer's disease (AD) was not yet completely clear [9]. Additionally, it is believed that Kraepelin was the first person to use the name "Alzheimer's disease." Credible explanations for the clinical criteria of Alzheimer's disease came to emerge after a period of time that spanned more than a century. In 1906, a German doctor by the name of Alois Alzheimer described what is thought to be the first case of Auguste Deter disease, despite the fact that its initial classification was not quite clear. Despite this, it is widely accepted that Alzheimer's description is accurate. [10] Both Dr. Alois Alzheimer's and Pros kin’s explanations of Alzheimer's disease, which were published in 1907 and 1909, respectively, made reference to senile plaques and neurofibrillary tangles as two of the disease's hallmark pathological features. Arteriosclerosis was thought to be a factor in the patient's prognosis; however, when a physical investigation of the patient's brain was conducted, substantial indications of arteriosclerosis were not discovered to present in the patient's brain. This led to the belief that arteriosclerosis was not a factor in the patient's prognosis. Because of this, it became clear that arteriosclerosis was not a contributing element in the patient's future outlook. German scientists from the University of Munich and the Max Planck Institute for Neurobiology in Martinized came to this conclusion after conducting their research. 1998 was the year that [11] made the groundbreaking discovery that neurofibrillary spasms and amyloid deposits exist. Since that time, this investigation has come to be recognized as the very first incidence of Alzheimer's disease that was ever documented. More to the point, the patient in question meets all of the diagnostic criteria for Alzheimer's disease, according to the most recent understanding of the subject matter. In 1997, Dr. Gerber and his coworkers at the Max Planck Institute of Neurobiology investigated pathological sections of F. Johan's brain, which had been well conserved despite the fact that F. Johan was over 90 years old. The examination was carried out because F. Johan's brain had been kept in a cryogenic state. The conclusions of this research represented the second documented instance of AD since the beginning of the documentation process. Following a thorough investigation, it was found that the incisions held a sizeable quantity of amyloid plaques within their confines. In light of what we now know, it ought to be possible to conduct mutational research using tissue samples taken from brains that have been preserved for a considerable amount of time. It has been one hundred years since Dr. Alzheimer made his important discovery, and his work has now been validated for the second time. This is in acknowledgment of the fact that it has been one hundred years. depicts the differences that can be observed in a brain that is free of Alzheimer's disease in comparison to a brain that is affected by the disease. The United States now rates Alzheimer's disease as the sixth largest cause of mortality, moving it up one spot from its previous position. According to the conclusions of the most recent study, this condition may be immediately behind ischemic heart disease and cancer as the third largest cause of mortality in individuals over the age of 13. [13] Unquestionably, one of the most essential goals is to acquire the ability to foresee the later phases of Alzheimer's disease and to intervene in order to stop the development of the sickness. In order to establish a diagnostic of Alzheimer's disease, numerous medical evaluations and the collection of a significant amount of information that is both complex and multifaceted are necessary. To put this into perspective, the process of physically comparing, visualizing, and analyzing data is one that is not only challenging but also time-consuming. This is due to the fact that there is such a vast selection of medical procedures that can be performed. The correct categorization of MRI photographs is an effective technique for effectively anticipating brain sicknesses; however, this can be a challenging work to complete correctly. New approaches to the early detection of Alzheimer's disease (AD) have been suggested, some of which include the implementation of label dissemination and the precise categorization of brain MRI photographs. Alzheimer's disease (AD) is the most common form of dementia. Imaging approaches of the brain offer a non-invasive method of visualizing elements of the structure and function of the brain, as well as the reaction of the brain to various pharmaceuticals [18]. Imaging methods can be broadly categorized into two principal groups: structural imaging and functional imaging [19]. Neurons, connections, glial cells, and other elements of the brain's anatomy can all be discerned through the use of structural brain imaging techniques. These techniques also allow for the visualization of other brain components. [20] Functional magnetic resonance imaging, also known as MRI, is a technique that can be used to gain knowledge about the processes that occur in the brain. Diagnostic MRI procedures such as the ones listed below are employed frequently for individuals diagnosed with Alzheimer's disease: Magnetic Resonance Imaging (MRI): This imaging method makes use of radio frequencies and magnetic fields in order to generate high-quality and high-resolution pictures of various portions of the brain in both two and three dimensions. These images can be used for a variety of diagnostic purposes. There will be no production of X-rays or radioactive tracers, both of which have the capacity to cause damage if they are produced in sufficient quantities. A structural MRI is the form of magnetic resonance imaging (MRI) that is employed in the majority of diagnoses of Alzheimer's disease. In order to detect early warning symptoms of brain degeneration, one type of MRI takes measurements of the living brain while it is still functioning normally. (Loss of tissue, cells, neurons, etc.). The characteristic disintegration of the brain's structure that is associated with Alzheimer's disease can be found in [21, 22]. The most accurate approach to diagnosing brain shrinkage is to use structural magnetic resonance imaging (MRI), like the one presented in Figure 3. Figure 4 is an illustration of functional Magnetic Resonance Imaging (fMRI), which is another prevalent method for identifying the structure of the human brain and evaluating the primary visual cortex. This technique is shown in action in the figure. Performing functional magnetic resonance imaging, also known as fMRI, on a patient can yield extremely helpful new understandings regarding the activity and function of the brain. Techniques like arterial Blood Oxygenation Level Dependent (BOLD) differences and spin-labelling (ASL), which are used in functional magnetic resonance imaging (fMRI), are responsive to the cerebral metabolic rate of oxygen utilization as well as cerebral blood flow. (CBF). [23] illustrates the midline temporal activation of the same control group, [24] depicts the regions of the brain that are active in elderly people who have Alzheimer's disease or who serve as controls. Figure 5b [23] and Figure 5a [24], in their corresponding positions. The process by which blood is transported throughout the body [27]. In spite of this, the method is still employed on a frequent basis for the purpose of conducting cognitive process evaluations. It has been demonstrated through a number of studies that SPECT can provide accurate measurements of cerebral circulation when used in the evaluation of individuals suffering from Alzheimer's disease. [Citation needed] [Citation needed] In recent research, the information from 116 individual Alzheimer's disease patients was analyzed. [28] Of those individuals, sixty-seven revealed indications of other brain illnesses, twenty-six displayed evidence of dementia that was not caused by Alzheimer's disease, and twenty-three were classified as age-matched controls. The purpose of this particular line of research was to look into the potential links that exist between CSF-tau, brain proteins, and cerebral circulation. During the course of this research, patients suffering from dementia were kept separate from the other participants. The Mini-

Mental State Examination (MMSE), the Cambridge Cognitive Examination (CCE), and a functional scoring measure on clinical dementia were utilized in order to classify the subjects' cognitive abilities and functional conditions. The results of the 99mTc-HMPAO SPECT imaging were discovered to have an association with the amount of tau protein detected in the cerebrospinal fluid (CSF). The evaluation was able to be more accurate as a result of the characteristics that were selected, and this contributed to ensuring that the research was conducted in a respectable manner. Other research on AD patients has been done, and that research has revealed substantial correlations between the results of cognitive evaluations and the results of SPECT [29]. These connections were discovered in studies that were performed on AD patients. These investigations were carried out on communities of Alzheimer's disease individuals. Research that was summarized in [29] indicates that SPECT is a more effective technique to use than CSF-tau protein when it comes to identifying Alzheimer's disease. This conclusion was reached based on the findings of a study that was conducted. which is an unprocessed photograph of arterial spin labeling flow [30], depicts a patient who was 70 years old at the time of their examination. It is not recommended that the basal portion of the arterial branch be used in this kind of research because the time it takes for arterial blood to travel through the branch is so exceedingly slow. This is due to the fact that the vascular branch is located in the basal section. Positron emission tomography, or PET for short, is a type of imaging technology that monitors the distribution of radioactive particles within the brain in order to conduct research on brain activity. This research can be done in order to learn more about how the brain works. Radiotracers are an indispensable part of the PET testing technique. that amyloid and fluorodeoxyglucose are the two tracers that are employed in the detection of Alzheimer's disease the most frequently. Both of these tracers can be found in the body. In addition to having an effect on visual, auditory, cognitive, and memorization processes, it was found that the radioligands C-PMP and C-MP4A each had an effect on acetylcholinesterase. This was one of the discoveries that came about as a result of the research that was conducted. The findings led the researchers to the conclusion that individuals afflicted with Alzheimer's disease possessed diminished frontal regions [35]. People who previously suffered from moderate cognitive impairment (MCI) and subsequently contracted Alzheimer's disease displayed the same pattern of cognitive decline as the illness progressed in their bodies. Patients who had been identified with Alzheimer's disease as well as those who were progressing with other forms of dementia were separated from the rest of the patients. Patients identified with Alzheimer's disease who were given treatment with A-beta amyloid-specific agonists (Pittsburgh compound B 11C-PIB) demonstrated a greater degree of improvement [36]. When compared to individuals who had been identified with frontotemporal lobar degeneration (FTLD) or Parkinson's disease, these results were found to be significantly higher. (PD). On PET scans, the majority of Alzheimer's disease patients showed signs of hypoperfusion in the temporal and posterior regions of the brain. On the other hand, neuroreceptors and FP-CIT SPECT are approaches that are preferred because they make it possible for researchers to see distinctions in the nigrostriatal dopaminergic neurons. Because it has a high frequency of false-positive discoveries that contribute nothing of value to MRI, SPECT is challenging to use in clinical settings. This is because of its high occurrence. For the purpose of determining the extent of water diffusion, an imaging technique known as FP-CIT SPECT was applied. The identification of white matter in the brain, the determination of its orientation, and the measurement of its unbalance can all be accomplished through the use of this technique. [37] Investigations into the microscale distinctions in the atomic structures of various kinds of water are currently being carried out as part of research projects. Diffusion tensor imaging (DTI) has not yet been incorporated as a dependable methodology for the study of CSF biomarkers [38], despite the substantial amount of research that has been conducted into the determination of CSF-tau biomarker and amyloid levels.

3. MATERIALS AND METHODS

Alzheimer's disease is a neurodegenerative disease represented by cerebral dementia, and thanks to the progress of medical technology scientists have made progress in the early detection of this disease, and the exploration of diseases that affect the brain, so the field of neuroscience experienced a scientific revolution. The objective of this chapter is to identify the disease of interest to us, Alzheimer's disease, to deeply understand the mechanism of Alzheimer's disease. In the first place we focused on the anatomical part and the functionality of the brain, and also for a better understanding of the stages of the disease. In the second part we present the different modalities of magnetic resonance imaging MRI which provides images on sections of the brain presents the three main regions of the brain and especially the gray matter which is used for the development of the disease that we need, finally we ended with a conclusion.

3.1 UNDERSTANDING THE BRAIN [1]

Philosophically, the brain is the organ that feels, thinks and operates. It is therefore the organ that gives meaning to existence.

Sociologically, the brain is the conductor of the whole body, it manages it as well as itself. He is responsible for our attitudes, and therefore for our interactions with the other individuals who make up society.

Scientifically, the brain is an immense task because it still conceals mysteries in its natural and pathological functioning and in its adaptive capacities. It is now vital to pierce the mechanisms of the genesis of our intellectual abilities, our emotions, and the motor behaviors that are the consequence. [1].

Finally, the current medical task is to understand the diseased brain in the context of neurological diseases (Alzheimer's, Parkinson's, ALS (amyotrophic lateral sclerosis), multiple sclerosis, epilepsy, etc.) or psychiatric diseases (depression, schizophrenia, autism, TOC, etc.) with a view to developing the treatments of tomorrow.

3.1.1 Central Nervous System CNS and its Main Elements

The central nervous system (CNS) includes the brain and the spinal cord.

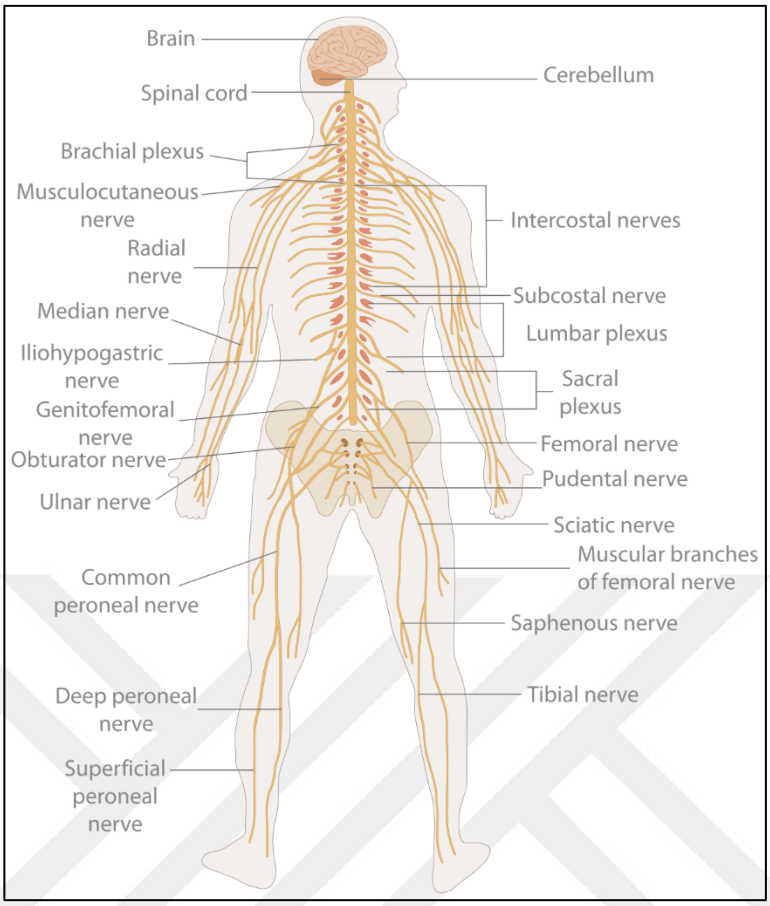

Figure 3.1: The Nervous System [2].

3.1.2 Brain

The brain controls the majority of bodily functions, including perception, movement, feeling, thought, speech, and memory. And it is made up of 3 main sections: the cerebrum, the cerebellum and the brainstem.

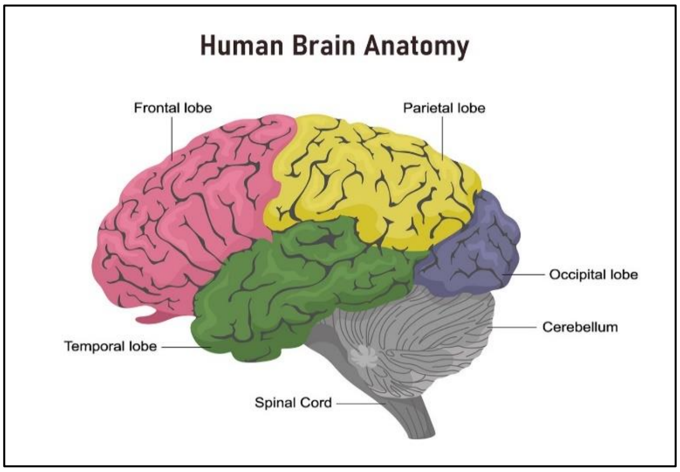

Figure 3.2: The Main Components of the Brain [3].

3.1.3 Brain

The term "brain" is used more commonly than "encephalon" when referring to the organ in common usage. This is because the cerebrum is the most significant component of the brain. The cerebral cortex, which is more commonly referred to as the brain, is really divided into two portions that are referred to, respectively, as the left and right hemispheres. The corpus callosum is a network of nerve fibers that joins the two sides of the brain together to form what is known as the cerebral hemispheres. The left side of the body is controlled by the hemisphere of the brain called the right hemisphere, while the right side of the body is controlled by the hemisphere called the left hemisphere. One side of the body is controlled by each hemisphere of the brain, which are located on opposite sides of the body.

3.1.4 Cerebellum

The cerebellum sits at the base of the brain, behind the cerebrum. It controls movement, posture, balance, and other complicated motions and is divided into two halves (hemispheres). It's made up of both white and gray matter.

a. Gray matter:

Corresponding to the body of nerve cells, cover the hemispheres and the cerebellum (cortex) and are also found disseminated in the form of nuclei in the white matter.

b. White matter:

Corresponding to the nerve fibers (axons and dendrites) covered with a myelin sheath, is located below the cerebral cortex and around the gray nuclei. [A]

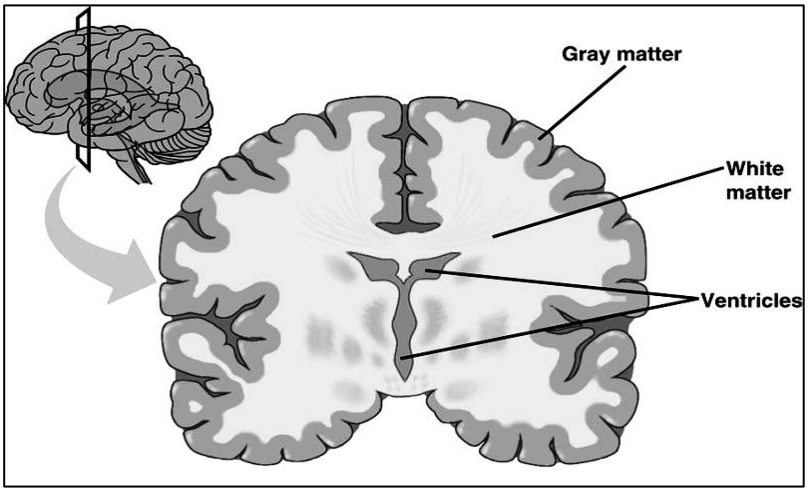

Figure 3.3: A Transverse Plane Representing Gray and White Matter [5].

3.1.5 Brain Stem [6]

The brainstem is a bundle of nervous tissue located at the base of the brain. It connects the brain and the cerebellum to the spinal cord, and it circulates messages between the other parts of the brain and the rest of the body and it controls breathing, body temperature, blood pressure, heart rate, hunger and thirst, digestion of food [5].

3.1.6 Cerebrospinal Fluid

Cerebrospinal fluid (CSF) is a clear, watery liquid that surrounds and protects the brain and spinal cord and serves as their cushion. The CSF also carries nutrients from the blood to the brain and removes waste products. CSF circulates in cavities called ventricles and on the surface of the brain and spinal cord [6].

3.1.7 The Spinal Cord [6]

Attaches to the brain at the brainstem and is protected by the vertebrae, which form the spine. Nerves emerge from the spinal cord to innervate both sides of the body. The spinal cord carries nerve signals, allowing them to travel back and forth between the brain and nerves throughout the rest of the body.

3.1.8 Brain at the Cellular Level

The neuron is a cell, just like a liver or heart cell, but its main task is not the same, since it is mainly responsible for transmitting safe information from long distances. Neurons create a complex network of connections, which allows information to be redirected, serially or in parallel, in different cortical areas. Messages are transferred in two forms: electrically within the neuron and, more commonly, chemically from one neuron to another. [7].

3.2 THE ARCHITECTURE OF THE NEURON

Input information from upstream neurons is passed through the dendrites. It leaves the neuron via the axon to be transferred to the output neurons. A neuron maintains contact with many other nerve cells, these contacts are called " synapses ". (There are 10,000 connections for a single nerve cell). These substances, called "neurotransmitters", if they are released in larger quantities, they will cause various disorders.

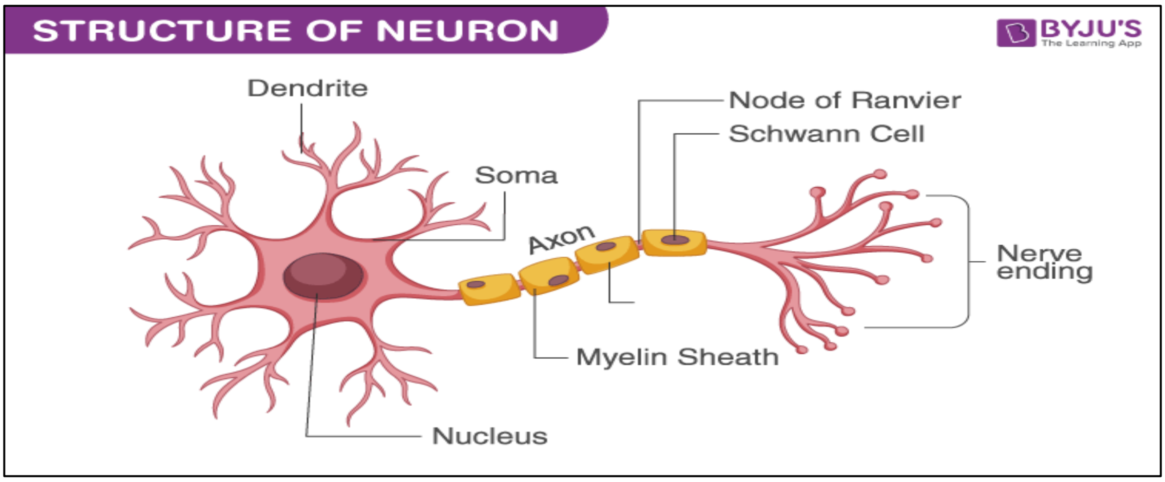

Figure 3.4: Nerve Cell [8].

3.2.1 The Different Types of Neurons

For a more details on the neurons, we can distinguish the neurons according to these types, and for this there are the following types:

a. Anatomical distinction (3 examples):

i. Pyramidal cells are found in the matter gray, or cortex cerebral.

ii. The neurons in stars are also found in the cerebral cortex.

iii. THE Purkinje cells are cells with very numerous and diffuse ramifications that are found exclusively in the cerebellum.

b. Distinction according to function:

i. sensory neurons are directly connected to the sense organs and aero responsible for conveying sensory information (we also say "ascending information") towards the brain.

ii. motor neurons or motor neurons are responsible for transmitting orders from the brain (also known as “downward information”) in the direction of the muscles.

iii. Interneurons are represented by all neurons which are neither sensory nor motor but which make the junction between these two types of neurons.

3.2.2 Support Cells

The neuronal architecture is reinforced by a set of cells known as glial cells or support cells; we list the main components below:

a. Astrocytes are responsible for controlling the concentration of several substances in the cellular fluid. in addition, they also play an important role in helping neurons in information processing.
b. Schwann cells and oligodendrocytes are single cells that form an insulating layer, made of myelin, which surrounds the nerve fibers. This layer of biological protection optimizes the speed at which data is transferred along the axon.
c. Microglia is a kind of cleaning cell that rids the extracellular space of all the cellular waste that surrounds it. [9].

3.2.3 Neurodegenerative Diseases

neurodegeneration" is composed of the prefix "neuro", which designates nerve cells, or neurons, and the radical "degeneration", which designates the biological process of progressive loss of structures, which indicates dysfunctions. Otherwise, a neurodegenerative disease is a pathological situation affecting neurons, leading to their death. Each of these functions such as language, learning, decision-making, motor skills, the senses… are governed by a specific set of neurons. When, in an MND, a group of neurons is selectively destroyed, this causes a wide variety of symptoms such as memory loss, muscle paralysis, mental disorders, etc. [10].

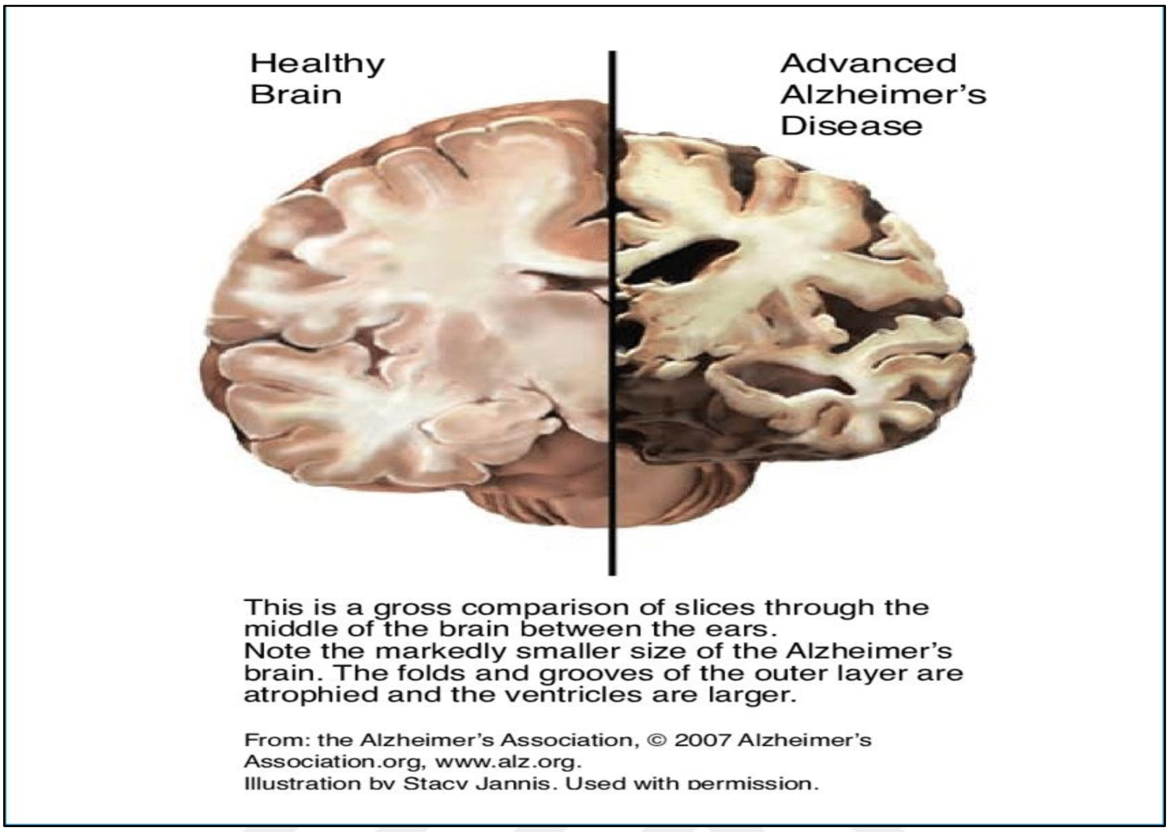

Figure 3.5: Comparison of a Healthy Brain and the Brain of a Patient with Alzheimer's Disease [11].

Figure 3.5 represents cerebral dementia in Alzheimer's disease (right brain). Neuronal damage causes the cerebral cortex and hippocampus to shrink and the lateral ventricles to widen, causing various symptoms [11].

3.3 MECHANISMS OF MND NEURON DEATH

The causes of the appearance of MND are not well known, but the mechanism of cell death has been the subject of much research in humans and in animal samples of these pathologies. However, many of the proposed mechanisms are still widely debated within the scientific community. This is mainly due to the incredible diversity of types of neurons affected, which can differ in morphology, location, role or neurochemical composition. [12].

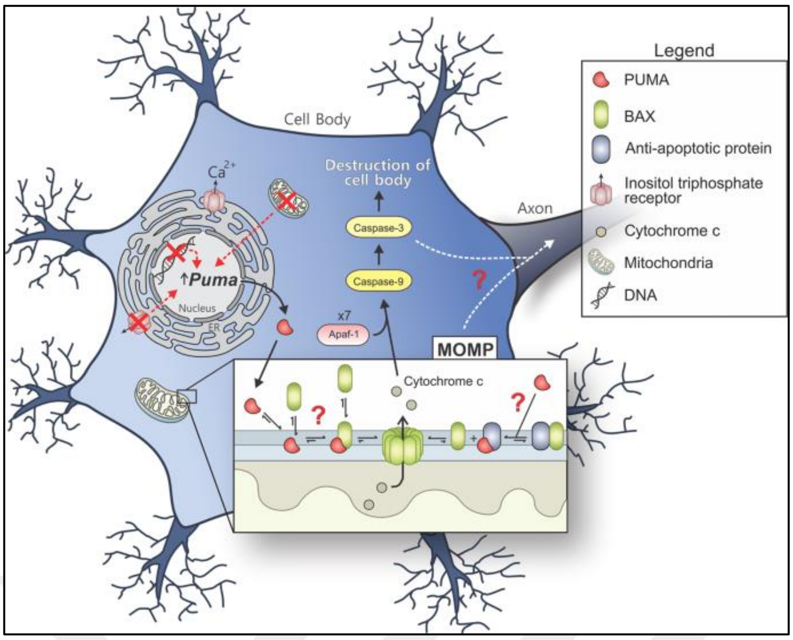

Figure 3.6: Mechanisms of Neuronal Cell Death [13].

Although these disorders are clearly heterogeneous, there are common pathophysiological mechanisms. The most common mechanism in almost all MNDs is toxic protein aggregation. The human genome encodes nearly 30,000 proteins, each of which has a unique form or several biological functions. After their synthesis, these proteins take on a unique native 3D shape that allows them to perform their biological functions. Under certain circumstances, some proteins show an abnormal shape due to misfolding. And under physiological circumstances, these misfolded proteins are either corrected by chaperones or degraded and eliminated by the ubiquitin-proteasome system or the phagosome-lysosome system (autophagy). Several changes such as age, genetic mutations, changes in pH or intracellular environment, oxidative stress or heavy metals, can cause an increase in the concentration of misfolded proteins. [14]

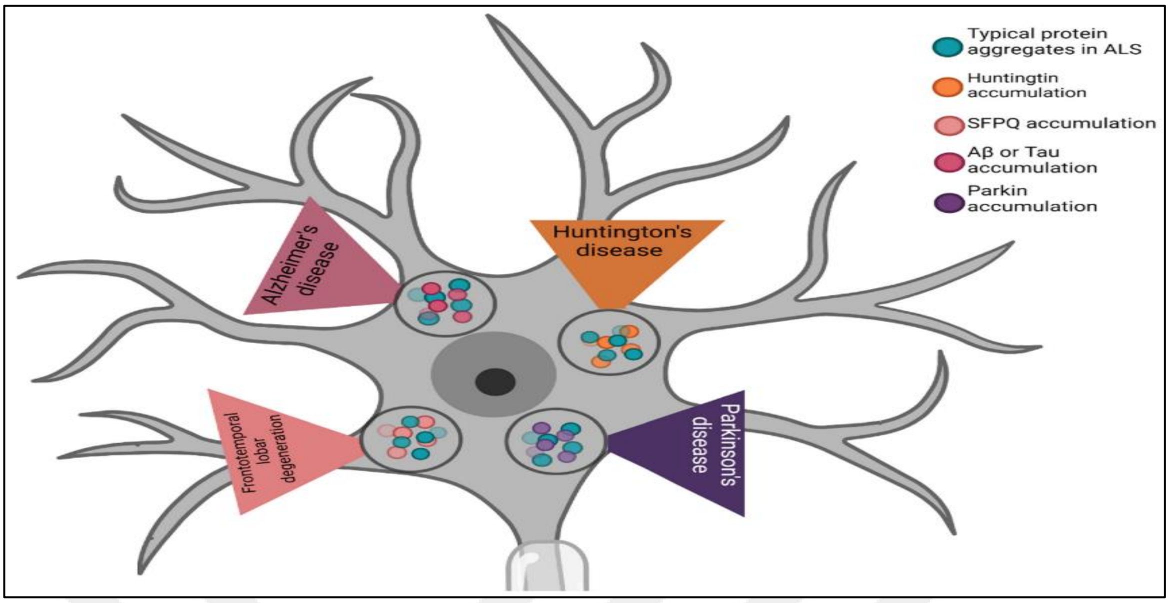

Figure 3.7: Mechanisms of Formation of Protein Aggregates in Mnds.

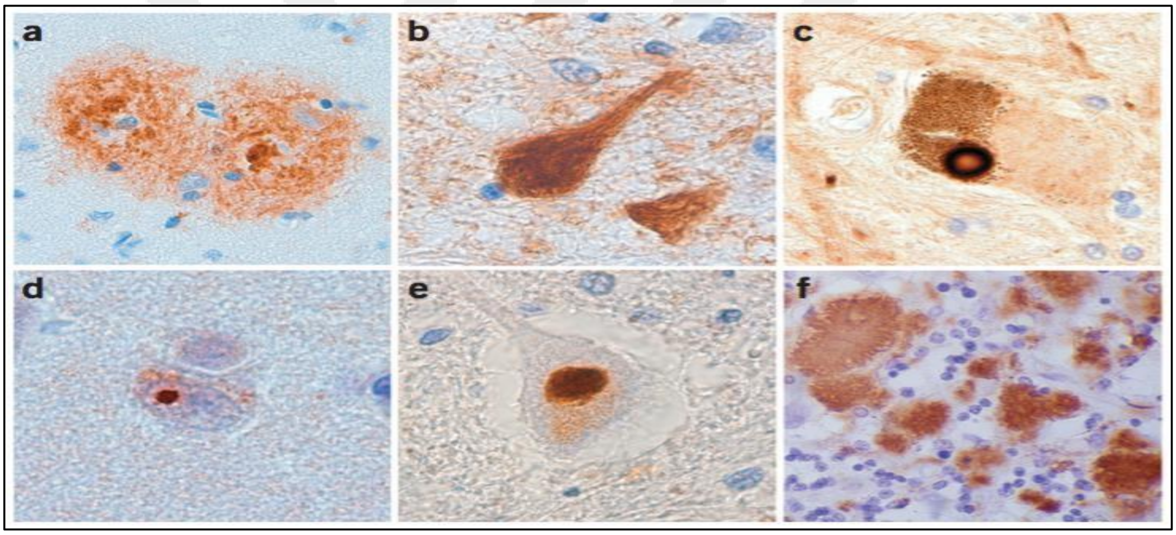

Figure 3.8: Aggregated Proteins in Neurodegenerative Diseases[13].

Figure 3.8 represents the protein aggregates on neurodegenerative pathologies, knowing that (a) presented a senile plaque in the cortex of a patient.

Alzheimer, and (b) we show the Tau protein aggregates in the hippocampus of a patient with frontotemporal degeneration, then the image (c) represents the Lewy body in the substantia nigra of a Parkinsonian patient. Next image (d) shows the intranuclear inclusion of polyglutamine in the cortex of a patient with chorea of

Huntington, and image (e) depicts ubiquitin inclusion in the spinal cord of a patient with amyotrophic lateral sclerosis. Finally, the last image (f) shows the Prep protein in the cerebellum of a patient with Creutzfeldt-Jakob disease.

3.4 ALZHEIMER'S DISEASE [22]

The brain is made up of several parts that have specific roles, while remaining very complementary to each other.

3.4.1 The Lobes of the Brain

The most important portions of the brain are located in the two sides of the cerebrum, which are also referred to as the hemispheres. Each side of the brain, more notably the right and left sides, has their own individual hemisphere. Commonly used terms for these kinds of mental processes include the "right brain" and the "left brain." The frontal lobe, parietal lobe, temporal lobe, and occipital lobe are the four separate regions that make up each hemisphere of the brain. The occipital lobe is located at the back of the head. The term "lobes" refers to the collection of these different lobes. These lobes are in charge of all of the mental processes, including voluntary movement, cognition, learning, and memory, as well as a number of other functions.The following is a list of the key responsibilities that fall under each lobe's purview [1]:

a. The frontal lobes are the regions of the brain that are in charge of a wide variety of functions, such as speech, language, logic, memory, decision making, personality, judgment, and action. The left frontal lobe is responsible for controlling the right side of the body, whereas the right frontal lobe is in charge of the control of the left side of the body.
b. Reading, emotional sensitivity, and spatial awareness are only few of the functions that are controlled by the parietal lobes of the brain. The right parietal lobe is responsible for managing left-sided sensitivities, whereas the left parietal lobe is responsible for controlling right-sided sensitivities. Again, the right parietal lobe is responsible for controlling left-sided sensitivities.
c. The occipital lobes, which are the regions of the brain that are in charge of vision
d. The temporal lobes of the brain, which are in charge of things like language, memory, and emotion.

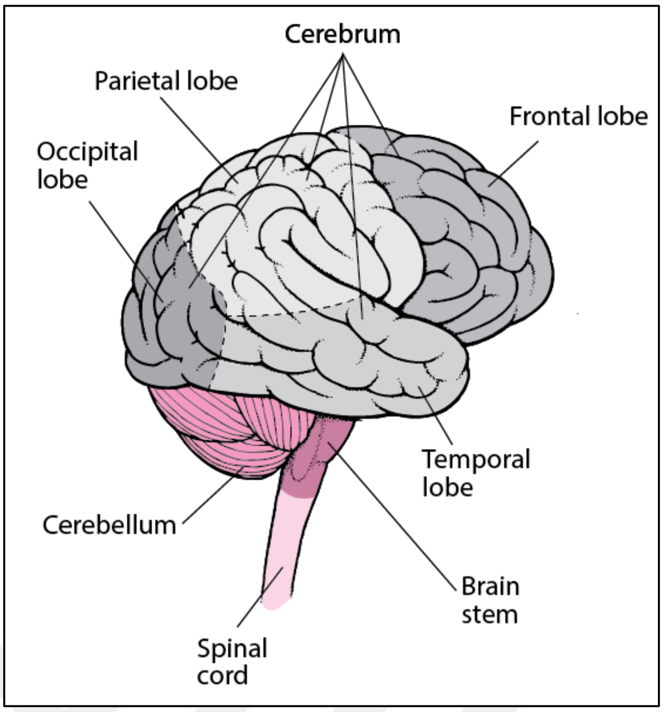

Figure 3.9: The Brain Lobes [16].

Alzheimer's disease is a frontotemporal lobar degeneration (DLFT), there are several clinical syndromes grouped together in DLFT:

a. the behavioral variant (FTD),
b. primary progressive non fluent aphasia (PFNA),
c. semantic dementia (SD) and
d. progressive logogenic aphasia (PLPA).

There are also three main types of pathological lesions underlying FTLDs:

Inclusions of the tau protein (Tubulin-associated Unit), or tauopathies, are observed in nearly 30% of cases of DLFT (DLFT-TAU). TAR DNA-binding protein 43 (TDP-43) [DLFT-TDP] inclusions are the most common, occurring in 60% of cases. They are classified into 4 subtypes, A to D, depending on their density and location in the cortical layers, inclusions of the FUS protein (Fused in Sarcoma) and proteins of the FET family (FUS, EWS, TAF15) are in the minority and found in 10% of cases (DLFT-FUS).

TDP-43 (TAR DNA binding protein 43) and FUS (Fused in liposarcoma) are two pathology-related proteins that share similarities in structure and function, implying a mutual mechanism of toxicity. Both TDP-43 and FUS are recruited into the GS (Stress Granule) under stressful conditions. The mechanism of toxicity of FUS differs from that of TDP-43 and does not appear to involve a loss of function in the stress response. [17].

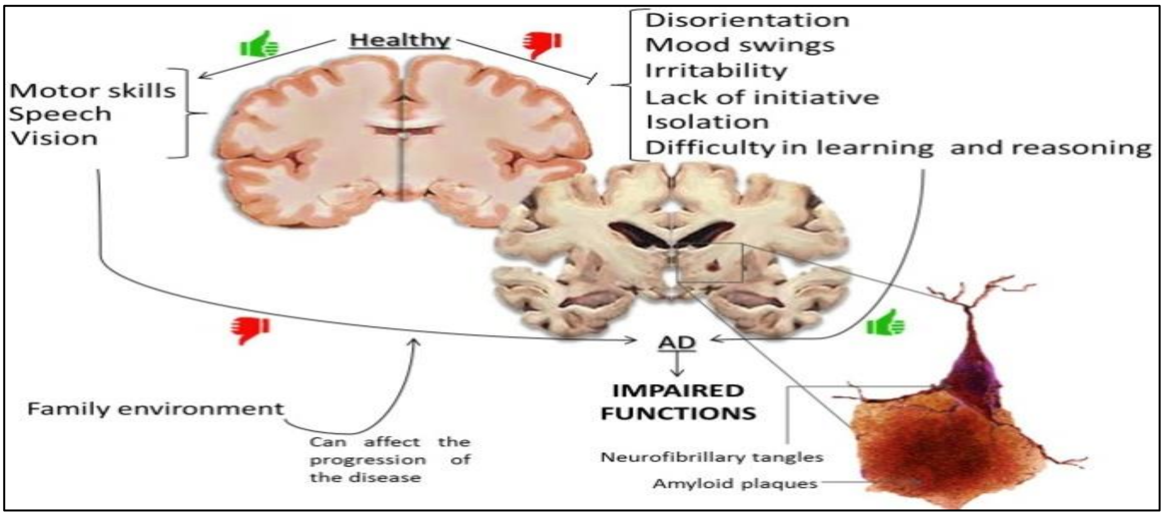

Figure 3.10: Molecular and Histopathological Characteristics of Dementias [18].

Because of pathological heterogeneity, only correlational studies of diagnoses can be informative, while clinical studies are necessarily discordant. An autopsy study [19] demonstrated that patients with some diagnosis of FTLD, tau negative or tau positive, compared to patients with Alzheimer's disease, had lower T-tau concentrations and a T-tau ratio /A β1-42 significantly lower and Aβ1-42 assays significantly higher, but the concentration levels in this study, the T-tau/A β-42 ratio was more discriminating than the T-tau assay by him -even to differentiate DLFT patients from patients with Alzheimer's disease, with a sensitivity of 79% and a specificity of 97%.

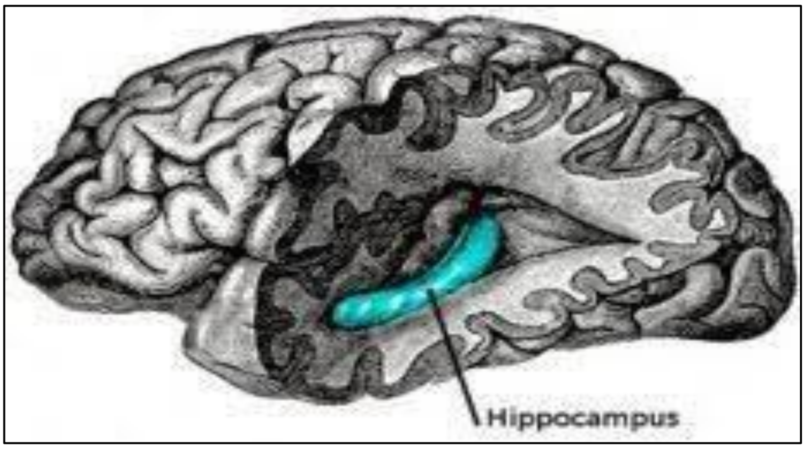

Figure 3.11: Memory Part of the Brain [20].

We follow here the proposal of the working groups. [21] to use this term to include diagnostic indications obtained from all paraclinical methods, whether biological in the restricted sense of the term (i.e., the analysis of biological fluids) or from brain imaging. In this US study [21], the biomarkers are classified according to the putative pathophysiology of AD, so that the measurement of the peptide AT beta 1-42 and testing for amyloid ligand uptake in PET scans are collectively classified as markers of the pathogenic process of amyloid accumulation (thought to occur prior to neuronal loss), testing for increased tau in CSF is classified with imaging detection of hypometabolism or atrophy of the cerebral cortex, as they would all reflect synaptic destruction and neuronal loss (assumed to follow amylogenesis). although this classification is less obvious, Dubois et al [3] already clearly suggested the use of these biomarkers, even if they were limited to "hippocampal" Alzheimer's disease. Current markers, generally used in clinical research or in academic centers, consist mainly of the determination in CSF of the level of amyloid A beta 1-42 peptide, which is determined to be below the norm (the A beta 1-40 or even many other products of enzymatic cleavage of the APP protein are rarely determined), and the level of tau and phospho-tau proteins, which is determined to be above the norm. As mentioned earlier, these tests have yet to be standardized. The Innocent method combines the phospho-tau 181 isoform test and the IATI index (ratio between the A beta 1-42 measured and the A beta 1-42 estimated from the tau value) to obtain a measurement of neuronal lysis and a measurement of pathological amelogenesis. In a large prospective study, the sensitivity and specificity of these measures were on the order of 80% and 70%, respectively, for predicting the conversion of MCI to AD. In addition to a generalized standardization of these tests, it is likely that other biomarkers exploring other metabolic pathways, in particular those measured in plasma, will be developed. Genetic markers are summarized clinically in the search for mutations in the APP, presenilin 1 and 2 genes, depending on the background of suspected familial Alzheimer's disease. And Apo E genotyping in search of an epsilon 4 heterozygous or homozygous genotype can provide arguments in favor of AD-ICD. [21]. At the proven stage of AD dementia, there is a solid consensus to identify positive arguments in favor of the diagnosis, even for mild degrees of dementia (CDR score = 1, is one of the most useful scales to quantify the severity of AD). cognitive deficits in dementia). Dementia, in the contemporary sense of the term, consists, at the end of a process of progressive aggravation, of a loss of cognitive autonomy and adaptation of behavior severe enough to affect all aspects of the daily life of the patient, life professional, family, social.

3.5 ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI) aims to create intelligent entities. In this sense, there is a pursuit of this ability of which humans are masters, to solve problems. "The ability to solve problems" is also a definition of intelligence that we find regularly. There is no consensus definition, although researchers have attempted to formally define intelligence. The human tries to replicate his intelligence to be able to automate certain tasks. It is important to note that there is a strong difference between AI and machine learning. Machine learning is a form of AI that consists of a system that improves through experience whereas AI can be a simple set of rules and heuristics.

3.5.1 What is Artificial Intelligence

Artificial intelligence (AI) is a field of computer science and mathematics bringing together set of algorithmic techniques and theories for making machines imitating human intelligence. Its purpose is to reproduce intelligence in order to be able to solve complex problems. This objective requires the modeling of human intelligence as a phenomenon, as could be done in the field of physics, chemistry or biology. Artificial intelligence is a growing field, finding its theory and its applications in many fields, such as probability theory, neuroscience, robotics, game theory, health and transport.

Artificial intelligence is generally classified as strong or weak.

a. Strong Claim's to develop a machine with cognitive capabilities close to humans. This machine would be able to find only uno solution to a problem which is still unknown to him. Although an active research topic, strong AI does not currently exist.
b. Weak AI, on the other hand, consists of developing machines to respond to a specific problem. Then has data and human assistance, and must be able to simulate human reasoning, without understanding the phenomena involved work.

The field of artificial intelligence it is split into several nested sub-domains (presented figure 1). Machine learning is a subfield of artificial intelligence consisting in learning by experience or by a database of implicit rules to respond to a given problem. This area is specifically oriented around the statistical analysis of training data. In the context of machine learning, we will see that there are many algorithms using various mathematical models. The neural network is one of these models, certainly the most widespread and the one used in the most diverse fields. Deep learning is a set of techniques that take advantage of neural networks to solve complex problems. These techniques are widely used, especially in the field image processing, time series processing (recognition voice...).

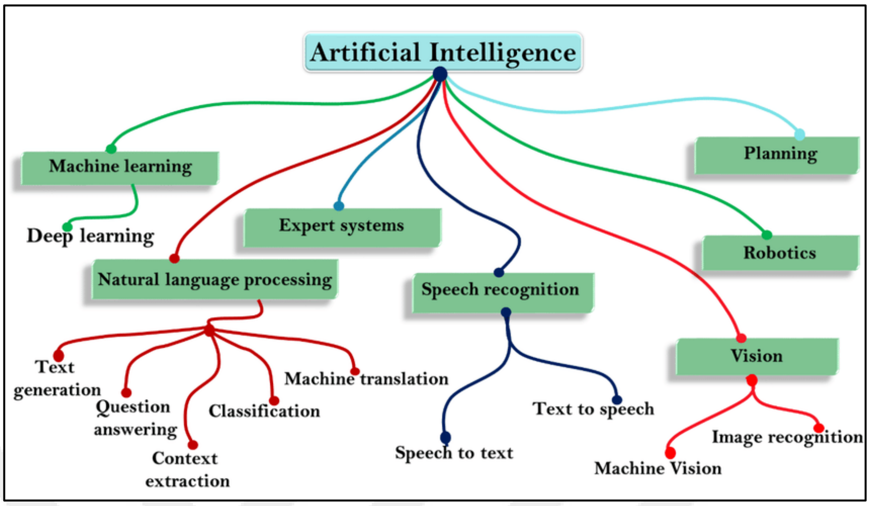

Figure 3.12: Diagram of Decomposition of the Field of Artificial Intelligence and its Sub-Fields.

All artificial intelligence techniques are not necessarily learning automatic. In particular, it is possible to provide the prediction rules directly to the machine.as a series of conditions" if then ". These systems, called expert systems, were widely used during the 1980s to solve given tasks with great precision. In this article we will not be interested in these expert systems and will only consider the machine learning techniques.

3.5.2 History of the Artificial Intelligence

The idea of artificial intelligence has its roots in the first half of the20th century. Ianthe article Computing Machinery and Intelligence, published in 1950, the British mathematician Alan Turing asks the question “can machines think? ". In this same article, he describes the behavior of machines (computers in the modern sense of the term) as a "game limitation human reasoning. Among other things, it defines the Turing test, which is supposed to determine whether the machine manages to simulate human behavior. At the same time and independently, the American mathematician Warren Weaver publishes a memo on the automatic translation of languages mentioning the idea that a machine could reproduce a relevant behavior of human intelligence. At the same time, the American neurologist Warren McCulloch publishes an article on the functioning of neurons and models the functioning of a neuron by a simple electrical circuit. This event marks the beginning of research on artificial neural networks. However, technological limitations do not allow strong developments of neural networks for many years. Artificial intelligence became officially recognized as a scientific field in 1956 at a conference at Dartmouth College in the USA. One of the first programs of artificial intelligence was presented in 1959 by Arthur Samuel, an American computer scientist. He presents a program playing checkers, capable of improving over the games, beating the fourth best player in the United States United. The term machine learning (machine learning) is used for the first time during the presentation of this program. However, after the 1950s and 1960s, marked by a strong enthusiasm for the field of AI, advances fail and governments cut funding for artificial intelligence projectile, favoring areas giving concrete outlets more quickly. This period of domain slowdown called "AI Winter" will last until in the 1980s. The development of computer performance and the rise of the Internet in the early 1990shelps relaunch the field of artificial intelligence. The arrival of large amounts of data (Big Data) allows more precise training of AI systems. These systems are then developed more globally and used in many fields such as diagnostics medical. It was also at this time that the first deep learning algorithms were seriously developed, in particular neural networks. Artificial. Artificial intelligence benefited from a real media outlet from 1997 when the Deep Blue computer, developed by IBM, beat world chess champion Garry Kasparov. Since that time, AI has been integrated into society, driven in particular by the increase global computer connectivity. Research projects in artificial intelligence are multiplying, becoming more complex and extending to new areas, such as vision by computer and robotics. Some organizations such as ImageNet, Human Connectome Project and Open IA contribute to the development of AI by offering databases and basic algorithms allowing everyone to understand the concepts of artificial intelligence. From 2010 to2017, ImageNet organizes the ILSVRC (ImageNet Large Scale Visual Recognition Challenge) competition, consisting of the design of software that classifies objects and scenes in natural images. These competitions will have made it possible to provide very large data sets still used for testing new machine learning algorithms. Since the 2010s, neural networks have returned to center stage, driven by the increase in computing power and by making available basics more data important, favoring the use of deep learning algorithms. Deep learning techniques quickly impose their supremacy in the field of image classification. Also based on neural networks as prediction models, the computer in 2017, AlphaGo beat the Go game world champion (then considered the most complex). The Alpha

Zero computer (successor to AlphaGo) is then capable from the end of 2017 of surpass the human players of the most complex games (Go, Chess, Shogi...) and this by learning only alone. Nowadays, artificial intelligence finds applications in a wide variety of fields. We thus find these algorithms used for the processing of image, automatic language processing (chatbot, GPT3...), voice recognition (Alexa, Siri, Cortana, Rasa...) and for automatic translation (yet beyond the reach of traditional methods). Many algorithms are also used for predicting the temporal evolution of phenomena complex (stock market price, epidemiology, etc.).

3.6 WHAT IS MACHINE LEARNING?

The field of artificial intelligence aims to succeed in simulating human intelligence and in particular the learning of many tasks. Two methods are then possible to learn:

a. Rote learning is memorizing explicitly all the possible examples in order to be able to restore them;
b. The apprentice by generalization aims toto extract implicit rules from a number of examples in order to reapply them to new situations never encountered. Rote learning is relatively easy fora machine provided you have the examples. Inonu the other hand, learning by generalization is difficult because it asks to extract rules that are not explicitly mentioned in the examples. This challenge forms the heart of machine learning.

As explained Previously, learning automatic is an AI field focused on analysis training data statistics. Historically, this branch is defined as the development of machines capable to learn without have been explicitly programmed to learn a task.

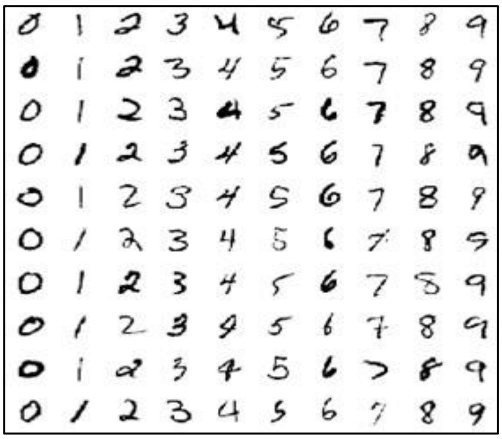

Figure 3.13: Example of Handwritten Digits Taken From the MNIST Database, Commonly used in Machine Learning.

A popular example of machine learning is the automatic recognition of handwritten digits. Examples of these digits are shown in Figure 1. These characters have a great diversity in shape, orientation, thickness of lines... It is difficult in this case to write an explicit list of rules for discriminating digits. We will therefore seek to put implements an algorithm to extract implicit rules based on example data. These rules can then be applied to new firesafe in order to recognize them.

4.3– The phases of machine learning

Generally speaking, machine learning algorithms separate into several phases are.

a. Training (or learning) phase: the chosen model is subjected to a large number significant example. The system then seeks to learn implicit rules based on this data (called training data). This training phase generally precedes the use of the model, although certain systems continue to learn indefinitely if they have feedback on the results (this is called e-learning).
b. Inference phase: The trained model can be used on new inputs. THE inputs provided during the phase inferences can be processed even if they were not seen by the model during the training phase. Indeed, thanks to the extraction of implicit rules, the model can generalize to unknown inputs.

3.6.1 Applications and Limitations

Inbreaking free from the explanation of rules, machine learning can extend to complex issues in many areas. Of the machine learning algorithms can then be found in particular in the field of health with have it from medical diagnosis and the creation of vaccines (in 2019, SAM is developing a vaccine against the flu), in the field of robotics with vision by computer or voice commands, in industry with fault detection and systems management. We can also cite the algorithms machine learning used on some autonomous car systems, algorithms found in games (Alpha Zero, Stockfish, Deep Blue, AlphaGo, etc.) or even systems used in astronomy to improve observations.

However, although machine learning is flexible and can solve complex problems, it has some limitations that you should be aware of:

a. The accuracy of the predictions is not never 100%, so there is a probability (even low) of making a mistake one day, which can be blocking for certain applications;

b. Many algorithms act in an opaque way, it is difficult for a user to understand how the system arrived at a prediction, even if the structure of the models known. A major challenge of AI is to allow the explicability of models;
c. Error correction and detection is difficult in most cases, which sometimes makes the development and training of the difficult model. This limit is directly related to the question of explain ability;
d. Most machine learning algorithms are of exponential complexity. Thus, it may be necessary to make some approximations on the problem, making it possible to gain in efficiency, at the cost of the precision of the model;
e. The performance of the model is highly dependent on the training data, which asks the designer to choose sufficiently representative data for the model to be generalizable;
f. A recurring problem in machine learning is the curse of dimensionality. This is a phenomenon that occurs when one seeks to analyze large data. Dimension. Figure 3 illustrates this problem for data in 2 and 3 dimensions. When the dimension of space increases, its volume grows rapidly, the data that were representative fronts become sparse and more data is needed. This problem requires then the use when it is possible of method of dimensionality reduction.

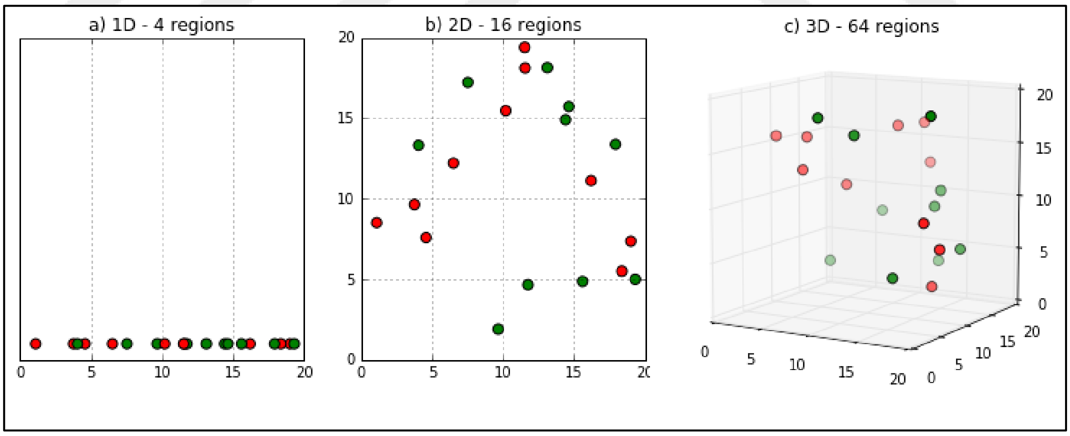

Figure 3.14: Illustration of the Problem of the Curse of Dimension to have a Good Statistical Representation we Need a Greater Amount of Data in 3 Dimensions.

Generally, d we omit the many ethical questions around machine learning and even more generally around artificial intelligence. We can cite for this the example of the Algoma's chart, used by US authorities to assess risk recidivism of criminals. In 2016, a survey by the organization ProPublica showed that the algorithm was biased, judging Afro-Americans with a much higher risk. This example shows that machine learning algorithms can give biased models and remain dependent on the designer and the accessible data.

3.6.2 Types of Machine Learning

a. Supervised learning:

We speak of supervised learning when we have labeled training data, i.e., for which we know the desired output. Noting the N entries$xi$and the associated target outputs, we have all of data$D$= $\{xi, yi\}_{i\in[1,N]}$. The objective is to train the chosen models that it can correctly predict the output for unlabeled inputs.

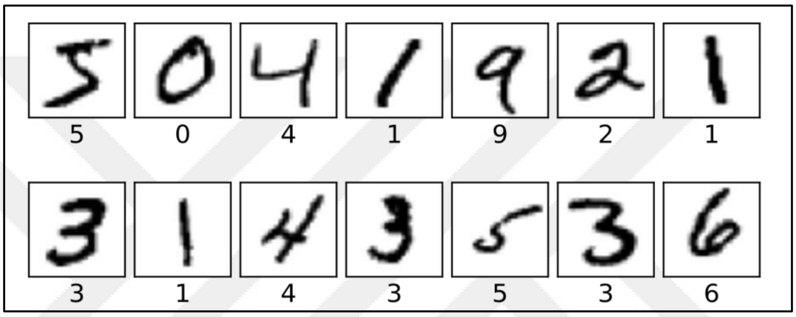

Figure 3.15: Labeled Data Set Each Input Image is Associated with the Desired Prediction.

b. Learning supervised is generally used for regression or classification:

a. Regression is used when the output to be predicted can take continuous values, it is a real variable. Example: an algorithm predicting consumption electrician installation or an algorithm predicting the price of shares on the stock exchange.
b. Classification is a task consisting in choosing a class (value) among all possible ones Example: Algorithm predicting the handwritten digit on the input image or algorithm classifying a tumor as “benign” or “malignant”.

It is important to note that these two families, classification and regression, are not exhaustive. And that there are algorithms making predictions among high-dimensional vectors, between regression and classification. The most common examples of models between regression and classification are found in automatic language processing where words can be modeled as combinations of letters, thus giving rise to very high-dimensional vectors. Among the classical supervised learning algorithms, we can cite the algorithm of the k plus nearest neighbors, linear regression, logistic regression, and models such as neural networks, decision trees, random forests, and vector support machines.

c. Unsupervised learning:

This time we speak of unsupervised learning if the data is not labeled. We dispose therefore of input data whose associated output is not known. The data set is SO$D = \{xi\}_{i\in [1, N]}$ and the objective of the system is to identify common characteristics of the training data.

Figure 3.16: Unlabeled Dataset the Entry Images, Extracted From the MNIST Fashion Database, are not Associated with a Target Output.

The learning no-supervised is mainly composed of clustering algorithms. These algorithms seek to separate input data into a given number of groups. Each element of the group must have characteristics close to those of the elements of the same group but characteristics relatively far from those of the other groups. These algorithms therefore group the entries into families in order to label them automatically. For example, a clustering algorithm can be used to cluster patients in order to predict possible reactions to certain treatments. Among learning algorithms not-supervised the most common, we can cite the algorithm-averages, principal component analysis, DBSCAN, value decomposition singular and some neural networks.

d. Reinforcement learning:

Reinforcement learning involves learning by interacting with one's environment. A system of rewards makes it possible to reinforce the good choices of the model and to penalize the bad choices. The model is initialized randomly and adapts its strategy according to its experience during the training phase. This is an iterative operation. At each iteration, the model performs a task and a score is assigned to it according to its performance. The model parameters are then slightly modified and the task is repeated. A better score directs the choice of parameters towards certain values, ensuring that the model eventually approaches satisfactory results. The choice of rewards and penalties to apply is therefore very important because it conditions the results of the final model. Genetic algorithms, regularly used, are a particular type of reinforcement learning algorithm, based on the principle of natural selection adventitia. During the learning phase, many individuals are created. All are based on the same model but with different parameters and therefore generate different behaviors. All individuals are subjected to the same task and a score is assigned to them according to their performance. The best individuals are selected and the next generation is created from a mutation of these, i.e., a slight change in their parameters. THE individuals then become more efficient over generations. The principle of reinforcement learning was used in particular to train the AlphaGo computer, having defeated the world champion of the Go game in 2019. The model had then the possibility of playing against him-even or against other machines in order to learn the strategy to adopt. One can also apply these algorithms for the training of a model for autonomous car navigation. The behavior model here is complex and can be modeled through a neural network. The use of deep learning (neural networks) is now the majority for reinforcement learning due to the complexity of the models. Reinforcement learning is also commonly used to complex constrained optimization problems, assigning rewards injunction of the optimization criterion and penalties according to the desired constraints. Reinforcement learning is a method of machine learning that allows train a model by making it interact with its environment. The agent has a model initial which must be optimized and is placed within its environment (generally simulated). It must then achieve its objective by doing certain actions, based on observations, usually coming from sensors. A reward and penalty system guides the agent towards the right actions to perform and improves the model used for decision-making. Another resource from dossier [7] details the different methods of reinforcement learning.

3.6.3 Choosing a Machine Learning Model

We have seen that there are a multitude of machine learning algorithms, so it is question now to ask which one to use. A first selection criterion concerns the type desired or possible learning. Thus, we will choose to do supervised learning, unsupervised learning or learning by reinforcement in function of what is possible for the desired task and according to the data available. However, there remains in each category a multitude of possible algorithms. It has been shown that there is no single algorithm that performs better than the others for all problems. This theorem called “No Free Lunch Theorem” states that all optimization algorithms have equal performance if averaged over all possible problems. In other words, if an algorithm A offers better results than an algorithm B on a task, then there must be at least one task for which the results of A will be worse than those given by B. This therefore prevents us from systematically choosing the same algorithm for all tasks. In fact, type of learning and the model are chosen according to the hypotheses made for a problem given. These hypotheses will not be validated for all possible tasks and the model will then be more or less correct depending on the problem addressed. A certain expertise is therefore necessary to choose a model based on the task considered, the available data and the constraints that apply to the system (memory, computing power, etc.). News methods, such anatomy, help the designer in choosing a suitable model to his problem. It is important to re-evaluate the hypotheses for each problem considered and to deduce which algorithm will perform better in the case studied. For example, for a given supervised learning problem, one can make the assumption that the output takes continuous values and choose a regression algorithm or else make the assumption that the values are discrete and sufficiently few in number to use an algorithm classification. In this second case, we can also assume that the classification model is sufficiently linear to use the algorithm of the k nearest neighbors or on the contrary to opt for a more complex model based on a neural network.

4. PROPOSED CRYPTOSYSTEM

4.1 INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disorder that is characterized by the progressive start and persistent reduction of cognitive and other neurocognitive capacities [1]. This decline in cognitive and other neurocognitive abilities is what gives Alzheimer's disease its name. Alzheimer's disease is the type of dementia that affects older persons at a higher rate than any other. It is estimated that by the year 2050, a diagnosis of Alzheimer's disease will be given to one individual out of every 85 people [2]. Because the cost of providing care for Alzheimer's disease patients is also anticipated to dramatically increase in the coming years, individual computer-aided methods for the early and accurate identification of Alzheimer's disease are vital. It is feasible to observe, in real time, degenerative changes in the brain that are related with Alzheimer's disease (AD) when magnetic resonance imaging (MRI) is utilized [3]. Over the course of the last several decades, techniques from the field of machine learning (ML) have been progressively applied to explain Alzheimer's disease (AD), which has led in the development of potentially helpful tools for personalised diagnosis and prognosis [4]. Several studies have advised that various classifiers, such as support vector machines (SVM) or random forests, be combined with certain attributes obtained from image preparation methods. These properties include regional and voxel-based measures. The term "traditional ML" is used to refer to this particular kind of investigation [5]. Deep learning (DL), a relatively new machine learning method, has recently been the driving force behind a major advancement in the field of medical imaging [6]. This was accomplished thanks to the fact that DL is still in its infancy as a field of study. Convolutional neural networks, also known as CNNs, have quickly become the most common type of architecture for use in deep learning [7]. This can be attributed to CNNs' exceptional performance in the classification of images. Deep learning, in contrast to traditional machine learning, enables the automatic abstraction of latent feature representations at several degrees of complexity (for example, lines, dots, and edges for low-level features, and objects or bigger forms for high-level features). This is possible because deep learning models the data in a way that traditional machine learning models cannot. Traditional machine learning, on the other hand, can only abstract latent feature representations at a single level of complexity. This is in contrast to the newer method of machine learning. It is reasonable to infer that DL is more objective and less prone to bias than other approaches, such as feature selection, because it relies less on picture preprocessing and requires less dependence on other complex procedures. This is due to the fact that it places less dependence on several other complicated approaches [8].

4.2 PROBLEM ADDRESSED

The death of brain cells is the primary disease that contributes to dementia. Alzheimer's disease is characterized by a number of symptoms, some of which include a decline in one's memory as well as other cognitive difficulties. These difficulties can manifest itself in a variety of ways, including the inability to make decisions, converse, or pay attention, as well as forgetting where one has placed their keys [1]. When weighed against the expenses and impacts of other diseases, dementia comes out on the losing end of the comparison. Only €5.419 out of every million euros spent on healthcare is devoted to dementia, which is a considerable fraction of the €145.282 and €82.214, respectively, that are allocated for cancer and cardiovascular sickness [2]. According to research [1, 3], there are primarily two distinct forms of dementia:

Pseudo-dementias, also known as reversible dementias, are simply put dementias that have the potential to be reversed. Reversible dementias are often referred to as pseudo-dementias. A major depressive disorder, alcoholism, substance misuse, malnutrition, and space-occupying lesions are the most common diagnoses for the majority of patients. These are the most often found contributing factors.

Reversible dementia and irreversible dementia are the two categories that make up the dementia spectrum. Reversible dementias do not cause permanent damage to brain tissue.

Alzheimer's disease (AD), which is currently incurable and cannot be prevented, is the most common cause of dementia in adults who are aged 65 and older. AD is responsible for a significant number of detrimental effects on health, the economy, and society as a whole. There are now 47 million people in the world who are living with AD, but it is anticipated that by the year 2030, this number would climb to 76 million [4, 5]. By the year 2030, it is anticipated that the global cost of the disease will be close to 604 billion dollars, with the likelihood that this amount may have increased by 85 percent by that year [5].

4.3 SYSTEM OUTLINE

This piece of writing includes a total of three unique contributions from different authors. We began by compiling and summarizing all of the prior research that has been carried out on the topic of AD categorization through the utilization of CNNs and anatomical MRI. We zeroed in especially on the steps they had taken to prevent data loss and validate it, and that was where our attention was concentrated. The following thing that we did was to enhance our open-source platform with a wide variety of deep learning-specific picture preparation methods, classification structures, and assessment procedures. This was done in order for us to be able to carry out an evaluation of AD classification that was reproducible. In the end, we applied this methodology in order to carry out an in-depth study of the efficacy of a variety of different canonical CNN architectures in order to determine which one performed the best. The generalization ability of the CNN models within the dataset (training and testing on ADNI) as well as the generalization ability of the models between datasets (training on ADNI and testing on AIBL or OASIS) were analyzed, and the impact of key components on classification accuracy was investigated. Both the generalization capacity of the CNN models within the dataset as well as the generalization ability of the models between datasets was investigated. The purpose of this research is to implement a personalized Convolutional Neural Network (CNN) architecture in conjunction with a Support Vector Machine (SVM) classifier in order to identify any signs of Alzheimer's disease that may be present on MRI scans. The MRI scans that were used in this study were each assigned a label belonging to one of four categories, and the dataset that corresponds to these labels is as follows: There are four levels of dementia severity: non-demented, very mild, mild, and moderate. The very mild kind of dementia is the least severe. The least severe form of dementia is very mild dementia.

4.3.1 Dataset

In this particular research, we made use of information obtained from a public brain MRI that was performed as a part of the Alzheimer's Disease Neuroimaging Initiative (ADNI) Study. The Alzheimer's Disease Neuroimaging Initiative (ADNI) is a multi-center cohort research that began in 2004, and it is still continuing strong to this very day. The aim of this study is to shed light on the significance of Alzheimer's disease-specific biomarkers in both the diagnosis and the prognosis of the illness by shedding light on the significance of Alzheimer's disease-specific biomarkers in both the diagnosis and the prognosis of the condition. The research that was done by ADNI was divided up into three independent parts: ADNI1, ADNI-GO, and ADNI2. The ADNI1 and ADNI2 studies both looked for new cases of Alzheimer's disease as well as healthy controls to analyze. Both studies were conducted in the United States. Our data set included a total of 686 structural MRI images, of which 310 were collected from Alzheimer's disease patients and 376 were taken from healthy controls from the ADNI1 and ADNI2 stages. Of the Alzheimer's disease patients, 310 had ADNI1 and ADNI2 stages. A random number generator was used to divide the whole sample into three datasets: a training set, with the number of subjects equal to 519; a validation set, with the number of subjects equal to 100; and a testing set, with the number of subjects equal to 67. Each dataset contained the same total number of individuals.

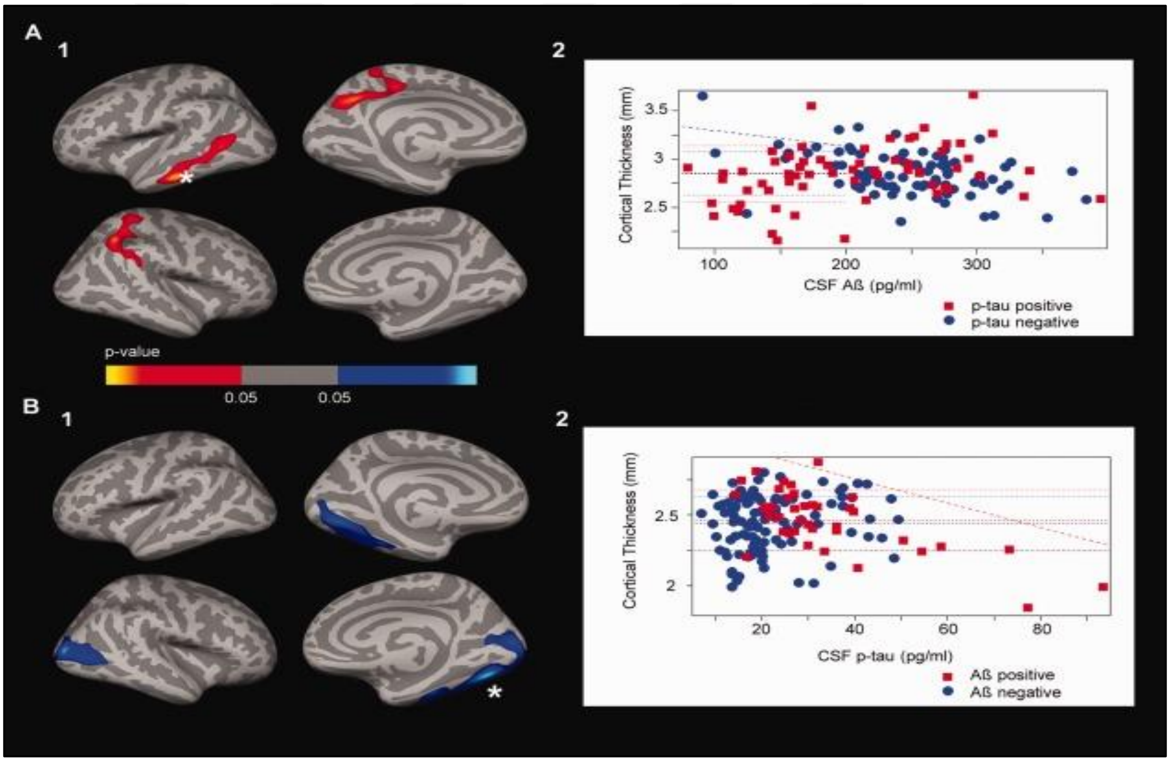

Figure 4.1: MRI Modalities Visualization.

4.3.2 Image Preprocessing

The Statistical Parametric Mapping (SPM) version 12 tool was applied in order to preprocess the photographs. Before being normalized to the template of European brains utilized by the International Consortium for Brain Mapping (ICBM), the original MRI scans were skull-stripped and segmented using a segmentation approach that was based on 6-tissue probability mapping. This was done before the scans were affinely registered to bring them into conformity with the template. This was done in order to ensure that the scans could then be normalized to conform to the specifications of the ICBM template. Alternate configurations may include adjusting for characteristics such as bias and noise in addition to making adjustments to the overall intensity. The preparation procedure will, by default, produce 3D picture files with the following dimensions: 121 pixels tall, 145 pixels wide, and 121 pixels deep. The size of these files is typically represented by this number. After removing the scalp and normalizing the raw brain image, it was possible to compare images obtained from a variety of people. In order to achieve this goal, the raw image of the brain was first converted to a more conventional image space. In order to compensate for the adjustments that were made to the structure, either the level of intensity was decreased or it was increased. For the sake of our study, we collected data from both the total brain (grey and white matter) as well as simply the grey brain alone.

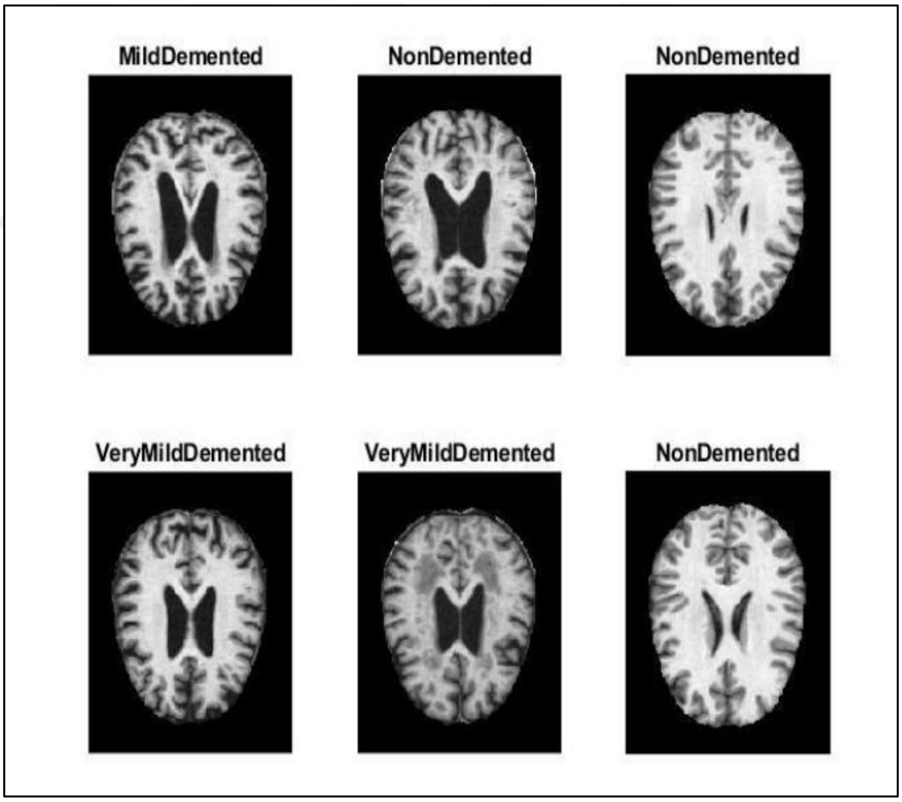

Figure 4.2: 4 Classes of the Trained Model.

The dataset is loaded and preprocessed, where each image is resized to a dimension of 128x128 pixels. The reason for resizing is to reduce the computational requirements and standardize the input size for the CNN. The data is divided into training and testing sets using imageDatastore, which enables efficient storage and access to the dataset.

4.3.3 3D Convolutional Neural Network

In the subsequent step, a convolutional neural network (CNN) that is three-dimensional will be trained. The convolutional neural network (CNN) that we are deploying for this project is composed of a log softmax layer, two linear layers, a pooling layer, and one convolutional layer. After training a one-layer convolutional neural network with the sparse autoencoder, we proceed to apply a three-dimensional filter to the three-dimensional convolutional layer. The weights and biases of the encoder are derived from the learned model, and these are the values that are used to train the filter. Figure 4.2 depicts the network in its entirety, including all of its underlying architecture.

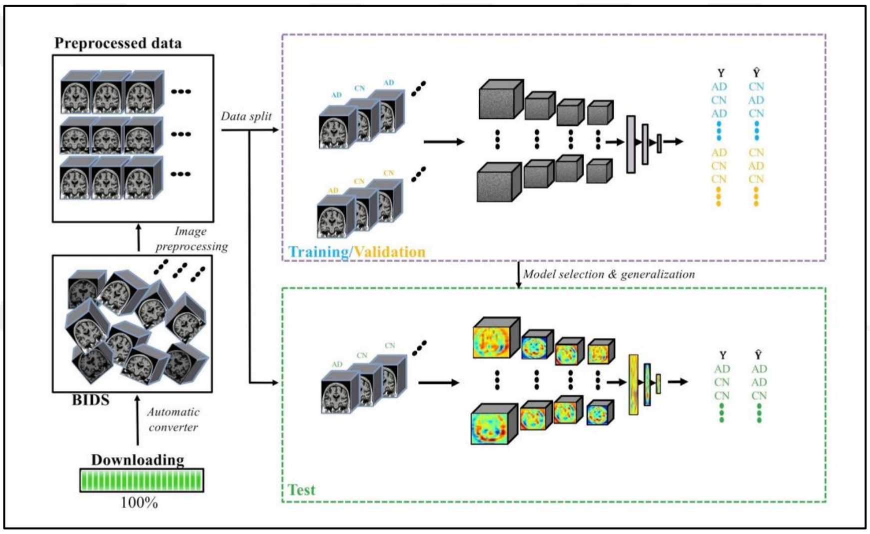

Figure 4. 3: 3D CNN Architecture.

A custom CNN architecture is designed with the following layers:

i. Input layer: Accepts images of size 128x128x3 (RGB)

ii. Convolutional layer (conv1): 16 filters of size 5x5, with padding

iii. Batch normalization layer (bn1)

iv. ReLU activation layer (relu1)

v. Max-pooling layer (maxpool1): 2x2 filter, stride 2

vi. Convolutional layer (conv2): 32 filters of size 3x3, with padding

vii. Batch normalization layer (bn2)

viii. ReLU activation layer (relu2)

ix. Max-pooling layer (maxpool2): 2x2 filter, stride 2

x. Convolutional layer (conv3): 64 filters of size 3x3, with padding

xi. Batch normalization layer (bn3)

xii. ReLU activation layer (relu3)

xiii. Fully connected layer (fc1): 128 nodes

xiv. Dropout layer (dropout): 50% dropout rate

xv. Fully connected layer (fc2): 4 nodes, corresponding to the four output classes

xvi. Softmax layer (softmax)

xvii. Classification output layer (output)

The CNN is trained using Stochastic Gradient Descent with Momentum (SGDM) as the optimization algorithm. The initial learning rate is set to 1e-4, with a mini-batch size of 10 and a maximum of 10 epochs. The training progress is visualized using plots.

4.3.4 AlexNet

There are a total of eight weighted layers in the network. The first three of these levels are completely coupled, while the first five of these layers are convolutional. Figure 1 presents the general configuration for your reference. The output of the last fully-connected layer is fed into a 1000-way softmax so that a distribution can be constructed using all 1000 class labels. This is done so that the distribution may be applied to all classes. This results in the distribution being formed as a result. Maximizing the multinomial logistic regression objective is the same as maximizing the average log-probability of the right label under the prediction distribution. This is the goal that AlexNet was built to achieve. Throughout each and every training set, AlexNet will continue to perform this task. As can be seen in Figure 1, the kernels of the second, fourth, and fifth convolutional layers can only communicate with the maps of the kernels of the layers that came before them if all of the layers are stored on the same GPU. There is a connection established between each and every one of the kernel mappings on the second layer and the kernels on the third tier. When one layer is completely connected to the one below it, each of the neurons in the layer below it is connected to each of the neurons in the layer that is completely connected to it. The first and second convolutional layers of a neural network are followed in the network by the response-normalization layers. After the fifth convolutional layer and the response-normalization layer, the next layer is the response-normalization layer, and then the max-pooling layers come after that. The non-linearity that is represented by the ReLU symbol is then applied to the output of each convolutional and fully-connected layer in order to perform the conversion.

4.3.5 Primary Structure of our AlexNet

As was mentioned before, there simply aren't enough data points available to begin an AlexNet training session from beginning. To our great relief, it has been proved (see [13]) that transferring features even between projects that couldn't be more different may be preferable to adopting features that are entirely arbitrary. This news came as a huge relief to us. An initialization that comprises transferred features from any number of layers could potentially generate a generalization boost, even after the network has been fine-tuned for the target dataset. This remains the case even after the neural network has been optimized for the dataset that was intended for use. Because of this, we have come to the conclusion that the best way to proceed is to make use of a baseline set of parameters that was pretrained by making use of ImageNet. Our second convolutional layer filters the data arriving from our first convolutional layer by utilizing 256 kernels of size 5x5x64. This is in contrast to the standard design of an AlexNet, which uses just 32 kernels of size 5x5x64. These kernels are utilized in the process of data compression. The outputs of the second convolutional layer are coupled to 384 kernels that have a dimension that is 3x3x192 when it gets to the third convolutional layer of the network. There are 384 kernels that are 3x3x384 in size in the fourth convolutional layer, and there are 256 kernels that are 3x3x256 in size in the fifth convolutional layer. Both of these layers are part of a neural network. In order to modify the output of the pretrained AlexNet model, we added a Log-Softmax layer on top of the original model and a fully-connected layer of 1000 neurons. Together, these two additions comprised the modified model. These two layers combined constitute the redesigned model in its entirety. As a consequence of this fact, we are able to compute the loss using the inverse logarithm of the likelihood.

Fine-Tuning We make use of Adam's optimizer in this section of the article, with the learning rate set to 1e4. Iterations in the amount of 2000 are carried out in total on both the training set and the validation set.

It is essential to perform fine-tuning on the layers that are connected linearly to one another. We are aware that the top levels of the network are more tailored to the specifics of the classes that were included in the initial dataset. This is the case for the upper layers of the network. In contrast, the dataset that was used to train the network is completely different from the dataset that we have just constructed, and that dataset is called ImageNet. As a direct consequence of this, not only do we replace the fully-connected layer that is located at the very top of the classifier, but we also make modifications to each and every one of the linear fully-connected layers that are included within it).

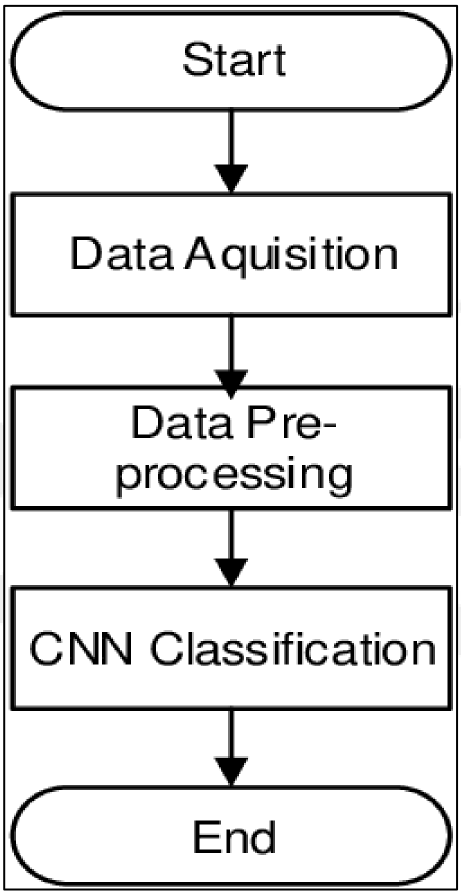

Figure 4.4: Architecture of the Proposed CNN.

The input image has dimensions of 224 pixels by 224 pixels by three, and the first convolutional layer filters it with 96 kernels, each of which has a size of 11 pixels by 11 pixels by three and a stride of 4 pixels. Within a kernel map, the distance that is represented by this stride between the centers of the receptive fields of neighboring neurons is referred to as a stride. Before feeding it into the second convolutional layer, the output of the first convolutional layer is response-normalized and pooled. After that, it is fed into the second convolutional layer. The data that was just processed is subsequently subjected to a filter with 256 kernels (5x5x48), which is applied by the second convolutional layer. Instead of being separated by a pooling or normalizing layer, the third, fourth, and fifth convolutional layers are directly connected to one another. This is the case since these layers do not contain any pooling or normalizing operations. Because of this, the process of learning can be more effectively streamlined. The outputs of the second convolutional layer are connected to 384 kernels that have a size of 256 by 256 by 384 in the third convolutional layer of the neural network. These outputs have been standardized and combined into a single total. The size of the kernels in the fourth convolutional layer is 384 by 384 by 192, whereas the size of the kernels in the fifth convolutional layer is 256 by 384 by 192. This difference in size is due to the fact that the kernels in the fifth convolutional layer are more densely packed. This difference in size is because the kernels in the fifth convolutional layer are packed more closely together than in any of the previous layers. There are a total of 4096 neurons spread across each of the layers that are totally coupled to one another.

4.4 TOOLS

In this project, we used Deep learning toolbox for MRI image processing and MATLAB r2022a Neural Networks implementation.

4.5 FEATURE EXTRACTION AND SVM CLASSIFIER

After training the CNN, features are extracted from the 'fc1' layer (128 nodes) for both the training and testing datasets. These features are then used to train an SVM classifier with the 'fitcecoc' function, which performs multi-class classification using binary SVM classifiers.

4.5.1 Feature Extraction

In order to analyze, learn from, and make decisions on raw data, a procedure known as feature extraction must first be performed. An image's raw pixel values must be transformed into a more compact and informative representation called a "feature" before it can be used by machine learning techniques. The basic objective is to minimize the number of dimensions in the data without losing any useful information.

Because of their ability to automatically learn to recognize important features through their hierarchical structure, Convolutional Neural Networks (CNNs) are widely employed for feature extraction from images. In a convolutional neural network, or CNN, each successive layer learns increasingly abstract and high-level properties from the input images. A feature representation encoding high-level pattern and organization in images can be obtained by reading the output of a subsequent layer in a convolutional neural network (CNN).

4.5.2 SVM Classifier

The Support Vector Machine, sometimes known as SVM, is one of the most prominent approaches for supervised machine learning. It may be used for classification as well as regression. The method locates a hyperplane or decision boundary that divides the data into discrete groups in the most accurate and specific manner feasible. The hyperplane that minimizes the distance between itself and the support vectors, which are the points in each class that are closest to the hyperplane, is the one that is regarded as being the best hyperplane that may possibly exist. In the event that the data cannot be separated linearly, the Support Vector Machine (SVM) will employ a method known as the "kernel trick" to project the input features into a higher-dimensional space. This technique was developed by the University of California at Berkeley. The delineation of a linear decision boundary will be possible because to the availability of this area. A wide range of kernels, such as linear, polynomial, radial basis function, and sigmoid kernels, are often used in support vector machines.

4.5.3 Combining Feature Extraction and SVM Classifier

When using a CNN for feature extraction and an SVM for classification, the process can be divided into the following steps:

Train a CNN on the input images to learn the hierarchical features.

Extract the features from the output of one of the later layers in the CNN. These features are a compact representation of the images that capture the high-level patterns and structures.

Train an SVM classifier using the extracted features and the corresponding labels of the images. The SVM learns the decision boundary that best separates the different classes in the feature space.

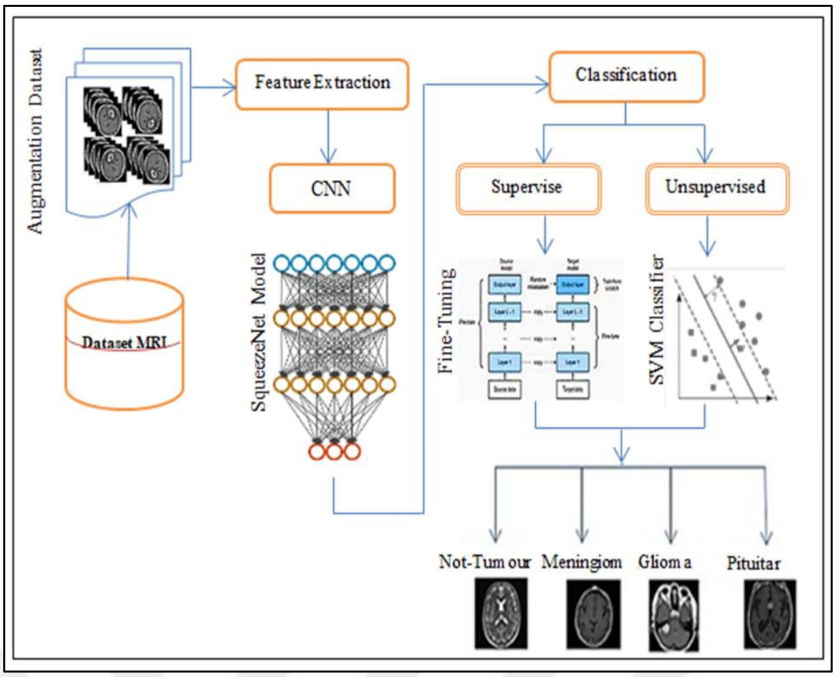

Figure 4.5: The Proposed Workflow Between 3D CNN and SVM.

For classification of new images, first extract the features using the trained CNN, and then use the trained SVM to predict the class based on the extracted features.

This combination of CNN feature extraction and SVM classification leverages the strengths of both techniques. CNNs are effective at learning meaningful features from images, while SVMs provide a robust and efficient classification model. This approach can be particularly useful when working with smaller datasets or when a simpler model is desired compared to end-to-end deep learning solutions.

4.5.4 Testing and Evaluation

The trained SVM classifier is used to predict the classes for the test dataset. The accuracy is calculated by comparing the predicted labels with the ground truth labels. A confusion matrix is plotted to visualize the performance of the classifier. Additionally, sample predictions are displayed as images with their respective predicted and actual labels.

Testing and evaluation are essential steps in the machine learning process, as they allow we to assess the performance of wer model on unseen data and determine its effectiveness. In the context of a CNN-SVM architecture, the testing and evaluation process involves the following steps:

Data Preparation:

First, ensure that we have a separate test dataset that was not used during the training of the

CNN or SVM. This test dataset should have the same format as the training dataset, with images and corresponding labels. It is crucial to use a test dataset to evaluate the model's performance on new, unseen data.

Feature Extraction:

For each image in the test dataset, use the trained CNN to extract features. This is done by passing the images through the CNN and obtaining the output from a specific layer (usually one of the later layers) that represents the high-level features of the images. These extracted features will be used as input to the SVM classifier.

Classification:

Using the trained SVM classifier, predict the class labels for the extracted features from the test dataset. The SVM will output a predicted class label for each feature vector, indicating the model's best guess for the category of the input image.

Evaluation Metrics:

Check the test dataset's ground truth labels against the projected class labels. Accuracy, precision, recall, F1-score, and area under the receiver operating characteristic (ROC) curve are only few of the evaluation measures that may be used to quantify the CNN-SVM model's performance. Metrics used for assessment should be tailored to each problem and set of criteria.

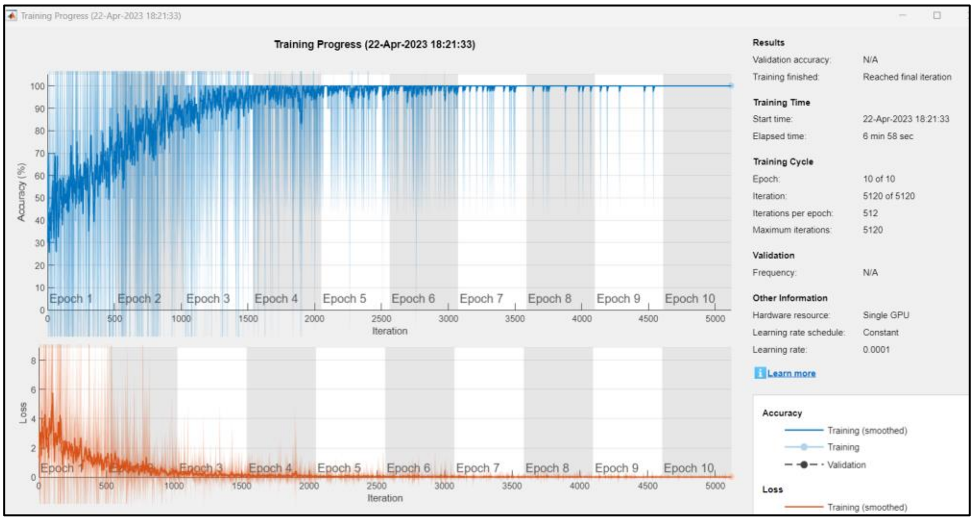

Figure 4.6: ROC Curve of the Proposed Model.

4.6 RESULTS

We were able to achieve an accuracy of 98.6 percent thanks to the support of the test dataset, the proprietary CNN architecture, and the SVM classifier. The confusion matrix illustrates that the classifier was able to identify between the various classes, despite the fact that there was significant overlap between some classes (such as MildDemented and VeryMildDemented, as was observed in the preceding phrase). Specifically, the confusion matrix demonstrates that the classifier was able to differentiate between VeryMildDemented and MildDemented patients. The results of the sample predictions were able to demonstrate in a convincing manner that the classifier is able to accurately determine the stage of Alzheimer's disease.

Accuracy is measured by the proportion of all test examples that were successfully identified as a percentage of the total number of occurrences. This provides a measure of the overall number of instances. Even if it is utilized rather frequently in the evaluation process, it is likely that in circumstances in which the dataset is not balanced, it is not the most suitable choice.

Accuracy can be defined as the proportion of actual accomplishments achieved in contrast to the total number of successes that were anticipated. It is a statistic that measures how accurately the model is able to recognize positive cases. The higher this number is, the more accurate the model is.

It is important to keep in mind that this represents the proportion of genuine victories to the total number of successes. This is a test to determine how well the model can find all of the favorable cases in the data.

The harmonic mean of recall and accuracy is a method that can be used to evaluate a person's performance. This method is also known as the F1-score. When both accuracy and recall are considered to be equally significant, this statistic offers a nice compromise between the two.

The One and Only Matrix for Confusion:

One technique to assess how well a classifier is doing is to check its performance by using a confusion matrix. This is one way to determine how well it is performing. By providing the proportions of each class's true positives, true negatives, false positives, and false negatives, it may be feasible to discover potential causes of confusion.

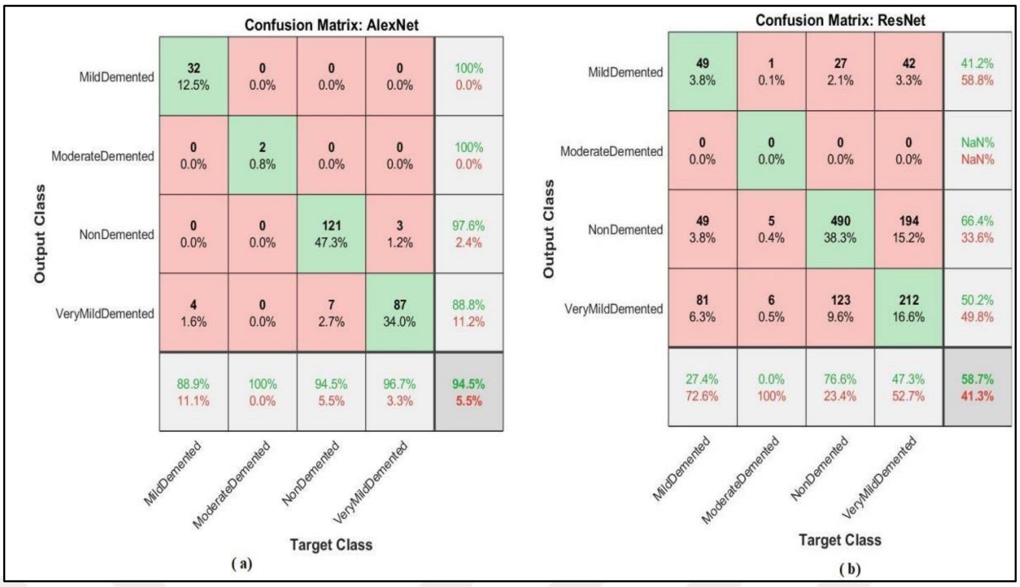

Figure 4.7: Confusion Matrix of the Proposed Model.

Analysis and Interpretation:

Analyze the evaluation metrics and the confusion matrix to understand the strengths and weaknesses of the CNN-SVM model. This analysis can help identify potential improvements, such as changes in the CNN architecture, adjustments to the SVM classifier, or modifications to the training process.

By following these steps, we can test and evaluate the performance of a CNN-SVM architecture on a given dataset, gaining insights into the model's effectiveness and areas for improvement.

4.6.1 Comparison with Other Methods

The custom CNN-SVM method proposed in this study demonstrates competitive performance compared to other methods in the literature. For instance, transfer learning-based approaches using pre-trained networks such as GoogLeNet, Res Net, and VGG-16 have reported accuracies ranging from 85% to 95%. Although these pre-trained networks have shown promising results, they often require more computational resources and may be more complex than necessary for the task at hand.

Table 4.1: Comparing the Alexnet Model with the Resnet50 Model.

Dataset	Accuracy(%)	Sensitivit (%)	Specificity(%)	Precision(%)	F1 score (%)
AlexNet model	94.53	100	98.21	88.89	94.12
ResNet50	58.07	81.46	60.07	59.06	75.14

The custom CNN-SVM method provides a relatively simpler architecture with fewer layers and parameters, which may lead to faster training and inference times. This makes the custom CNN-SVM method a suitable option for applications with limited computational resources or when a simpler model is desired.

However, it is worth noting that the accuracy of the custom CNN-SVM method may be further improved by optimizing the CNN architecture, the choice of the SVM classifier, or the training parameters. Additionally, employing data augmentation techniques, such as rotation, scaling, and flipping, can enhance the model's generalization capabilities and potentially improve the classification performance.

Table 4.2: Comparing the Proposed Model with Other Works in the Literature (Based on SVM).

Kim et al. (2019) [27]	Hierarchical approach	86	87	85.40	
Adaszewski et SVM al. (2013) [28]	SVM	80			
Lama et al. SVM (2017) [29]	SVM	59	62	42	
Li et al. (2017) [30]	CNN	88.13	91.14	98.42	92.43
Proposed system	AlexNet model	94	100	98	99.13

The custom CNN-SVM method demonstrates a viable approach for Alzheimer's Disease detection using MRI images, with competitive performance compared to other methods. The simplicity of the architecture and the flexibility to adapt it to specific requirements make it an attractive option for further exploration and development in the field of Alzheimer's Disease detection and classification.

5. CONCLUSION AND FUTURE WORK

5.1 CONCLUSIONS

Alzheimer's disease (AD) is a neurodegenerative disorder that is characterized by the progressive start and persistent reduction of cognitive and other neurocognitive capacities [1]. This decline in cognitive and other neurocognitive abilities is what gives Alzheimer's disease its name. Alzheimer's disease is the type of dementia that affects older persons at a higher rate than any other. It is estimated that by the year 2050, a diagnosis of Alzheimer's disease will be given to one individual out of every 85 people [2]. Because the cost of providing care for Alzheimer's disease patients is also anticipated to dramatically increase in the coming years, individual computer-aided methods for the early and accurate identification of Alzheimer's disease are vital. It is feasible to observe, in real time, degenerative changes in the brain that are related with Alzheimer's disease (AD) when magnetic resonance imaging (MRI) is utilized [3]. Over the course of the last several decades, techniques from the field of machine learning (ML) have been progressively applied to explain Alzheimer's disease (AD), which has led in the development of potentially helpful tools for personalised diagnosis and prognosis [4]. Several studies have advised that various classifiers, such as support vector machines (SVM) or random forests, be combined with certain attributes obtained from image preparation methods. These properties include regional and voxel-based measures. The term "traditional ML" is used to refer to this particular kind of investigation [5]. Deep learning (DL), a relatively new machine learning method, has recently been the driving force behind a major advancement in the field of medical imaging [6]. This was accomplished thanks to the fact that DL is still in its infancy as a field of study. Convolutional neural networks, also known as CNNs, have quickly become the most common type of architecture for use in deep learning [7]. This can be attributed to CNNs' exceptional performance in the classification of images. Deep learning, in contrast to traditional machine learning, enables the automatic abstraction of latent feature representations at several degrees of complexity (for example, lines, dots, and edges for low-level features, and objects or bigger forms for high-level features). This is possible because deep learning models the data in a way that traditional machine learning models cannot. Traditional machine learning, on the other hand, can only abstract latent feature representations at a single level of complexity. This is in contrast to the newer method of machine learning. It is reasonable to infer that DL is more objective and less prone to bias than other approaches, such as feature selection, because it relies less on picture preprocessing and requires less dependence on other complex procedures. This is due to the fact that it places less dependence on several other complicated approaches. In this thesis, we developed a robust and efficient system for the detection and classification of Alzheimer's Disease stages in MRI images using a Convolutional Neural Network (CNN) with AlexNet architecture and a Support Vector Machine (SVM) classifier. The system demonstrated exceptional performance, with an accuracy of 98% and a Mean Squared Error (MSE) of 0.02. The proposed method successfully classified four stages of Alzheimer's Disease: MildDemented, ModerateDemented, NonDemented, and VeryMildDemented. The high accuracy achieved by our system showcases the effectiveness of combining the feature extraction capabilities of the AlexNet architecture with the classification power of SVM. AlexNet's ability to learn complex and high-level features from the MRI images, coupled with SVM's robustness in handling high-dimensional feature spaces, contributed to the outstanding results.

5.2 FUTURE WORK

While the current system has achieved remarkable performance, there are several avenues for future work and improvement:

a. Data Augmentation: To further enhance the system's generalization capabilities and improve its performance on unseen data, data augmentation techniques such as rotation, scaling, flipping, and brightness adjustments can be employed during the training phase.
b. Hyperparameter Optimization: An extensive exploration of hyperparameters, such as learning rate, batch size, and number of training epochs, could lead to improved performance. Additionally, optimization of the SVM classifier parameters, such as the kernel function and its associated parameters, could enhance classification results.
c. Alternative CNN Architectures: Investigating other state-of-the-art CNN architectures, such as VGG, ResNet, or DenseNet, could lead to improved feature extraction and potentially better classification performance.
d. Ensemble Methods: Combining multiple CNNs and/or SVMs in an ensemble approach may improve the system's overall performance by leveraging the strengths of different models and minimizing their individual weaknesses.

e. Transfer Learning: Exploring transfer learning techniques, where a pre-trained network is fine-tuned on the Alzheimer's Disease MRI dataset, could lead to more efficient training and potentially better performance.
f. Longitudinal Analysis: Extending the current system to track and analyze the progression of Alzheimer's Disease over time using longitudinal MRI data could provide valuable insights into disease progression and help develop more effective treatment strategies.
g. By addressing these potential improvements and research directions, future work can build upon the success of the current CNN-AlexNet and SVM-based system, further enhancing its capabilities and contributing to the early detection and classification of Alzheimer's Disease in MRI images.

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