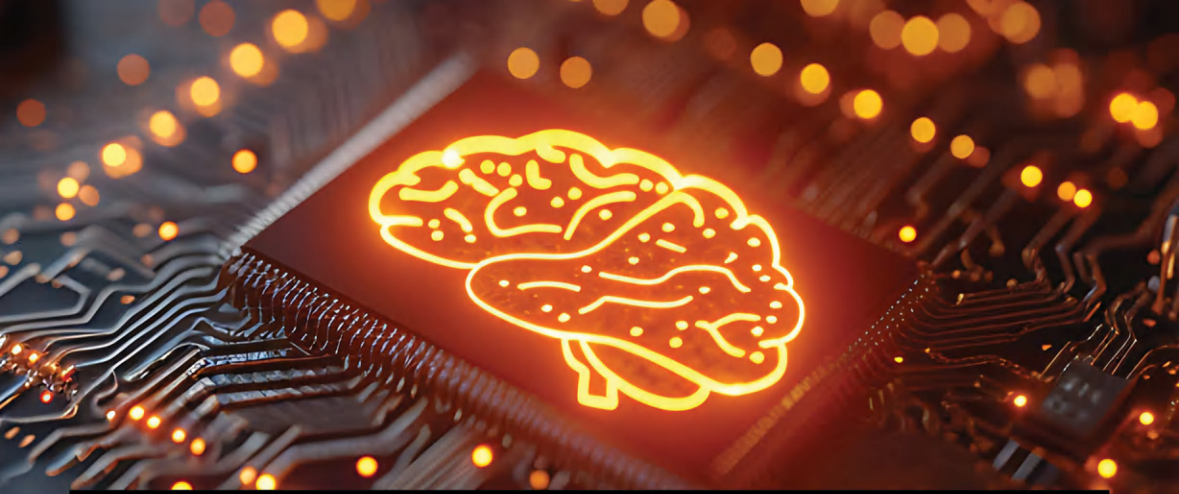

COMPUTATIONAL INTELLIGENCE ALGORITHMS FOR THE DIAGNOSIS OF NEUROLOGICAL DISORDERS

Edited by
S. N. KUMAR, SHERIN ZAFAR,
AND SAMEENA NAAZ

EDGE AI IN FUTURE COMPUTING

CRC Press
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Computational Intelligence Algorithms for the Diagnosis of Neurological Disorders

This book delves into the transformative potential of artificial intelligence (AI) and machine learning (ML) as game-changers in diagnosing and managing neurodisorder conditions. It covers a wide array of methodologies, algorithms, and applications in depth.

Computational Intelligence Algorithms for the Diagnosis of Neurological Disorders equips readers with a comprehensive understanding of how computational intelligence empowers healthcare professionals in the fight against neurodisorders. Through practical examples and clear explanations, it explores the diverse applications of these technologies, showcasing their ability to analyze complex medical data, identify subtle patterns, and contribute to the development of more accurate and efficient diagnostic tools. The authors delve into the exciting possibilities of AI-powered algorithms, exploring their ability to analyze various data sources like neuroimaging scans, genetic information, and cognitive assessments. They also examine the realm of ML for pattern recognition, enabling the identification of early disease markers and facilitating timely intervention. Finally, the authors also address the critical challenges of data privacy and security, emphasizing the need for robust ethical frameworks to safeguard sensitive patient information.

This book aims to spark a conversation and foster collaboration among researchers, clinicians, and technologists, and will assist radiologists and neurologists in making precise diagnoses with enhanced accuracy.

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Preface

Neurological disorders represent a significant and growing challenge in modern medicine, affecting millions of individuals worldwide. With advancements in computational intelligence (CI), artificial intelligence (AI), and machine learning (ML), we are witnessing a paradigm shift in how these disorders are diagnosed, monitored, and managed. The fusion of cutting-edge computational methods with neuroscience has the potential to revolutionize early detection, enhance treatment efficacy, and provide deeper insights into the complexities of the human brain. This book, *Computational Intelligence Algorithms for the Diagnosis of Neurological Disorders*, aims to present a comprehensive overview of the latest research and developments in this interdisciplinary field. It brings together leading experts from across the globe to explore the role of computational techniques in addressing neurological conditions such as Parkinson's disease, Alzheimer's disease, autism spectrum disorder, and brain tumors, among others.

Structured into three major sections, this book begins with an introduction to neurological disorders and the challenges associated with computational neurology. Ethical considerations in neurodisorder diagnosis and treatment are also discussed, emphasizing the need for the compassionate and responsible application of artificial intelligence. The second section delves into neuroimaging and diagnostic techniques, highlighting advancements in magnetic resonance imaging (MRI), deep learning applications, and targeted drug delivery. These technologies have significantly enhanced our ability to detect, classify, and analyze neurological disorders with higher precision and accuracy. The final section focuses on the application of ML and AI in neurological disorder diagnosis. From supervised learning models to deep learning and federated learning approaches, this section demonstrates how AI-driven solutions are shaping the future of neurorehabilitation and patient care.

The objective of this book is to serve as a valuable resource for researchers, medical professionals, computer scientists, and students interested in the intersection of computational intelligence and neurology. By fostering a deeper understanding of AI's role in neuroscience, we hope to contribute to more effective diagnostic methodologies and ultimately improve patient outcomes. We extend our sincere gratitude to the authors, researchers, and professionals who have contributed to this book. Their dedication and expertise have made it possible to present a comprehensive and insightful compilation of knowledge. We also appreciate the support of the institutions and organizations that have encouraged this endeavor. We hope that this book inspires further research and innovation in computational intelligence for neurological disorder diagnosis, paving the way for breakthroughs that will transform the future of medical science.

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Part I

Introduction and Challenges

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1 Introduction to Neurological Disorders

T. Manonmani, Mohit Malik, and P. Abinaya

1.1 INTRODUCTION

Neurological disorders can cause a significant impact on individual's quality of life. They are defined by their impact on the brain and the nerves that extend throughout the body, including the spinal cord. This group of disorders affects the nervous system, can impact individuals of any age, and are prevalent across the globe, significantly impacting quality of life. These disorders encompass a wide range of conditions, including epilepsy, Alzheimer's disease, multiple sclerosis (MS), Parkinson's disease, and stroke, among others. Additionally, the economic implications of these disorders are substantial, as they frequently necessitate prolonged treatment, rehabilitation, and caregiving.

Neurological disorders have a rich history of recognition, dating back to ancient civilizations.

The Edwin Smith Papyrus, an ancient Egyptian text, provides early documentation of brain injuries, highlighting the civilization's rudimentary understanding of neurology [1]. In ancient Greece, physicians like Hippocrates discussed epilepsy, suggesting it was a natural occurrence rather than one caused by divine or supernatural forces. During the Middle Ages, explanations for neurological disorders often stemmed from superstition, with many conditions framed as demonic possession or divine punishment [2]. However, during the Renaissance, scientific inquiry revived, leading to significant advancements in our understanding of the brain. Andreas Vesalius was instrumental in developing detailed anatomical illustrations of the brain, and Thomas Willis later made significant contributions by coining the term "neurology" and enhancing our understanding of brain function [3]. In the nineteenth century, neurology emerged as a distinct field of medical study. Pioneers like Jean-Martin Charcot advanced the study of brain diseases such as MS and Parkinson's disease through clinical observation and systematic study [4]. The twentieth century saw the introduction of neuroimaging technologies, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans, alongside advances in molecular biology, which have revolutionized the analysis and treatment of neurological disorders [5]. These milestones have paved the way for modern neurology, transforming diagnosis and treatment and deepening our knowledge on brain's complexities.

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1.1.1 Neurodiversity

Neurodiversity alludes to the concept that neurological differences, such as Autism, attention deficit hyperactivity disorder (ADHD), dyslexia, and others, are natural variations in the human brain. Rather than viewing these conditions as deficits or disorders, neurodiversity emphasizes that each brain functions uniquely, bringing different strengths and challenges. People having these conditions often exhibit talents like creativity, hyperfocus, and problem-solving skills that enrich society.

Figure 1.1 encapsulates the core idea of neurodiversity, highlighting different neurological conditions, strengths, and properties that are associated with neurodiverse individuals. The figure highlights conditions like dyscalculia, dyslexia, ADHD, Tourette syndrome, autism spectrum disorder (ASD), developmental coordination disorder (DCD), and acquired neurodiversity, showing how these often come with unique cognitive or creative advantages. For instance, dyscalculia, characterized by difficulties with math and number processing, is associated with enhanced creativity [6]. Many individuals with dyscalculia possess enhanced creative abilities and may excel in fields that require innovative problem-solving or out-of-the-box thinking. Dyslexia is a condition that makes it hard for people to read because they struggle to recognize speech sounds and understand how these sounds connect to letters and words (also known as decoding). Dyslexia-affected people often show real and genuine ways of communicating and solving problems, making up for their difficulties in normal learning procedures with their own unique perspectives [7]. ADHD is a disorder characterized by a consistent pattern of inattention, hyperactivity, and impulsiveness that disrupts daily functioning or growth. Although individuals having ADHD might have trouble concentrating and controlling their impulses, their strong ability to focus on things they find interesting can be a valuable skill. Tourette syndrome [8] is a brain condition that involves repeated, involuntary movements and sounds known as tics. People with Tourette's often come up with unusual ways to deal with their tics, which can lead to creative and innovative approaches to problems in other parts of their lives.

Neurodiversity refers to changes in brain function or structure due to various life experiences such as injury, illness, or aging. This includes circumstances like traumatic brain injury (TBI) or stroke. People who develop neurological differences

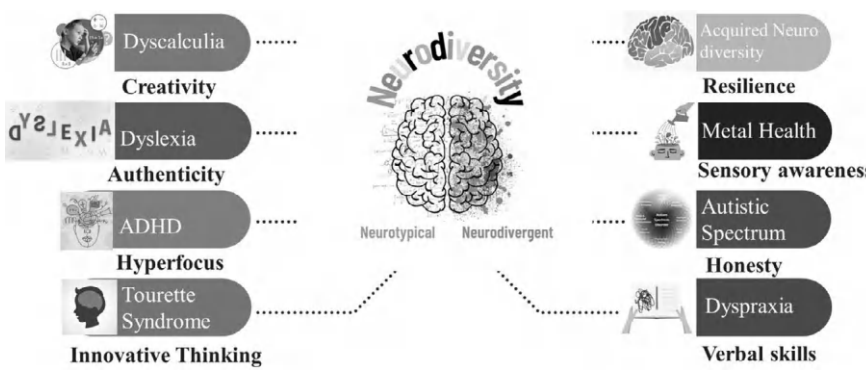

FIGURE 1.1 Neurodiversity: Highlighting strength in every mind.

often show incredible strength and flexibility in learning how to navigate and thrive despite their challenges. This often includes conduct with issues such as anxiety, depression, or other emotional conditions that can affect thinking and general health. Many individuals with neurodiversity, including those who are very sensitive to mental health, are highly attuned with their surroundings and have improved abilities to process sensory information. ASD, despite its difficulties in social communication, is also connected to traits like truthfulness and increased awareness of sensory experiences.

Finally, people having DCD often face difficulties with motor skills but demonstrate strong verbal skills [9]. By recognizing and supporting neurodiverse individuals, we can foster inclusive environments where everyone's contributions are valued. Neurodiversity encourages us to appreciate diverse ways of thinking and to challenge traditional views of "normal" brain function.

1.1.2 Types of Neurological Disorders

Degenerative disorders like Alzheimer's and Parkinson's are distinguished by the progressive loss of nerve cells and accelerated decline in brain function. For instance, Alzheimer's disease causes loss of memory, a low in mental abilities, and challenges in performing daily tasks. Parkinson's disease is linked to tremors, stiffness, slowness in movement, and trouble walking. Cerebrovascular diseases, like strokes, happen when the blood supply to the brain is interrupted, causing harm to brain cells. This can cause different symptoms, such as weakness or paralysis, problems with speaking or comprehending, issues with vision, and alterations in emotions or behavior.

Figure 1.2 highlights various types of neurological disorders. Seizure disorders, including epilepsy, are characterized by recurrent and unprovoked seizures resulting

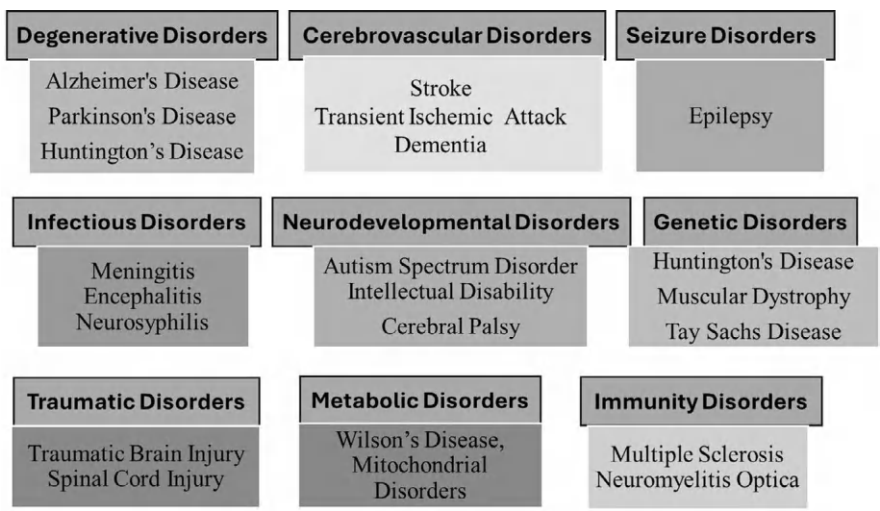

FIGURE 1.2 Types of neurological disorders.

from abnormal electrical activity in the brain. The intensity of these seizures can vary from brief, mild episodes to extended, severe convulsions. Neurodevelopmental disorders refer to conditions that impact the development of the nervous system either prenatally or during early childhood. ASD is marked by challenges in social interaction, communication, and behavior. Cerebral palsy represents a physical disability that influences movement and coordination. Traumatic disorders arise from physical injuries to the nervous system, such as TBI or spinal cord injury. TBI may lead to cognitive impairments, physical restrictions, emotional difficulties, and changes in behavior.

Injuries in spinal card can result in paralysis or a loss of sensory function below the injury site. Infectious diseases such as meningitis and encephalitis arise from infections that impact the nervous system. Meningitis is inflammation of the meninges, which are the protective membranes encasing the brain and spinal cord, whereas encephalitis denotes inflammation of the brain itself. Both conditions can manifest severe symptoms, including fever, headaches, neck stiffness, seizures, and alterations in mental status. Genetic disorders stem from inherited mutations within genes. Huntington's disease is a progressive neurodegenerative condition resulting from a dominant mutation in a single gene. Muscular dystrophy encompasses a range of genetic disorders characterized by progressive muscle weakness and degeneration. The specific symptoms, underlying causes, and treatment options for neurological disorders [10] can differ significantly based on the type of disorder and the individual's unique situation.

1.1.3 Causes and Symptoms of Neurodisorders

Neurodegenerative disorders and other neurological conditions affect the brain and nervous system in various ways, leading to a range of symptoms that can significantly impair a person's cognitive, motor, and sensory functions. Figure 1.3 represents the pictorial representation of major brain disorders. Brain disorders such as Alzheimer's disease, Parkinson's disease, and Huntington's disease are characterized by the progressive degeneration and death of neurons. These conditions are often driven by abnormal protein accumulations in the brain, which disrupt normal

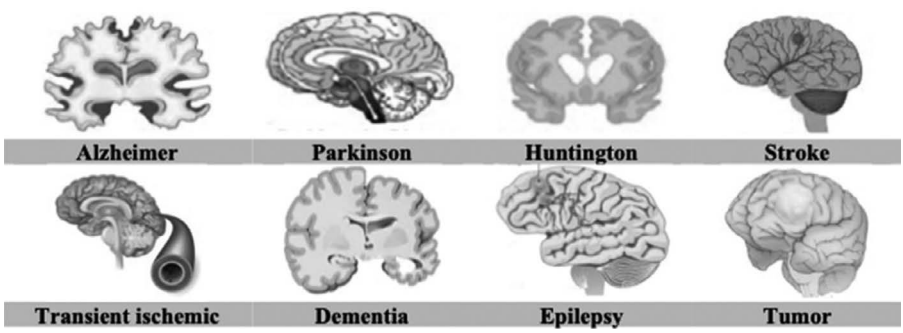

FIGURE 1.3 Pictorial representation of brain with various disorders.

neural functions. The most prominent symptoms include cognitive decline, memory loss, and motor dysfunction. For instance, in Alzheimer's disease, the buildup of beta-amyloid plaques and tau tangles contributes to the destruction of neurons responsible for memory and learning, leading to profound cognitive impairments [11]. Parkinson's disease specifically affects the dopaminergic neurons in the substantia nigra region of the brain. The depletion of dopamine, a neurotransmitter crucial for regulating movement, results in a range of motor symptoms, including tremors, muscle rigidity, and bradykinesia (slowness of movement). Over time, these symptoms progress, leading to difficulty in performing even simple tasks [12]. In contrast, MS is an autoimmune disorder rather than a classic neurodegenerative disease. The immune system mistakenly targets and damages the myelin sheath, the protective covering of nerve fibers, impairing the transmission of signals between the brain and several parts of the body. As the damage accumulates, individuals experience muscle weakness, vision problems, and overwhelming fatigue [13].

Table 1.1 depicts various types of neurodisorders with their cause and symptoms. Cerebrovascular disorders, such as stroke and transient ischemic attacks (TIA) [14], are caused by interruptions in the blood supply to the brain. These interruptions, often the result of blood clots or the rupture of blood vessels, deprive brain cells of oxygen, leading to cell death. The consequences can be severe, including paralysis, difficulties with speech, and cognitive impairments. In the case of a stroke, the damage may be permanent, while TIAs serve as warning signs of potential larger strokes [15]. Furthermore, seizure disorders like epilepsy stem from abnormal electrical activity within the brain. Due to electrical disturbances, seizures will result, which manifest as convulsions, loss of consciousness, or sensory disruptions. Seizures [16] vary in intensity and frequency and can significantly disrupt an individual's life if left untreated.

Migraines, triggered by genetic and environmental factors, cause intense headaches, nausea, and light sensitivity [17]. Amyotrophic lateral sclerosis (ALS), often of unknown origin, leads to progressive muscle weakness, speech difficulties, and eventual paralysis [18]. Neurodevelopmental disorders, such as ASD and ADHD, are associated with atypical brain development that can manifest in early childhood as social, communicative, or attention-related challenges [19]. Infectious causes, such as bacterial, viral, or parasitic infections, affect the nervous system, exemplified by conditions like meningitis or encephalitis [20]. Genetic mutations may lead to inherited neurological conditions, such as familial forms of Alzheimer's disease or muscular dystrophy [21]. These diverse causes highlight the complexity and multifaceted nature of neurological disorders. Huntington's disease, a genetic disorder, causes involuntary movements, cognitive decline, and mood changes [22]. Neuropathy, commonly resulting from diabetes or toxins, leads to numbness, pain, and tingling in extremities. Cerebral palsy, typically caused by brain damage during birth, results in motor impairments and poor balance [23]. Dementia, often due to age-related brain degeneration, results in memory loss and cognitive impairment. Finally, Guillain-Barré syndrome, an autoimmune disorder triggered by infections, causes muscle weakness and breathing difficulties [24]. These disorders, while varied in their causes, often share symptoms related to neurological dysfunction, emphasizing the complex nature of the nervous system. This overview of neurological disorders

TABLE 1.1
Neurodisorders Causes and Symptoms

Category	Cause	Symptoms
Alzheimer's disease	• Age-related degeneration • Genetic factors • Accumulation of amyloid plaques	• Memory loss, confusion • Cognitive decline • Difficulty speaking and understanding language
Parkinson's disease	• Loss of dopamine producing neurons, genetic mutations	• Tremors, muscle rigidity • Slowed movement, balance issues
MS	• Autoimmune attack on myelin sheath • Genetic and environmental factors	• Muscle weakness • Numbness or tingling • Fatigue, vision problems • Loss of coordination
Stroke	• Blood clot (ischemic stroke) • Haemorrhage (bleeding in the brain)	• Sudden numbness or weakness • Difficulty speaking or understanding speech • Vision problems, loss of coordination
Epilepsy	• Unusual electrical activity in the brain • Brain injury, genetic factors	• Seizures • Temporary confusion • Loss of awareness or consciousness
Migraine	• Genetic predisposition • Hormonal changes • Environmental triggers	• Intense headaches • Sensitivity to light and sound • Nausea and vomiting
Amyotrophic lateral sclerosis (ALS)	• Unknown (may involve genetic mutations or environmental factors)	• Muscle weakness • Difficulty speaking, swallowing • Paralysis, breathing difficulties
Huntington's disease	• Genetic mutation in the huntingtin (HTT) gene	• Involuntary movements • Cognitive decline, behavioral changes
Neuropathy	• Diabetes, infections • Autoimmune diseases, toxins	• Numbness or tingling, pain • Muscle weakness
Cerebral palsy	• Brain damage during birth or early childhood • Infections	• Motor skill impairment • Muscle stiffness • Poor balance and coordination
Traumatic brain injury (TBI	• External trauma (e.g., accidents, falls)	• Headaches, memory loss • Mood swings, difficulty concentrating • Dizziness and confusion
Dementia	• Degeneration of brain tissue • Vascular damage • Genetic factors	• Memory loss, cognitive decline • Confusion • Behavioral changes
Guillain-Barré syndrome	• Autoimmune attack on peripheral nerves • Often triggered by infections	• Muscle weakness, difficulty walking • Tingling in extremities • Breathing difficulties

highlights the complex mechanisms and varied symptoms associated with conditions that affect the nervous system. Each disorder requires tailored medical intervention, focusing on both managing symptoms and, where possible, slowing disease progression.

1.1.4 Diagnosis of Neurological Disorders Using Neuroimaging Techniques

Neuroimaging remains a cornerstone in the diagnosis of neurological disorders. Neurological disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, and MS, often progress over time. Early diagnosis helps with prompt intervention, which can slow the progression of the disease, improve quality of life, and in some cases halt further damage. Diagnosing neurological disorders has evolved significantly in recent years, with advancements in technology and medical understanding improving accuracy, speed, and depth of diagnosis. Some of the notable trends and techniques in diagnosing neurological disorders include: Techniques like MRI and CT scans provide detailed images of the brain, aiding in the detection of conditions such as stroke, brain tumors, and MS [25]. More advanced versions like functional MRI (fMRI) allow real-time tracking of brain activity by measuring blood flow, useful in diagnosing epilepsy and neurodegenerative diseases [26]. These techniques allow researchers to visualize brain activity, map neural pathways, and investigate the underlying mechanisms of cognition and behavior. In this section, we explore various neuroimaging methods, each offering unique insights into the brain's functioning.

Structural MRI provides detailed images of brain anatomy, helping to identify brain abnormalities, such as tumors or damage [27]. Functional MRI measures brain activity by detecting changes in blood flow, allowing researchers to observe which areas of the brain are active during specific cognitive tasks. Positron emission tomography (PET) scans [28] can detect amyloid plaques and tau tangles, which are hallmark biomarkers of Alzheimer's, allowing early diagnosis before significant cognitive decline occurs. Radioactive tracers [29] are used to map areas of the brain that consume more energy, typically highlighting regions involved in certain functions like memory, language, and emotion.

Electroencephalography (EEG) is widely used to diagnose epilepsy by recording electrical activity via electrodes placed on the scalp, making it useful for studying temporal dynamics of cognitive processes with high time resolution. It can detect abnormal patterns that indicate seizures and is also used to assess sleep disorders and monitor brain activity in comatose patients [16]. Magnetoencephalography (MEG) measures the magnetic fields produced by neural activity, offering precise temporal resolution while also mapping brain function spatially [30]. Diffusion tensor imaging (DTI) is a form of MRI that visualizes white matter tracts, helping to map the brain's intricate network of connections and studying conditions like MS and brain injuries [31]. near-infrared spectroscopy (NIRS) is a noninvasive method that uses infrared light to monitor blood oxygenation, providing insights into brain function, especially in infants or during motor tasks [32]. Each of these methods

provides a different perspective, contributing to a holistic understanding of the brain. Although each imaging modality has its strengths and limitations, advancements in neuroimaging technology continue to expand our ability to explore brain function in health and disease.

1.1.5 Technological Advancements in Neurodisorder Analysis

Recent advancements in neuroscience and technology, however, have dramatically transformed the landscape of neurodisorder analysis. Breakthroughs in neuroimaging, computational modeling, and artificial intelligence are paving the way for earlier diagnosis, personalized treatments, and a deeper understanding of brain dysfunction. Following are the technological advancements that not only enhance our understanding of neurodisorders but also offer hope for earlier, more accurate diagnoses and the development of novel, individualized treatments, significantly improving patient outcomes.

AI and ML have revolutionized neurodisorder analysis by enabling pattern recognition in large, complex datasets. AI models can now predict the progression of neurodegenerative diseases, differentiate between various neurodisorders, and identify biomarkers that are often undetectable through traditional methods [33]. Deep learning models trained on brain imaging data have significantly improved diagnostic accuracy and provided predictive insights into treatment responses for conditions like MS and epilepsy [34].

With the growing understanding of the genetic basis for many neurological disorders, genetic testing has become an essential diagnostic tool, particularly for diseases like Huntington's disease, Parkinson's disease, are various forms of epilepsy [35]. Advances in next-generation sequencing (NGS) technologies allow for the rapid sequencing of genes, aiding in early diagnosis and personalized treatment. The identification of biomarkers for neurodegenerative diseases is a growing area of research. Cerebrospinal fluid (CSF) analysis to detect proteins like amyloid-beta, tau, and alpha-synuclein is helping to diagnose diseases such as Alzheimer's and Parkinson's disease [36]. Blood-based biomarkers are also being developed for noninvasive diagnosis [37]. Electromyography (EMG) and nerve conduction studies (NCS) are used to assess the health of muscles and the nerves controlling them. EMG and NCS are critical in diagnosing peripheral nerve disorders, such as neuropathy, and neuromuscular junction diseases like amyotrophic lateral sclerosis (ALS). MEG records the magnetic fields produced by neuronal activity in the brain and is useful in pinpointing seizure locations in epilepsy patients. It provides greater spatial resolution than EEG and is a valuable tool for presurgical planning in epilepsy [38]. Wearable devices such as smartwatches and biosensors are emerging as diagnostic tools for neurological disorders. They continuously monitor physiological data like movement, heart rate, and sleep patterns, which can help in diagnosing and managing conditions like Parkinson's disease and epilepsy [39]. With advancements in computational tools, cognitive testing has gone digital. Cognitive assessments using apps and online platforms are being used to detect early signs of cognitive decline or memory impairment, often in the context of dementia [40].

1.1.6 Treatments for Neurological Disorders

Treating neurological disorders requires a multidisciplinary approach that often includes medication, rehabilitation, surgery, and cutting-edge therapies such as neurostimulation and gene therapy. The choice of treatment varies depending on the type and severity of the disorder, with recent advancements improving the management and outcomes of conditions such as Alzheimer's, Parkinson's, MS, and epilepsy.

Medications remain the cornerstone of treatment for many neurological disorders. For example, levodopa is widely used to manage Parkinson's disease by replenishing dopamine levels in the brain [41]. Similarly, anticonvulsants, such as valproate and carbamazepine, are standard treatments for controlling seizures in epilepsy [22]. In Alzheimer's disease, cholinesterase inhibitors and NMDA receptor antagonists, like donepezil and memantine, help slow cognitive decline. Rehabilitation, including physical therapy, occupational therapy, and speech therapy, plays a critical role in managing the symptoms of neurological disorders, particularly after strokes or traumatic brain injuries. Rehabilitation helps patients regain motor skills, improve speech, and maintain cognitive functioning. In certain cases, surgery is required to treat neurological conditions. For instance, deep brain stimulation (DBS) is an established surgical procedure for Parkinson's disease and epilepsy, involving the implantation of electrodes that modulate abnormal brain activity [42]. Epilepsy surgery, where parts of the brain responsible for seizures are removed, is another option for patients with drug-resistant epilepsy [43]. Neurostimulation techniques, including transcranial magnetic stimulation (TMS) and vagus nerve stimulation (VNS), are gaining prominence in the treatment of neurological disorders like depression and epilepsy. TMS involves using magnetic fields to stimulate nerve cells in the brain, helping with depression resistant to other treatments, while VNS uses electrical impulses to stimulate the vagus nerve to control seizures [16].

Gene therapy and stem cell research are pioneering areas offering potential cures for previously untreatable neurological disorders. In conditions like spinal muscular atrophy (SMA), gene therapy using Zolgensma has been a breakthrough by addressing the genetic root cause of the disorder [44]. Stem cell-based therapies are being explored for their potential to regenerate damaged neural tissue, with early success in conditions such as MS [27] Lifestyle modifications and complementary therapies [45] can also support neurological health. Mindfulness, yoga, and acupuncture have been found to alleviate symptoms and improve quality of life for patients with chronic neurological conditions [46].

With the ongoing integration of cutting-edge technologies like machine learning, neurogenetics, and stem cell research, the future of neurological disorder treatment is poised to become more personalized and effective. These advancements bring hope not only for better management of symptoms but also for potential cures to previously untreatable conditions.

1.1.7 Recent Research Advancements in Neurodisorder Treatments

In recent years, significant evolution in the treatment of neurological disorders have emerged, offering new hope for patients facing conditions that were once

deemed untreatable or difficult to manage. Table 1.2 summarizes the advancement of research findings in treating neurodisorder diseases. However, breakthroughs in neuropharmacology, gene therapy, neuromodulation, and specialized medicine have revolutionized the therapeutic landscape, improving both patient outcomes and quality of life.

The rapid progress in treating neurological disorders over the past five years has transformed the outlook for many patients. From gene therapy to targeted neurostimulation, these innovations offer promising new avenues for managing and potentially

TABLE 1.2
Research Advancement in Treating Neurodisorders

Neurological Disorder	Research Advancement	Description	Authors
Alzheimer's disease	Anti-amyloid drugs (Aducanumab)	Targeting amyloid-beta plaques to slow cognitive decline in early Alzheimer's	[47], Alexander et al., 2021
Parkinson's disease	Deep brain stimulation (DBS)	Targeting more precise brain areas, improving motor function and reducing side effects	[42], Benabid et al., 2020,
Multiple sclerosis (MS)	Disease-modifying therapies	Ocrelizumab, a B-cell depleting therapy, shown to slow progression of primary progressive MS	[48], Hauser et al., 2020
Spinal muscular atrophy (SMA)	Gene therapy (Zolgensma)	One-time gene therapy targeting the genetic cause and improving motor function in infants	[44], Mendell et al., 2019
Epilepsy	Responsive neurostimulation (RNS)	Implantable device delivering targeted electrical stimulation to prevent seizures	[16], Fisher et al., 2021
Stroke	Endovascular thrombectomy	Mechanical clot removal for treating ischemic stroke	[49], Campbell et al., 2019
Amyotrophic lateral sclerosis (ALS)	Tofersen antisense therapy	Antisense oligonucleotide therapy for patients with this genetic subtype	[50], Miller et al., 2022
Migraine	Monoclonal antibodies	Monoclonal antibodies prevent migraine attacks	[17], Goadsby et al., 2020
Huntington's disease	RNA interference therapies	Therapies targeting the huntingtin gene to reduce its production	[51], Tabrizi et al., 2020
Traumatic brain injury (TBI)	Transcranial magnetic stimulation (TMS)	Used to enhance cognitive rehabilitation to improve memory and executive functions	[52], Nielson et al., 2021
Autism spectrum disorder (ASD)	Oxytocin-based therapies	Oxytocin nasal spray to improve social behaviors and emotional responses	[53], Parker et al., 2021
Chronic pain	Neuromodulation	Treating chronic pain associated with neurological disorders	[54], Deer et al., 2020

curing neurological diseases. As research continues to evolve, the future holds the potential for even more personalized and effective treatments, significantly improving the lives of those affected by these debilitating conditions.

1.1.8 Precautionary Measures against Neurological Disorders

Many neurological disorders are linked to genetic factors or aging, but there are several precautionary measures that individuals can take to reduce the risk of developing or exacerbating these conditions. These measures, primarily centered on maintaining overall brain health, can help prevent disorders such as stroke, dementia, Parkinson's disease, and other cognitive impairments. A balanced diet rich in antioxidants, vitamins, and healthy fats is crucial for brain health. The Mediterranean diet, with fruits, vegetables, whole grains, fish, and healthy fats like olive oil, has been linked to a lower risk of Alzheimer's disease and other neurodegenerative disorders [55]. Omega-3 fatty acids, found in fish and flaxseed, are particularly beneficial for reducing inflammation and protecting neurons. Regular exercise supports neurogenesis, improves blood flow to the brain, and reduces the risk of stroke and cognitive decline. Aerobic exercises like swimming, walking, and cycling have been shown to enhance memory, executive function, and overall cognitive health [56]. Consistent physical activity can also mitigate the progression of conditions like Parkinson's disease.

Engaging in mental exercises such as puzzles, learning new skills, reading, or playing musical instruments helps keep the brain active and promotes neuroplasticity. Studies suggest that lifelong learning and cognitive training may minimize the risk of dementia by improving cognitive reserve [57]. Chronic stress is linked to a higher risk of neurological disorders, particularly anxiety, depression, and cognitive decline. Practices like mindfulness meditation, yoga, and deep breathing can help reduce stress and improve emotional regulation, contributing to better long-term brain health [58]. Sleep is vital for the brain's restoration, memory consolidation, and removal of toxic waste products. Chronic sleep deprivation is interrelated with an increased risk of neurodegenerative diseases like Alzheimer's. Ensuring seven to nine hours of quality sleep per night and maintaining a consistent sleep routine can significantly benefit brain health.

Avoiding substances that can harm the brain, such as excessive alcohol, recreational drugs, and tobacco, is essential for preventing neurological disorders. These substances can lead to neuron damage, impair cognitive function, and increase the risk of conditions like stroke and dementia [59]. For stroke and cognitive decline, high blood pressure, high cholesterol, obesity, and diabetes are major risk factors. Managing these conditions through medication, diet, and lifestyle modifications helps maintain healthy blood flow to the brain and prevents damage to neurons [60]. Routine medical checkups can prevent conditions like stroke or diabetes, both of which are closely linked to neurological disorders. By adopting these precautionary measures, individuals can remarkably reduce their risk of developing neurological disorders and improve their overall brain health. While not all neurological disorders are preventable, a proactive approach to brain health can mitigate risk factors and enhance cognitive resilience throughout life.

1.2 CONCLUSION

The field of neurological disorders continues to be one of the most complex and evolving areas of medical science. As this chapter has explored, neurological conditions such as Alzheimer's disease, Parkinson's disease, epilepsy, and neurodevelopmental disorders have profound impacts on individuals and society. Despite the challenges in diagnosing and treating these disorders, advancements in neuroimaging techniques, genetic research, and therapeutic interventions have significantly improved our understanding of these conditions. Technological innovations, including artificial intelligence and gene therapy, offer new hope for more accurate diagnoses and personalized treatments. These breakthroughs are paving the way for managing neurological disorders more effectively, ultimately enhancing the quality of life for patients. Furthermore, an increased focus on preventive measures, such as healthy lifestyle choices and cognitive training, underscores the importance of proactive approaches to brain health. As research continues to advance, the potential for new treatments and preventative strategies grows, offering promising future directions for addressing the global burden of neurological disorders. By integrating cutting-edge technology with personalized medicine and rehabilitation, the medical community is better equipped to meet the needs of individuals affected by these complex conditions.

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2 Navigating the Complexities of the Brain *Challenges and Opportunities in Computational Neurology*

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2.1 INTRODUCTION TO COMPUTATIONAL NEUROLOGY

Computational neurology is the independent subdivision that involves using methods that belongs to neuroscience and creative mathematical models of the brain and the nervous system. These models act and analyze complex neural problems and processes, which involves in neuroperformances, interneuron relations, and neuropathological diseases. Therefore, when we use this in our daily lives, computational applications help create new developments in neurology about the functioning of the brain. Applications like this may be beneficial to scholars and junior doctors to discover new treatments for neurological disorders. This enhances the brain−computer interface method and helps to understand the impact of head injuries on human behavior.

Following are the methods that get to know about the behavior of the brain [1]:

1. Disease diagnosis and treatment: Conditions like epilepsy and Parkinson's disease affect neural networks. It is difficult to imitate these conditions on a computer, so instead they are simulated. Such simulations are essential to researchers so that they can provide crucial ideas for determining some of the fundamental characteristics of the disease and the required treatment.
2. Brain−computer interfaces: Neurological computation is utilized to construct and develop the brain−computer interface (BCI), where people manage devices without actually thinking about them. The applications of BCI can aid those with motor disorders like language, emotional, cognitive, hearing, and visual impairment, especially in the area of assistive technology, communication, and neurology for patients with physical disorders during their rehabilitation.

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3. Neural prosthetics: Neural prosthetic devices are designed and analyzed to determine the shapes of neural implant devices proposed that are favorable and can be used by a person who become paralyzed through the spine or any other reasons.
4. Brain imaging analysis: Multiple methods are used to analyze the data that are aggregated from various procedures like MRI and electrical mapping processes. Brain imaging complements the beneficial strategies through which scientists research where and to what level the human brain involves and interacts with a range of diverse mental processes and neuropsychiatric illnesses.

Neurocomputing is a branch that deals with mathematical and computing neurology to gain knowledge about the human brain and other related organs. It refers to the developmental process of computational models, algorithms that can analyze and develop neural systems through the real environment. Computational neurology is evolving rapidly by combining neuroscience and computer science to understand the structure and functions of the brain. There are some features like modern developments, futuristic tools, and potential revolutionary impact of computational neurology. The following are modern development tools that help in neurology:

1. Neural networking: The neural networking method is inspired by structure of the brain. The artificial intelligence (AI) system can learn and adapt as the human brain to understand and solve new age problems in an accurate way. The neural network will help to adapt to the problems faced in future. In this method, neurology can adapt to the situation and can understand the difficulty in it to solve problems in an inspiring way.
2. Neuroinformatics: It helps to develop database and tools that can analyze brain data. Neuroinformatics can also analyze new functions in brain to upgrade or to develop new features in treating people in a possible way without failing.
3. Simulations: Computational models can mimic brain activity to help researchers test hypotheses. It is an emerging approach to integrate the knowledge dispersed throughout the field of neuroscience.

Revolutionary impact:

1. Personalized medicine: Treatments are tailored for neurological disorders. Such treatments include a variety of approaches, like medication, rehabilitation, assistive devices, pain management, etc.
2. Brain enhancement: It has the potential for cognitive enhancement and memory augmentations.
3. Neurological disorder treatment: New insights and treatments for Alzheimer's, Parkinson's, and similar disorders.

Futuristic tools:

1. Neural dust: This is the method to insert tiny implantable sensors to monitor brain activity.
2. Optogenetics: It uses light to control specific brain cells.
3. Quantum computing: This may enable simulations of complex brain processes.

Figure 2.1 explains the schematic of computational and theoretical approaches in computational neurology, from fundamental research to clinical applications. Dark gray boxes are small or focused data, light gray boxes are larger or more heterogeneous data, and arrows represent relationships. Sometimes AI, data mining, and machine learning methods are also used in relatively smaller or less heterogeneous data to guide mechanistic modeling. Here we can see the focused data to the clinical decision support system (CDSS) have many steps to follow and get the result. Here small and focused data are processed to models like mechanistic modeling and probabilistic or statistical analysis. In the same way, large and heterogeneous data will be processed, but in this process of modeling no mechanistic modeling process will be included. Only probabilistic and statistical analysis modeling will be used as primary modeling tools.

Modeling neural dynamics involves developing mathematical and computational models to understand the behavior of neural systems, from single neurons to large-scale brain networks. By modeling neural dynamics, researchers and clinicians can better understand the brain, develop more effective treatments, and improve human performance, leading to a better quality of life. Neuroimaging machine language (ML) is the application of new computational methodologies to study and interpret brain image data [3]. The future of this field also looks very promising, as a breakthrough in the identification of neurological disorders and the development of the individual plan for their treatment are guaranteed.

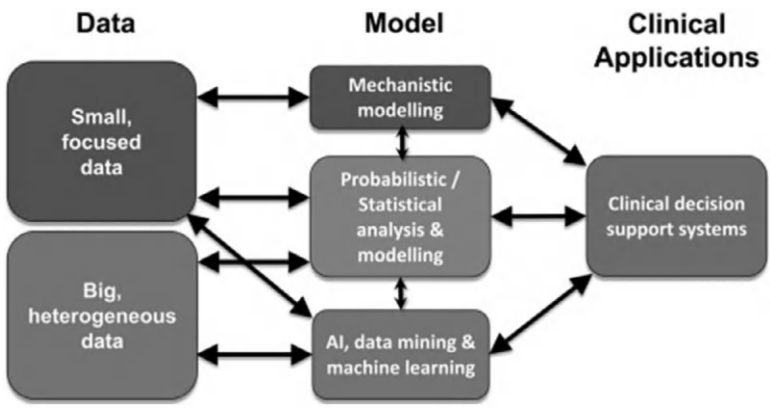

FIGURE 2.1 Architecture of data mining neurology [2].

Some applications of machine learning in neuroimaging include [4]:

- Image segmentation: ML-based methods can be utilized for segmenting respective areas in MRI and CT scans to identify diseases in their early stages, such as Alzheimer's or multiple sclerosis.
- Disease classification: Incorporating first principles and analysis of aspects of neurological disorders as features of the dataset allow machine learning models to be developed that can discern between various disorders from images and assign more precise recommendations for management. Patterns that could be identified through brain imaging datasets could help train machine learning models to distinguish between various neurological disorders accurately, resulting in precise diagnosis and treatment recommendations.
- Biomarker discovery: Biomarker discovery can happen because of machine learning algorithms; they can carry out a detailed analysis of large databases of imaging scans of the brain and find correlations with certain diseases or conditions that are hard to detect otherwise but could be used as biomarkers for diagnosis of the disease at an early stage or for monitoring the progress of the disease.
- Treatment response prediction: This knowledge of predicted responses to treatments can be captured using AI techniques such as machine learning models where the ability to forecast how an individual patient will respond to the specific form of treatment could be determined from brain imaging. By scrutinizing patients' brain images, machine learning models show predictions regarding their responses to a particular therapy, thereby enabling better management by doctors who take into account individual patient differences.

In terms of practical applications, based on the advances in machine learning technologies, neuroimaging studies can enhance the daily lives of patients by offering better diagnoses, prognoses, and treatment solutions for their diseases and by explaining the biological processes that contribute to neurological disorders. Moreover, it opened up opportunities for the invention of new technologies and devices for early diagnosis and status progressional for managing worse brain disorders and improving the quality of life of people affected.

2.2 NEUROINFORMATICS AND BIG DATA

Neuroinformatics combines neuroscience, computer science, and information technology to examine the brain and its related functions. Neuroinformatics is therefore a field that concentrates on developing tools as well as techniques for gathering, analyzing, and interpreting huge amounts of data about the brain including genetic information, clinical data, and neuroimages.

Some notable examples include [5]:

- Disease classification: Patterns present in brain imaging datasets may be able to train machine learning models to accurately distinguish between different neurological disorders, thereby leading to accurate diagnosis and subsequent treatment recommendations.

- Biomarker discovery: ML algorithms can analyze large-scale datasets from finally in imaging scans to detect subtle patterns associated with specific diseases or conditions that could act as possible biomarkers for early detection or monitoring of the progression of these diseases.
- Drug innovation and development: Through using neuroinformatics and big data analytics, one can find potential drug targets, anticipate their responses to drugs, and optimize treatment approaches for neurological diseases.
- Brain mapping and connectivity analysis: Neuroinformatics tools enable the study of brain connectivity networks as well as brain region mapping; it lets us know how various parts of the brain communicate and work in tandem.

Therefore, if neuroscience leverages neuroinformatics along with big data, researchers will enhance their knowledge about the brain, improve diagnosis accuracy, come up with individualized treatment options, follow these methods to resolve related disorders, and better understand the problems that these brain-related neurodiseases will pose in the future.

2.3 COMPUTATIONAL TOOLS AND SOFTWARE

In neuroinformatics and big data, computational tools and software are used to refer to the programs that help in analyzing, processing, and interpreting massive neural data. These tools allow scientists to:

- Store, manage, and share their data
- Evaluate complex brain functions
- Interpret the results and visualize them
- Merge different sources of data

Some examples of computational tools and software include [6, 7]:

- Freesurfer: Automated reconstruction and analysis of brain structures from MRI data
- FSL: A comprehensive library for MRI and functional fMRI analysis
- AFNI: fMRI data analysis and visualization software
- NEST: Simulator for large-scale neural networks
- BrainPy: Python library for neural data analysis and modeling
- NeuroDebian: Neuroimaging and neuroinformatics software platform
- OpenNeuro: Open access neuroimaging repository

The computational tools and software applications include:

1. Research on neurological disorders
2. Development of a BCI
3. Neuroscientific discovery-making

4. Personalized medicine services
5. Drug development industry
6. AI and ML
7. Healthcare analytics
8. Neuroeducation (NE) and cognitive enhancement (CE)

These computational tools thereby allow researchers to unlock insights from complex neural data that drive innovation within neuroscience as well as the healthcare technology sector.

2.4 NEURAL ENGINEERING AND NEUROMODULATION

The development of innovative technologies for understanding, interfacing, and modulating neural activities of the brain is what neural engineering and neuromodulation involve. These disciplines are a mix of engineering principles, neuroscience as well as computer science, aiming to:

- Build brain–machine interfaces (BMIs)
- Construct neural prosthetics or implants
- Design neuromodulation therapies

Neural engineering and neuromodulation have the goals of [8]:

- Restoring function in neurologically damaged individuals
- Increasing intelligence
- Treating mental health disorders
- Enhancing human performance

Neural engineers value the heterogeneity of their colleagues and seek out multiple perspectives to inform the development of their technology. The subspecialties are illustrated in Figure 2.2. This illustration highlights the professionals actively involved in developing and translating neural technology. These professionals include subspecialties ranging from scientists, technical experts, clinicians, and others involved in the clinical setting.

Applications and uses of [9, 10] neural engineering include:

1. BCIs: providing communication, control, and interaction
2. Neuroprosthetics: substitute or repair injured neural systems
3. Neuromodulation therapies: for example, Parkinson's disease, epilepsy, and depression treatments
4. Neurological disorder treatment: producing new therapies for paralysis, Alzheimer's disease, and stroke
5. Cognitive enhancement: aid attention, memory building, and learning
6. Neurofeedback training: teach self-control over brain functioning
7. Neurological rehabilitation: boost recovery abilities and enhance plasticity
8. Neuroscientific research: explore brain functioning as well as behavior patterns

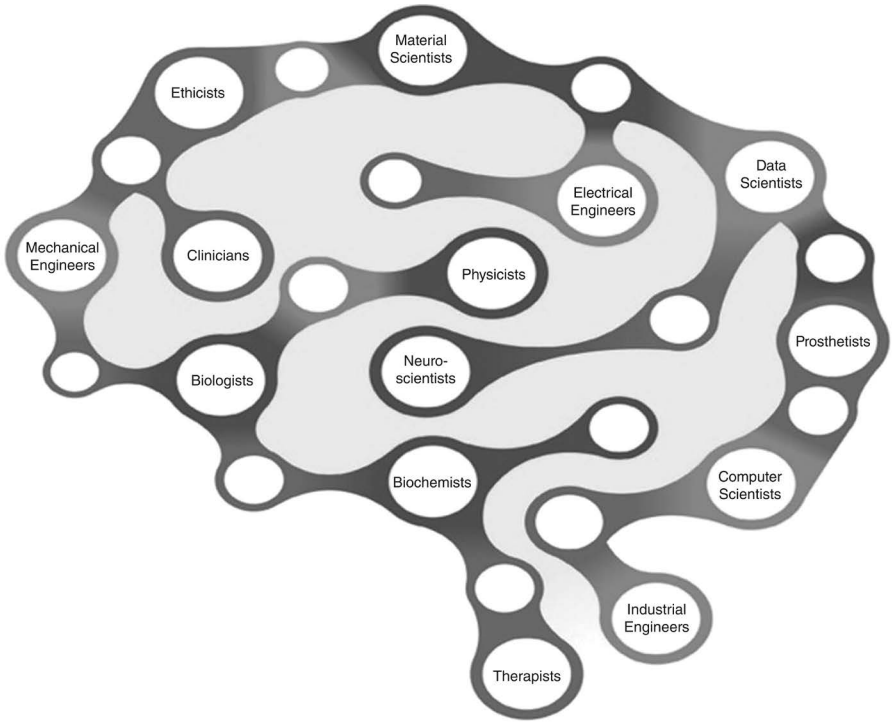

FIGURE 2.2 Neural engineers and the professional chain [8].

Some examples of neural engineering and neuromodulation include [11, 12]:

1. Deep brain stimulation (DBS): electrodes that are implanted in the body to manipulate signals transmitted from the brain; used as a treatment for Parkinson's disease, dystonia, and obsessive-compulsive disorder.
2. Transcranial magnetic stimulation (TMS): a procedure that involves the use of magnets to influence activities of desired areas in the brain to cure depression, anxiety, and chronic pain.
3. BCIs: Allow patients with paralysis, neural disorders, or tetraplegia, who could not speak or manipulate anything, to use their minds to command devices and participate in social activities.
4. Neuroprosthetics: prosthetics such as artificial limbs and organs that could be operated through signals from the brain to enable those who have had their limbs or organs amputated or damaged to have their limbs or organs replaced.
5. Neurofeedback training: forms mental and neural pathways, which increases attention, memory, and overall intellectual performance.
6. Optogenetics: exploits light to manipulate granulocyte-macrophage (GM) brain cells, map the mind/brain, and influence behaviors.

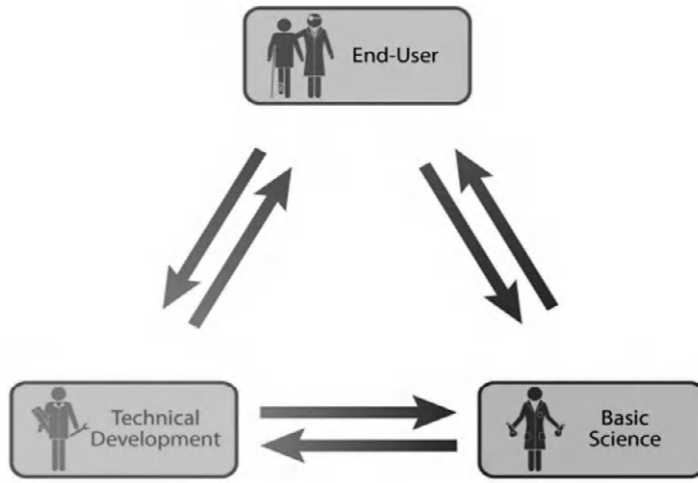

FIGURE 2.3 Neurotechnology developmental cycle [13].

7. Neural dust: innovative nanobots inserted into the human skull that record the brain's signals and may cure brain-related diseases.
8. Graphene-based BCIs: semi- and fully implantable systems that can record and interpret signals from the brain so that devices can be operated with a high degree of accuracy.

All of these progressive technologies can bring significant change to the healthcare industry, act socially beneficial by positively affecting the patient's standard of living, and alter the human condition for the better. Figure 2.3 explains about the developmental cycle of the neurotechnology process.

2.5 TOWARD PERSONALIZED MEDICINE IN NEUROLOGY

Personalized medicine in neurology is defined as the practice of providing medical treatment concerning a patient's genetic, environmental, and social individuality. Some key aspects include [14, 15]:

- Genomic medicine: in its simplest form, utilizing genetic information to forecast susceptibility to diseases and the likely individual response to treatment
- Precision neurotherapeutics: an individualized approach to treatment using the possibilities of pharmacogenomics to create highly specific treatments for certain dysfunctions in the patient's brain
- Pharmacogenomics: changing or modifying the type of drugs given depending on the patient's genetic makeup
- BCIs: designing neural interfaces to be personalized to the point that one can optimize their use for communication as well as control

- Neuroimaging biomarkers: to develop imaging markers that would define the disease early and help monitor the effectiveness of the treatment modalities employed
- Personalized neurorehabilitation: assuming individual rehabilitation strategies by checking with the afflicted segment of the brain and typical demeanor
- Lifestyle medicine: personalizing nutrition, exercise, and other aspects of a lifestyle according to a person's genetic makeup and functions of the brain

Applications and uses of key aspects that indicate personalized medicine in neurology include:

1. Genomic medicine: introducing genetics to help identify tendencies and reactions to intervention in diseases.
2. Precision neurotherapeutics: the service provision that would entail the application of specialized pharmacology that would in effect be targeted toward treatment that in most cases is concerned with specific aspects of a given patient's brain.
3. Pharmacogenomics: employing the reaction that occurs at the genetic level of an individual using pharmacogenomic and pharmacogenetic testing to establish which drug is appropriate for the patient or the most suitable dose.
4. BCIs: methods and approaches for tailor-made neural systems.
5. Neuroimaging biomarkers: identifying the imaging markers useful in the early detection of the disease or in following up those treatments or therapies that are being offered to the patients.
6. Personalized neurorehabilitation: the competency of establishing and passing such rehab charts due to the evaluation of brain functions and behavior.
7. AI in neurology: applying AI not only in the primary inherent big data analysis but also in the prognosis of that concrete individual treatment plan.

The concept of individualized patient healthcare professional treatment in neurological science relates to increasing the probabilities of enhanced handling, recovery, and patient satisfaction with their treatment regimen tailored to suit the specific needs of the patient.

Computational neurology involves computational methods and applying mathematical formulations to understand and become involved briefly in model neurological processes. These methods and models offer different types of perspectives and tools to analyze and understand the complex dynamics of the nervous system from the standpoint of computational neurology. Some methods are explained in Table 2.1 [16].

TABLE 2.1
Computational Neurology Methods

1. Neuronal models	• Hodgkin–Huxley model: This model describes how any potential action in neurons is initiated and propagated. It uses a set of differential equations to model the membrane potential ***V(t),*** ionic current, and gating variables: $$C_m \frac{dV}{dt} = -I_{ion}(V,\ n,\ m,\ h) + I_{ext}$$ • Leaky integrate-and-fire (LIF) model: This is a similar model that describes a neuron's membrane potential V(t) with leakage and input currents: $$C_m \frac{dV}{dt} = -\frac{V - E_L}{R_m} + I(t),$$ where C_m is the membrane capacitance, I_{ion} is the total ionic current, and I_{ext} is the external current. The ionic current I_{ion} is given by: $$I_{ion} = gNam3h\left(V - E_{Na}\right) + gKn^4\left(V - E_k\right) + gL\left(V - E_L\right),$$ where gNa, gK, and gL are the conductance's of sodium, potassium, and leak channels, respectively, and E_{Na}, E_K, and E_L are their reversal potentials. The gating variables m,h, and n follow their own differential equations. R_m is the membrane resistance and E_L is the resting potential. If V reaches a threshold V_{th}, the neuron "fires" and the potential is reset.
2. Network models	• Hopfield network: This type of recurrent neural network serves as an associative memory system. The energy function E for a Hopfield network with binary units can be expressed as: $$E = -\frac{1}{2}\sum_{ij} w_{ij} s_i s_j + \sum_i \theta_i s_i.$$ • Boltzmann machine: This is a stochastic recurrent network that models complex probability distributions. The energy of a state s is: $$E(s) = -\sum_{i<j} w_{ij} s_i s_j - \sum_i b_i s_{i,}$$ where s_i are the binary states, w_{ij} are the weights, and θ_i are the thresholds. The network seeks to minimize this energy function to converge to a stable state. b_i are biases. The probability of a state is given by the Boltzmann distribution: $$P(s) = \frac{e^{-E(s)/T}}{Z},$$ where T is the temperature and Z is the partition function.

(*Continued*)

TABLE 2.1 (*Continued*)
Computational Neurology Methods

3. Signal processing	• Fourier transform: It is used to analyze the frequency components of neural signals. For a signal $x(t)$, its Fourier transform $X(f)$ is: $$X(f)=\int_{-\infty}^{\infty} x(t)e^{-j2\pi ft}\,dt.$$ • Wavelet transform: Wavelet transform provides time-frequency representation of signals. Continuous wavelet transforms (CWT) of a signal $x(t)$ with wavelet function φ is: $$w_x(a,b)=\frac{1}{\sqrt{a}}\int_{-\infty}^{\infty} x(t)\varphi*\left(\frac{t-b}{a}\right)dt,$$ where a is the scale parameter and b is the translation parameter.
4. Information theory	• Mutual information: This measures the amount of information obtained about one random variable through another. For random variables X and Y, mutual info $I(X;Y)$ is: $$I(X;Y)=\sum_{x\in}\sum_{y\in} p(x,y)log\frac{p(x,y)}{p(x)p(y)}.$$
5. Optimization and learning	• Gradient descent: This optimization method is used in training neural networks. For a loss function $l(\theta)$, the update rule is: $$\theta_{t+1}=\theta_t-\dot{\eta}^{\nabla L(\theta_t)},$$ where $\dot{\eta}$ is the learning rate and $\nabla L(\theta_t)$ is the gradient of the loss function with respect to parameters θ.
6. Neurodynamic	• Fitzhugh–Nagumo model (FNM): This model is a simple version of Hodgkin–Huxley model that captures the essential dynamics of excitable systems: $$\frac{dV}{dt}=V-\frac{V^3}{3}-W+I$$ $$\frac{dW}{dt}=\epsilon(V+a-bW),$$ where V is the membrane potential, W is the recovery variable, and ϵ, a, and b are parameters controlling the dynamics.

2.6 CONCLUSION AND FUTURE DIRECTION

Computational neurology has the potential to revolutionize the fields of neuroscience and neurotechnology by providing a deeper understanding of the brain and its functionalities. It uses models like mathematics to simulate neuroprogressive processes. Researchers can gain insights into the underlying mechanism of

neurological disorders, like Alzheimer's, Parkinson's, and epilepsy. This knowledge can be used to develop more effective treatments and interventions for these conditions.

Moreover, computational neurology plays a crucial role in the development of BCIs, which help to improve the quality of life for individuals with severe motor disabilities. Additionally, computational neurology will help to build neural prosthetics, such that devices will restore lost sensors and functions by directly interacting with the nervous system. These prosthetics can give a good change in people who are suffering from spinal cord injuries or any other neurological diseases. Early diagnosis of neurological disorders, BCIs, and neurofeedback training improve skills and neurostimulation therapies and drug developments and use of AI in computational neurology.

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3 Challenges and Opportunities in Computational Neurology

S. Vijayanand and C. Priya

3.1 INTRODUCTION

The human brain is one of the most complex systems in the known universe, consisting of approximately 86 billion neurons that form a vast network of trillions of interconnected synapses [1]. This intricate biological circuitry enables our thoughts, perceptions, behaviors, emotions, and the very essence of consciousness itself. Unraveling the mysteries of how the brain processes information, learns, stores memories, and gives rise to the richness of human experience has been one of the greatest scientific challenges humanity has undertaken. Computational neurology, also known as computational neuroscience, is an interdisciplinary branch of science that integrates knowledge of neuroscience, computer science, physics, mathematics, and other sciences to develop and utilize computational models and simulations in studies on the structure and functions of the brain and nervous system [2]. Computational neurology researches the basic principles and mechanisms driving neural computation, cognition, and behavior by incorporating insight from strong computational methodologies and a wide variety of disciplines. During the last few decades, the exponential increase in computing power was complemented by rapid advances in neuroimaging technologies and access to large-scale neural data to bring computational neurology to the forefront in brain research. Sophisticated computational models and simulations have provided insight into the complex dynamics of neural circuits, the representation of information in the brain, and neural correlates for several cognitive functions previously unmatched [3].

Yet, along with these impressive achievements, the key challenges to computational neurology come from the complexity of the brain and from the limitations of models and methodologies at our disposal. Activities of the brain span a very wide range of spatial and temporal scales, from the nanoscale of molecular and ionic interactions to the macroscopic scales of the organization of brain regions and networks [4]. Capturing this multiscale nature of brain dynamics within a unified computational framework still constitutes one of the major challenges. Besides, the brain is highly plastic and able to adapt; it keeps readapting and reorganizing its neural circuits due to environmental input, learning, and experience throughout its

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life. This dynamic and ever-changing nature of neural computation, in turn, presents another level of difficulty in developing computational models able to represent and account for it with precision.

This chapter will touch on some of the most important challenges pending in computational neurology, including, but not limited to, the problem of the complexity of the brain; the limitations of current data acquisition techniques; issues with model validation; the integration of disciplines and methodologies; and the interpretability of complex computational models. Moreover, we shall discuss exciting opportunities and possible future directions awaiting us as we continue to expand the boundaries of brain research using computational approaches. In returning to these challenges and capitalizing on the newest achievements in machine learning, artificial intelligence, neuromorphic computing, and brain–computer interfaces (BCIs), computational neurology could evoke nothing but breathtaking discoveries that may not only substantially advance the understanding of the brain but also enable the development of radically new applications in such areas as precision medicine, enhancement of cognition, and building smart systems inspired by biological intelligence [5].

What is now required is interdisciplinarity, sharing not only knowledge and insight but embedding these various standpoints and methodologies within one great endeavor. It is only by serious effort across disciplines that the secrets of the brain will be unwoven and the full power of computational neurology unlocked. The major challenge in the field of computational neurology is to take care of the huge complexity of the brain along with the various spatial and temporal scales. The brain contains almost 86 billion neurons at the microscale, with each making several thousand connections with other neurons through synapses. Indeed, the work from this dense interconnectedness gives rise to the amazing ability of information processing by the brain. Similarly, continued development in computational models is put into practice in order to simulate the dynamics of the brain from higher to finer scales. The recent editorial publications published bring out how cognitive function–simulating models and mental disorder–simulating models facilitate grasping not only normal brain activities but also pathological states like schizophrenia and depression [6]. However, even the most negligible percentage of neural circuitry in the brain involves computationally intensive tasks to model and simulate. A single neuron itself is a highly complex computational machine that integrates and processes incoming signals through detailed electrochemical dynamics. The modeling of behavior by billions of interacting neurons, all singular in their properties and again singularly connected with others, quickly becomes computationally infeasible for even the most powerful supercomputers.

The brain also acts over a huge range of spatial scales, from the nanoscale interactions of molecules and ions to the macroscopic organization of brain regions and networks. It is a big challenge to capture the multiscale nature of brain dynamics using current computational models, which tend to focus on one particular scale or level of abstraction. The temporal complexity of brain activity also poses a formidable challenge. Neural computations occur across a wide range of timescales, from the millisecond dynamics of action potentials to the slower processes of synaptic plasticity, learning, and memory consolidation that unfold over hours, days, or even years.

Bridging these disparate timescales within a unified computational framework is an area of active research.

3.2 CHALLENGES IN COMPUTATIONAL BRAIN MODELING

3.2.1 Complexity of Neural Networks

The human brain encompasses approximately 86 billion neurons, each forming connections (synapses) with thousands of other neurons in incredibly dense, recursively networked architectures [7]. The total number of synapses is estimated around 100–500 trillion. This vast, heterogeneous connectivity gives rise to the brain's prodigious information processing capabilities. However, the sheer combinatorial complexity makes modeling entire brain networks a grand challenge for computation. Current neural simulations are highly simplified compared to biological reality, often abstracting away much of the intricate biological details [8]. Capturing the dynamic, nonlinear interactions of such an immense network is extraordinarily difficult, requiring massive computational resources and novel modeling approaches. Even modeling a small fraction of the brain's neural circuitry is a formidable task. For instance, the Blue Brain Project's reconstruction and simulation of a rat cortical microcircuit, comprising around 31,000 neurons and 37 million synapses, required a supercomputer and took years of effort. Scaling such detailed simulations to the level of the entire human brain, with its billions of neurons and trillions of synapses, remains an immense computational challenge.

3.2.2 Bridging Multiple Scales and Modalities

Brain functions and neural coding emerge across multiple spatial and temporal scales, from molecular events within synapses, to neuronal membrane potentials, to network-level oscillations, to systemwide cognitive functions. Bridging these scales in unified computational models is extremely complicated since each scale involves different types of data, theories, and modeling approaches. For example, biophysical models simulate neurons as multicompartment structures based on cable theory, while cognitive models use systems of interacting units approximating brain areas or functions. Integrating bottom-up molecular data with top-down cognitive constraints in a neurobiologically constrained manner is a key challenge [2]. Additionally, the brain exhibits a wide range of dynamics across different timescales, from the millisecond dynamics of action potentials to the slower processes of synaptic plasticity, learning, and memory consolidation that unfold over hours, days, or even years [9]. Capturing these disparate timescales within a unified computational framework remains an open challenge in the field.

3.2.3 Limitations of Neural Data

Despite significant development in multimodal neuroimaging and neural recording techniques using fMRI, PET, EEG, calcium imaging, and multielectrode arrays, at

almost all scales, there are gaps in neural data acquisition both in terms of spatial and temporal resolutions. Most data are a small snapshot of the activity of the brain rather than the complete information flow at any instant of time. Techniques are typically biased either to the particular spatial scale or to a particular temporal scale; for instance, functional magnetic resonance imaging (fMRI) has excellent spatial resolution with poor temporal resolution, while electroencephalography (EEG) has excellent temporal resolution with poor spatial resolution. The invasive nature is also the main limit to most neural recording methods, constraining the extent and duration of data collection, particularly in human subjects. Lacking proper data coverage in a multiscale and multimodal setting places tremendous challenges toward constructing comprehensive multiscale neural models able to represent complex brain dynamics correctly. But the key point to observe is that current neuroscience methods are mostly bound to a restriction of measurement correlate, not directly observing the activity of single neurons and their connections themselves, using blood flow changes or electrical potentials as proxies. This presents a barrier in establishing accurate computational models that can be true representatives of the mechanisms beneath [10].

3.2.4 Data Acquisition Challenge

Another important challenge in computational neurology is the issue of high-quality, comprehensive data on the structure and function of the brain. While modern techniques of neuroscience, including fMRI, EEG, BCI, and multi-electrode arrays, have provided unparalleled insight into the activity of the brain, all these methods still suffer from overwhelming limitations. Several challenges remain in the development of BCIs. Such challenges may involve further real-time neural signal processing, enhancing the accuracy and reliability of BCI systems, and improving user comfort for extended use. While neuroimaging techniques like fMRI offer very good spatial resolution, allowing the researcher to spatially locate brain activity with high spatial precision, their temporal resolution is rather poor, making it difficult or impossible for them to capture rapid dynamics of neural activity occurring on a millisecond timescale. In contrast, techniques such as EEG and magnetoencephalography (MEG) provide excellent temporal resolution but poor spatial resolution, which makes it very difficult to spatially locate sources of activity in the brain with either high precision or accuracy [11]. Moreover, most current neuroscience techniques remain indirect measures in that they usually record correlates of neural activity, such as altered blood flow (fMRI) or electrical potentials (EEG/MEG), rather than directly observing the activity of individual neurons and their connections. This is a formidable obstacle to the creation of realistic computational models that can truthfully capture the real neural mechanisms at a cellular and synaptic level [12].

Another major challenge is to obtain a comprehensive structural dataset on the intricately interconnected neural circuitry of the brain. Although techniques such as diffusion tensor imaging (DTI) and tractography give some insights into the structural connectivity at large scales, they often remain at too low a resolution and specificity to pinpoint exactly which neurons are connected with which [13]. In addition, these techniques cannot easily capture the dynamics of structural plasticity that are

so important in processes like learning and memory formation. New and better data acquisition methodologies will become increasingly important as computational models further increase in complexity and require data at higher resolution across scales and modalities. Several new technologies – nanoelectronics, optogenetics, and molecular sensors – may overcome some of these limitations by allowing more direct and high-resolution recordings of neural activity and connectivity [14]. This might include nanoelectronic devices, like nanoelectrode arrays and nanowire field-effect transistors, which could potentially record the activity of single neurons or even synapses with high spatial and temporal resolution. Another tool known as optogenetics involves the use of genetically engineered light-sensitive proteins for selectively controlling the activity of specific neurons and thus offers a powerful tool for the investigation of neural circuits and the study of causal relationships between neural activity and behavior. Besides, advanced molecular sensors and imaging techniques have been reporting how to observe biochemical processes within neurons and synapses at high spatial and temporal resolution with techniques such as fluorescence resonance energy transfer (FRET) and bioluminescence resonance energy transfer (BRET), among others [15, 16].

3.2.5 The Model Validation Challenge

Even with the most sophisticated computation models and best data, validation of the veracity and predictive capability of such models remains one of the major challenges in the field of computational neurology. Unlike most other scientific disciplines, it is often impossible or difficult to observe and directly measure the underlying modeled process in the brain. While optogenetics and multi-electrode arrays are two popular experimental techniques for obtaining data on model validation, they usually remain confined to particular parts of the brain or specific neural circuits and thus lack generalization to the complex whole-brain dynamics. Additionally, numerous models involve simplifying assumptions or abstractions, which may not accurately capture all the finer details of biological complexity in neural systems [17]. The lack of ground truth data and the inherent complexity of the brain make it difficult to discern whether a computational model is correctly instantiating the underlying neural mechanisms or simply reproduces the observed behavior via other mechanisms or compensatory dynamics. This problem is extremely concerning in the case of the brain's large-scale models and simulations because a great number of parameters and interactions could render disentanglement hard for the actual causal relationships. Besides, the brain is highly plastic; it structurally changes its neural circuitries based on environmental inputs, learning, and experience continuously. This dynamic nature of the working of the human brain adds another layer of complicating factors in the validation of computational models. Since the brain itself is so dynamically changing, the models themselves need to be updated and fine-tuned continuously to keep pace with all the changes that are happening in the neural structure and function [18]. This can be attempted by developing finer methods of model validation and testing, which may include the use of synthetic data or virtual brain models as ground truth references. The improvement of experimental techniques, including closed-loop optogenetics and all-optical electrophysiology, might actually provide a

completer and more accurate dataset from which to validate computational models at all scales [19].

Another promising direction could be the elaboration of more interpretable and explainable computational models that can provide insight into the underlying mechanisms and causal relationships, rather than simply reproducing the observed behavior. Approaches from explainable artificial intelligence (AI) could be adapted and applied to the models in computational neurology, allowing researchers to gain more insights and to validate the inner workings of such complex systems [20]. Finally, solving the model validation problem will be a multifaceted approach: better experimental techniques, better computational methodology, better interpretability, and further knowledge of biological principles and constraints of neural computation [12]. Such work will be accomplished mainly through interdisciplinary collaboration and the integration of a variety of perspectives and methodologies.

3.2.6 The Integration Challenge

Computational neurology is a very broad field, borrowing principles and methods from neuroscience, computer science, physics, mathematics, engineering, and many other disciplines. Whereas this interdisciplinary nature is a clear strength, enabling the combination of various points of view and tools, it also implies a number of complications concerning communication, collaboration, and integration of varied theoretical frameworks and modeling approaches. The barriers to successful communication and knowledge transfer are set by complex disciplinary terminologies, conventions, and conceptual frameworks [8]. For example, "information processing" may mean quite different things to a computer scientist and to a neuroscientist, depending on what might be inferred or assumed from that term – a potential source of misunderstanding or conflict.

Other modeling approaches and techniques may be more appropriate for specific aspects of brain function or for specific spatial or temporal scales. A further challenge is to integrate such various approaches into one coherent computational framework. For instance, biophysically detailed models can describe activities in single neurons or small circuits very well, but abstract models may be more suitable when studying large-scale brain networks or cognitive functions [21]. Overcoming integration challenges requires effective collaboration and sharing of knowledge between researchers from various disciplines. Interdisciplinary training programs, conferences, and research initiatives can help build mutual understanding and enable the exchange of ideas and methods between disciplines.

3.2.7 The Interpretability Challenge

Whereas models of the brain computationally grow in their complexity and sophistication, interpretations and understandings of the inner mechanisms and outputs from such models are all becoming increasingly difficult. Indeed, most of the currently used techniques in machine learning and AI – such as deep neural networks – are often criticized for being "black boxes" whose inner workings are hardly explainable and interpretable in terms of mechanisms. In the setting of

computational neurology, interpretability is not only key to furthering our comprehension of the brain but also in the validation of accuracy and biological plausibility in computational models. No matter how good a model has performed in the capture of real brain activity or behavior, failing to give insights into the neural mechanisms means such a model will carry limited value in the improvement of our understanding of the brain [22].

Interpretation and explanation of the inner workings of such complex computational models involve the development of techniques and frameworks; these are indeed active areas of research in interpretable machine learning and explainable AI. At the same time, all this faces great difficulties in application to the domain of computational neurology because of its complexity and the multiscale nature of brain dynamics [3]. Overcoming the interpretability challenge will require advances in model interpretability techniques themselves, as well as deeper insight into the biological principles and constraints that determine neural computation. Such progress will be dependent on many collaborations between computational neuroscientists, machine learning researchers, and neuroscientists. Techniques like lateralized readiness potential (LRP) and attention maps have already seen some success in interpreting the representations learned by deep neural networks, and such techniques can be adapted for models derived from computational neurology [23]. Another next step might be toward developing more interpretable and biologically plausible computational models, based on either the principles of predictive coding or energy-based models, when more transparently and explainable furthering the framework through which neural computation is studied.

3.2.8 Knowledge Gaps in Neural Theory

Despite this, many open questions remain with respect to our theoretical understanding of neural coding, learning, and memory formation among other fundamental neural processes. The many frameworks, including but not limited to connectionism, dynamical systems, Bayesian coding, and others, speak to these issues from supplementary perspectives without any unifying theory. This is a particularly hard procedure in linking higher-order cognitive functions with their biophysical neural mechanisms. Indeed, now more than ever, reliable simulations of neural phenomena across multiple scales and modalities call for robust generalizable computational frameworks incorporating empirically validated theories. For example, although much is now known about the biophysical mechanisms contributing to synaptic plasticity and the cellular basis of learning and memory, the translation of these low-level processes into a coherent theory capable of accounting for complex cognitive functions such as reasoning, decision-making, and language remains an open challenge [24]. Similarly, understanding how information is represented and processed in distributed neural networks, and how those representations give rise to conscious perception and subjective experience, remains rudimentary. Likewise, understanding how information is represented and processed in the brain, particularly within distributed neural networks, along with how those representations give rise to conscious perception and subjective experience, remains undeveloped thus far [25].

3.2.9 Computational Scaling Challenges

Although strong computing power and technologies such as GPU acceleration enable more complex neural simulations than were possible in the past, modeling the whole human brain at scales approximating biological reality is far from possible using currently conceivable methods. In contrast, a biophysically detailed simulation of the whole human cortex – 16 billion neurons with thousands of compartments each – may well require an exascale supercomputer with unparalleled computation and memory. Novel computational paradigms driven by the neural architectures themselves may well be called for in naturalistic modeling of whole-brain circuitry. One of the key challenges in this regard is the immense complexity and heterogeneity of neural circuits, which exhibit a vast range of cellular and molecular diversity, as well as intricate spatial and temporal dynamics. Capturing this complexity in a comprehensive computational model requires not only massive computational resources but also a deeper understanding of the organizational principles and computational motifs that govern neural information processing [26].

3.3 OPPORTUNITIES AND APPLICATIONS

Despite the immense challenges, computational neurology is opening up exciting opportunities and applications that are propelling the field forward at a rapid pace. This section covers some of the key areas of progress and impact.

3.3.1 Next-Generation Brain Mapping and Modeling Initiatives

Major scientific efforts are presently made to develop ultra-high-resolution maps and computational models integrating multiscale multimodal data about brain structure and dynamics. The latter will, for example, digitally reconstruct and simulate the entire human brain down to the molecular level. The Human Brain Project is developing a research infrastructure integrating neuroinformatics, brain simulation, and high-performance analytics to advance brain science, and computing projects like these drive innovation in data management, visualization, and modeling frameworks, and simulation at unprecedented scales. These large-scale initiatives of brain mapping and modeling provide much-needed insight into the organization and function of the human brain but also serve as test beds in developing novel techniques and computational technologies. For example, the Blue Brain Project has pioneered the use of highly optimized simulation algorithms and hardware accelerators to enable efficient simulations of large-scale neural circuits [27].

3.3.2 Computational Disease Models and Therapeutics

Computational models, by simulating the neural underpinnings of various brain disorders, such as Alzheimer's, Parkinson's, epilepsy, stroke, and psychiatric conditions, are becoming indispensable tools for understanding disease mechanisms, identifying biomarkers, therapy screening, and rationalizing specific treatment strategies for each individual [28]. The models linking molecular pathways to

neural circuits and impairments in cognition could be applied further to devise targeted therapeutic interventions, from new medicinal treatments to protocols for neural stimulation to cognitive remediation approaches. Computational models have been applied, for example, to explore how various genetic and environmental risk factors affect the course of development and progression of Alzheimer's disease, by providing insight into the underlying pathological mechanisms and possible therapeutic targets. For instance, in epilepsy, the use of computational models has been vital in identifying seizure generation and spreading commanding processes. These have contributed to better ways to forecast seizures, prevent them, or stop them [29].

3.3.3 Brain-Inspired Artificial Intelligence

Insights from computational neurology are inspiring new directions in AI by developing algorithms and architectures that better approximate the computational principles of the brain. Neuromorphic computing aims to build energy-efficient, fault-tolerant, and adaptive neural networks modeled on biological neural circuits and dynamics. Neuroprosthetic devices could enhance or restore sensory, motor, and cognitive capabilities by directly interfacing with the nervous system. Deep learning methods loosely inspired by neural circuits are achieving remarkable performance in machine learning tasks, with biology suggesting pathways toward more human-like reasoning, unsupervised learning, and transfer learning capabilities. For example, the development of attention mechanisms in deep learning was inspired by the selective attention processes observed in the brain. Similarly, the field of meta-learning, which aims to develop systems that can quickly adapt and learn new tasks, draws inspiration from the principles of synaptic plasticity and brain reorganization. Integrating neuroscience principles into AI development is crucial for advancing AI beyond current limitations. It introduces the concept of the "embodied Turing test," which focuses on creating AI systems capable of interacting with their environments in ways similar to animals. By mimicking biological sensorimotor and cognitive abilities, NeuroAI could lead to more generalizable and robust AI systems. This shift emphasizes evolving AI that can learn and adapt autonomously, inspired by how the brain naturally processes information [30].

3.4 NEUROTECHNOLOGY BREAKTHROUGHS

With improvements in neural data acquisition and increasingly biologically realistic brain simulations, a new era of neurotechnology breakthroughs is within prospect. Direct neural interfaces such as BCIs form a new paradigm that allows devices to be directly controlled by neural signals; it may give patients with sensory or motor impairments a way to recover lost abilities. Computational models play a crucial role in the extraction of meaningful signals from neural activity and translating those into control signals. Neural prosthetics, including artificial retinas and cochlear implants, will restore vision, hearing, and other senses or motor functions to individuals. Neurotechnology will commercially enable brain-controlled interfaces in gaming, computing, and more. However, major challenges remain to be addressed regarding

biocompatibility and long-term stability and in developing effective decoding algorithms and control strategies for these neurotechnology.

3.5 ETHICAL CHALLENGES

While the opportunities brought about by computational neurology are great, the increased capability for monitoring and decoding and the possibility to manipulate neural activity bring up significant ethical challenges. Systematic frameworks need to be introduced for the protection of neural data against privacy and security threats. Enhancement of cognitive capabilities also poses interesting philosophical issues regarding the modification of the frontiers of human characteristics and concerning possible coercion or unfair advantage. Above all, there will be proactive governance and regulation for emerging neurotechnologies, whether that be for military or consumer exploitation. As integration with the brain becomes more feasible, new human rights may have to be established in regard to cognitive liberty and mental privacy [31]. What is needed are ethical guidelines that can ensure responsible development and fair access to neurotechnological capabilities. Interdisciplinary collaborations among neuroscientists, ethicists, policy makers, and other stakeholders are essential in negotiating these complex ethical issues and ensuring that neurotechnologies under development and deployment align with the values and priorities of society [32].

3.6 OPPORTUNITIES AND FUTURE DIRECTIONS

Despite the significant challenges facing computational neurology, the field also presents exciting opportunities and potential for transformative discoveries. With ever-increasing computational power, continuing data acquisition capabilities, and improving modeling techniques, the breakthroughs toward understanding of the brain and neural computation are really at hand. One of the most promising areas of research involves the development of large-scale, biologically realistic simulations of the entire brain or significant parts of it. Projects like the Human Brain Project and the BRAIN Initiative in the United States are pursuing this ambitious goal by capitalizing on the most recent advances in high-performance computing, neuroimaging, and data integration.

It will likely be many years, possibly even decades, before simulation of the whole human brain at the level of individual neurons and synapses becomes possible. However, even models of more modest size – that is, smaller brain areas or circuits – could have great value in illuminating the principles of neural computation and emergent properties of complex neural networks. It is exciting to see computational neurology come of age in concert with two other emerging fields: neuromorphic computing and BCIs. Neuromorphic computing is engaged in the design of hardware and software systems powered by the architecture and computational principles of the brain, with the prospect of more energy-efficient and powerful computational paradigms.

On the other hand, BCIs try to create a way for the brain to communicate with external devices directly and thus help people with disabilities to control some assistive technologies or even restore some lost sensory and motor functions.

Computational neurology can help build precise models of neural activity and, for these applications, decoding algorithms. Equally important, the integration of computational neurology with disciplines like machine learning and AI opens exciting possibilities toward the advancement of knowledge in intelligence and cognition. Building computational models with the ability to simulate or even surpass human-level performance on specific cognitive tasks may yield valuable insights into the neural mechanisms underlying these various abilities.

However, it is critical to remember that while artificial neural networks and other machine learning models are sometimes inspirations and thus very handy in attempts to study the brain, they are after all simplified abstractions and need not provide all the rich complexity and biological constraint of real neural systems. The challenge then lies in determining what computational principles are shared between AI and biological intelligence but taking into account the unique characteristics and constraints pertinent to each. Other promising directions for computational neurology include personalized brain modeling and simulation: individualized models and simulations particular to a given patient or experimental participant. Now researchers could integrate detailed neuroimaging, genetic, and other individual-specific data to create highly accurate computational models of a person's unique brain structure and function.

Personalized models of the brain could have many applications in precision medicine – simulation and prediction of different treatments or interventions and their outcomes on the individual's brain. They will also contribute to elaborating neurofeedback or stimulation therapies targeted at specific pathologies, including depression, anxiety, or chronic pain. In addition, personalized brain models might also provide unparalleled research tools, allowing scientists to investigate the impact of specific genetic variations, or even various lesions or other individual differences, on neural computation and behavior in silico. However, developing personalized models requires serious development in data acquisition and integration and modeling techniques alone; not less important is addressing ethical and privacy concerns about the collection and use of sensitive personal data.

3.7 CONCLUSION

Computational neurology stands at the forefront of our quest to know about the brain, arguably one of the most complex and fascinating systems in the known universe. While the challenges facing this field are enormous, ranging from sheer complexity of the brain to limitations in current data acquisition and modeling techniques, the potential rewards are immense. This type of advance in the creation of accurate and informative computational models of the brain – a logical next step in the advance of our core understanding of neural computation and the biological basis for cognition – would unleash transformative applications assured by brain-computer interfaces, neuromorphic computing, precision medicine, and the design of AI systems inspired by the principles of biological intelligence. Overcoming the challenges will require a concerted, interdisciplinary effort involving neuroscientists, computer scientists, engineers, mathematicians, and experts from various other domains. Fostering collaborations, knowledge sharing, and the integration

of disparate methodologies and theoretical frameworks will be crucial for making significant progress. Additionally, continued investment and innovation in cutting-edge technologies for data acquisition, high-performance computing, and advanced modeling techniques are essential to push the boundaries of what is computationally feasible. As our computational capabilities and empirical understanding of the brain continue to grow, we may witness profound breakthroughs that could reshape our conception of intelligence, consciousness, and the fundamental nature of our existence as thinking, feeling beings. The development of biologically inspired AI systems that can match or even surpass human cognitive abilities could have profound implications for fields ranging from healthcare and education to scientific discovery and technological innovation. This, in turn, may lead to revolutionary neurotechnologies that can enhance human capabilities, restore lost functions, or cure neurological conditions by accurately monitoring, decoding, and potentially manipulating neural activity. Along with responsible development, fair distribution, with increasingly powerful technologies, protection of individual privacy, autonomy, and cognitive liberty is to be pursued. Fundamentally, the quest to unlock the brain through computation is not a purely scientific one but also highly existential – to understand computational principles at the core of our very own minds and consciousness is to be closer to fundamental insights into the nature of existence, the origins of subjective experience, and where we fit in the universe. While daunting challenges line the road ahead, the possible rewards make computational neurology a frontier worth exploring, for perhaps it contains keys to unlock some of the deepest secrets of our universe and ourselves.

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4 Ethical Issues in Neurodisorder Diagnosis

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4.1 INTRODUCTION

Among the many ways that medical artificial intelligence (AI) may enhance neurological procedures are by helping patients get diagnosed, actively treating their symptoms in between in-person consultations, anticipating and averting likely flare-ups, and more. Differential symptoms are displayed by people with a variety of mental and behavioral disorders. Verbal output, whether spoken or written, body language, tone of voice, and facial expressions can all be used to diagnose a patient. There are many moral and legal issues that medical sector must deal with. While AI has made great strides in society and may lead to better treatment results, not all cultures can afford it [1]. The most recent technology is still unavailable in many developing and low-income countries. Not to mention, there are a lot of concerns we have to deal with, such moral dilemmas, data privacy and protection, informed consent, societal divides, medical advice, empathy, and compassion. The Indian Committee of Clinical Exploration (ICMR) has planned moral direction records every once in a while, for advancing moral and top-notch research in India. Experts and ethics committees are expected to adhere to these guidelines [2]. These guidelines aim to offer guidance without restricting innovation or suggesting specific diagnostic or therapeutic approaches for diseases, but to facilitate safe and effective use of AI technologies in biomedical research and healthcare delivery. With the broad implications of AI-based technologies in healthcare, these guidelines apply to health professionals, technology developers, researchers, entrepreneurs, hospitals, research institutions, organization(s), and laypersons who wish to use health data for biomedical research and healthcare delivery using AI technology and techniques. AI is continuously using for the development of "smart" healthcare devices, which have the ability to learn difficult patterns from big and complex datasets like neurodisorders and many other mental diseases. Virtual health assistants, tailored medications, and smart digital tablets are some AI-driven computer programs that will assist primary care doctors in more precisely identifying patients who need special treatment and care and in developing protocols that are tailored to each patient. AI can be used by doctors to take notes, evaluate patient conversations, and upload necessary data straight into electronic health record systems [3]. But AI may be abused when applied incorrectly due to biases and other factors. So, AI in smart healthcare creates a number of new ethical questions.

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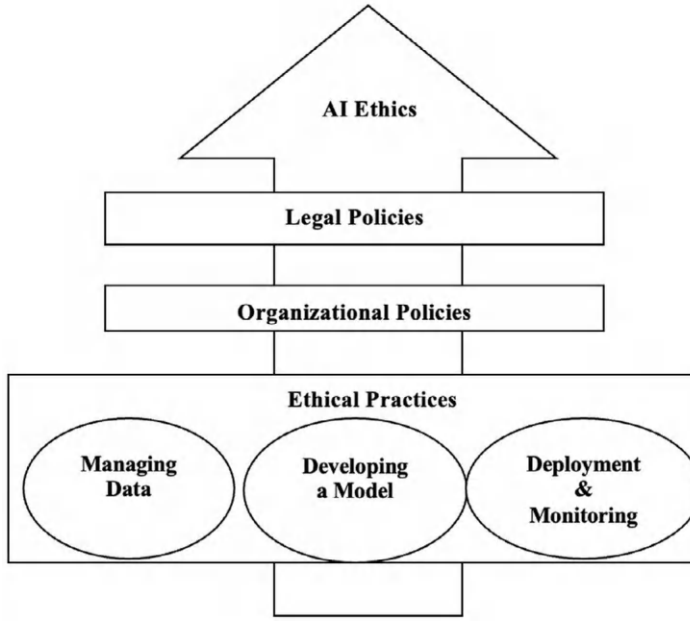

FIGURE 4.1 Flowchart depicting different ethical policies in healthcare.

The flowchart in Figure 4.1 makes it evident that there are mainly legal policies and organizational policies. Then there are some ethical practices:

1. Data management, which includes data collection, data protection, data cleaning, and data reporting.
2. Model development includes model training, model verification, and model reporting.
3. Deployment and monitoring includes stakeholder engagement and user-centered design, updates and ongoing validation, and supervision and auditing.

4.2 RELATED WORKS

In the beginning of healthcare research, every study in health and biomedical science, whether it uses AI or traditional approaches, must follow fundamental ethical rules: respect for individuals (autonomy), promoting well-being (beneficence), avoiding harm (nonmalfeasance), and fairness in distribution (distributive justice). Each rule aims to guarantee the safeguarding of the respect, rights, safety, and welfare of both the community and the individuals involved. These basic principles have been broadened into 12 overarching principles in the ICMR National Ethical Guidelines, 2017 [2].

The primary classification of the literature review is depicted in Figure 4.2.

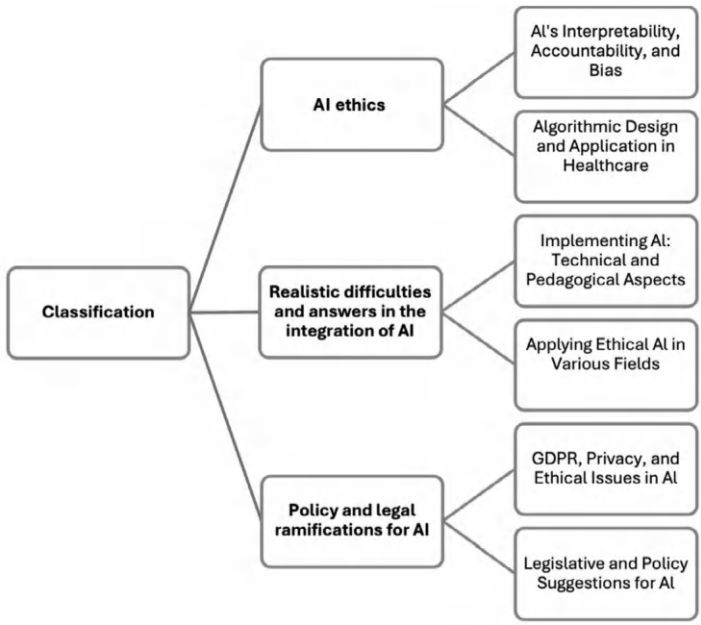

FIGURE 4.2 Primary classification of the literature review [1].

There are ten ethical principles in Figure 4.3, which shows different issues specific to AI for health.

These principles are:

- *Autonomy:* Utilization of AI in healthcare can improve patients' treatments more efficiently. Such a system has the capacity to operate on its own and weaken human independence, putting the power of making decisions into the hands of machines. Humans ought to possess the entire management of the AI-driven healthcare system. AI technology must always respect the autonomy of the patient.
- *Data privacy:* AI technology must guarantee the privacy and protection of personal data in every phase of growth and implementation. Having the trust of everyone is important for all stakeholders, such as healthcare recipients, who are concerned about safety and security. Data privacy should focus on stopping unauthorized entry, alteration, or deletion of personal information. AI can be used to support individual needs, but it should not impose excessive limitations on a person's real or perceived freedom.
- *Accountability and liability:* Accountability is defined as the responsibility of a person or group to take responsibility for its actions, be accountable for its activities, and present the outcomes in a clear and easily understandable way. AI technologies are designed to be implemented in the healthcare

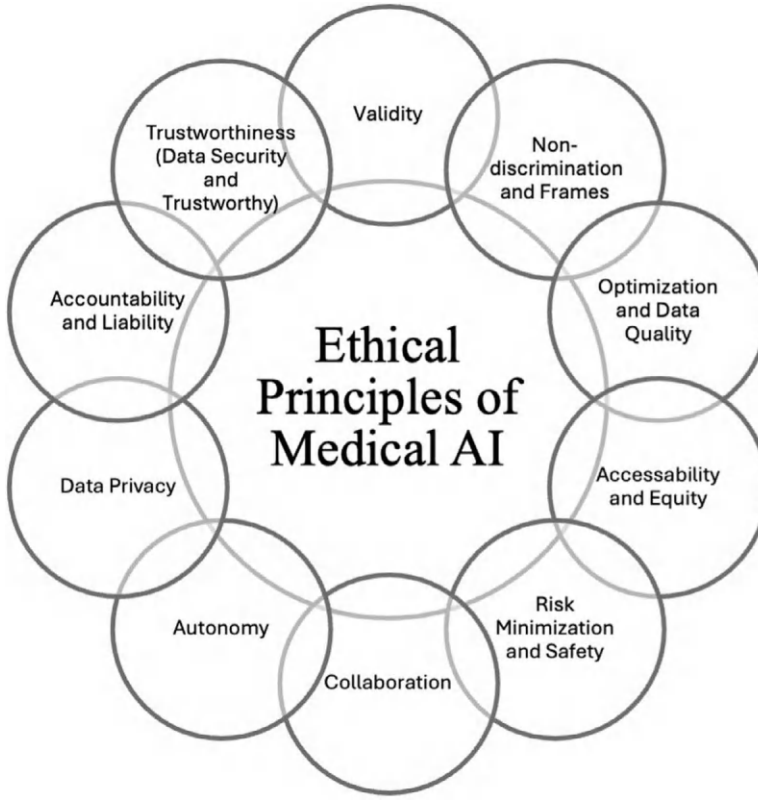

FIGURE 4.3 Objectives of ethical principles in neurodisorder research of AI.

industry and need to be prepared for examination by relevant authorities at any given moment [4]. AI technologies need to go through routine internal and external assessments reviews to guarantee their peak performance. It is necessary to make these audit reports accessible to the public.

- *Trustworthiness:* Reliability is the most sought-after attribute of a prognostic tool for utilization in AI healthcare. Clinicians must develop trust in the tools. AI technologies also utilize the same approach. To successfully utilize AI effectively, clinicians and healthcare providers should possess a straightforward, organized approach and a reliable method to evaluate the credibility and dependability of AI technologies.
- *Validity:* AI technology in healthcare needs to go through thorough clinical and field validation prior to being used on individuals. These are crucial in order to guarantee safety and effectiveness. The AI-based algorithms' deviation could be increased because of variations in the datasets utilized to train AI algorithms. When AI technology has an influence on every person or medical facility, there should be a well-functioning system for receiving feedback for implementing essential changes.

- *Nondiscrimination and fairness:* To avoid biases and inaccuracies in the algorithms and guarantee accuracy In order to maintain quality, it is necessary to adhere to some principles. Inaccuracies and biases can lead to less than optimal or faulty results [5]. External, independent algorithmic audits of AI technologies and ongoing evaluation of feedback from end-users should be conducted to reduce errors and prejudices. The developers/researchers working on AI must recognize and consider any biases present and ought to address the steps that are needed to fix them.
- *Optimization and data quality:* AI is a technology that relies heavily on data, and its results are largely determined by that data. The information is utilized to train and test AI. Data bias is seen as the primary danger to data-focused technologies such as AI for the purpose of maintaining good health. It is important to exercise due diligence to verify the quality of the "training data."
- *Accessibility and equity:* Utilizing computers for both progress and implementation of AI, the presence of a broader infrastructure is necessary for the widespread implementation of healthcare technologies. AI developers and authorities must ensure fairness in how AI technology is distributed. Organizations are required to strive to offer equal chances and accessibility to AI technology within various user demographics [6]. The accessibility of these technologies for underprivileged populations that are socially and economically disadvantaged should be the focus of AI developers and other stakeholders.
- *Risk minimization and safety:* It is the responsibility of all stakeholders to ensure participant safety engaged in the creation and implementation of AI technology. Patients/participants must be protected, with their dignity, rights, safety, and well-being of topmost importance. Strong control mechanisms are essential to avoid unintentional or intentional misuse. Having secured systems and software is crucial and necessary due to the sensitive data in the healthcare industry.
- *Collaboration:* AI technology in healthcare contexts suffers from a severe lack of confidence. More than 60% of patients, according to recent surveys, don't trust AI in healthcare. This mistrust stems from worries about data privacy, possible biases, and the opaqueness of AI decision-making procedures. Thus, the moral and societal responsibility of using AI ethically transforms it from a purely technical task.

Integrating AI into every part of medical systems looks difficult and not reachable. Medical robots and humans may not progress at the same speed in upcoming years because of the unique emotions that humans have. It is impossible for doctors and other healthcare professionals to communicate with or take advice from other healthcare professionals through robotic systems. Nevertheless, it appears unlikely that patients will prefer "machine–human" to "human–human" medical interactions [7]. The recovery of patients will be significantly influenced by the compassionate and empathetic care that medical professionals must provide. Achieving this task is not feasible with artificial doctors and nurses. When

patients engage with robotic medical professionals, they may not show empathy, courtesy, or proper conduct due to the machines' absence of human traits such as compassion. One of the key disadvantages of AI in the field of medicine is this. AI is widely used in healthcare [8]. Some examples are booking appointments online, checking in online at hospitals, converting medical documents into digital format, sending reminders for follow-up appointments and vaccinations, calculating medication dosage, and issuing alerts about possible side effects of combining medications.

4.2.1 Advantages of Incorporating AI in Neurodisorder

There are many advantages to integrating AI into healthcare, including revolutionizing patient care. AI-enabled applications, chatbots, and interfaces allow virtual health assistants to provide individualized services. The workload for healthcare providers is lessened by these digital assistants, which help with vital sign monitoring, medication reminders, appointment scheduling, and identification of patient problems [9]. Virtual health assistants have proven effective in-patient triaging and are available around the clock to improve healthcare accessibility. Some of the advantages are:

- *Optimization of workflow:* AI helps healthcare workers by automating repetitive tasks, freeing them up to concentrate on important decisions and patient care.
- *Improved diagnosis:* AI-powered diagnostic instruments offer fast and precise evaluations.
- *Individualized care programs:* AI uses patient data analysis to customize treatment plans based on response, genetics, and individual traits.
- *Accurate forecasting:* AI models can effectively address possible health issues by predicting disease trends.
- *Effective management of resources:* AI aids in resource optimization, enabling healthcare providers to better manage personnel, assets, and facilities.
- *Simplified administrative duties:* By automating administrative procedures, more patient-centric tasks can be completed with less paperwork and bureaucracy.
- *Instantaneous decision assistance:* AI helps medical professionals make educated decisions during patient consultations and treatments by providing timely and pertinent information.
- *Ongoing education:* Healthcare workers can remain up to date on the most recent developments in medicine thanks to medical AI.
- *Remote observation:* AI-driven monitoring systems make it possible for physicians to track patients' health outside of conventional clinical settings by facilitating remote patient monitoring.
- *Increased involvement of patients:* AI technologies improve dialogue between patients and doctors, encouraging greater understanding, compliance, and engagement with treatment regimens.

4.2.2 Challenges of AI

In spite of many benefits of AI in healthcare, there are many challenges that a healthcare professional has to deal with [10]. Some of these are:

- The major ethical dilemma in AI-powered mental healthcare is data privacy issues, like data breaches and exploitation of patient information for commercial use, which require strict protection measures.
- Bias in algorithms is a significant issue in mental health assessment and care; AI algorithms use extensive datasets that may have biases, resulting in discrepancies in diagnosis and treatment suggestions that impact marginalized communities.
- Informed consent is highly essential in healthcare as it allows patients to make informed decisions based on complete information. The right is equally significant while utilizing AI in medicine, despite some thinking that black-box AI systems do not influence it. A patient should be given the option to say no to AI-informed treatments if they are concerned [11].
- Keeping up with ethical guidelines in AI-based mental healthcare, lack of transparency in AI can impede understanding of how decisions are made. Understanding how AI operates and makes decisions is essential for patients and healthcare providers to ensure responsible use. Furthermore, it is crucial to hold AI accountable for its outcomes in cases of adverse events or mistakes.

We give a summary of ongoing research endeavors aimed at creating an AI focused on humans. These initiatives involve a core reevaluation of user-focused data control and handling, alongside the creation of safe and privacy-protecting machine learning (PPML) algorithms and implementing clear and transparent algorithms and incorporating machine learning fairness principles and methodologies to address biases and discriminatory outcomes. According to our perspective, it is essential to focus on humans, as they are both the doers and the main focus of the discussion of the choices determined by algorithms [12]. If we can make sure that these criteria are fulfilled, we should harness the benefits of AI-powered decision-making but also reduce the associated dangers of potential adverse effects on individuals and the entire society [13].

4.3 CONCLUSION

In the future, research in AI-driven healthcare will focus on improving algorithms for better interpretation, minimizing biases, and maintaining strong privacy protections. Continuous updating of ethical guidelines is essential to adapt to technological advances, and promoting interdisciplinary collaborations is necessary to tackle intricate challenges. The investigation of cutting-edge technologies like robotics, augmented reality, and blockchain in healthcare offers promising opportunities for future studies. Grasping the lasting effects on society and tackling accessibility issues will be essential in fully utilizing AI for improving global healthcare [14].

This study lays the groundwork for ongoing discussions, partnerships, and examination of ethical dilemmas as AI further influences the healthcare field. In this research, we found that there are just as many supporters as detractors of this new era of AI-augmented practice. Many aspiring and current doctors are concerned about the decline in employment opportunities brought about by the rising use of technology. While machines can interpret human behavior logically and analytically, they cannot develop human qualities like creativity, emotional intelligence, interpersonal and communication skills, critical thinking, or creative thinking. AI is going to be increasingly used in healthcare and hence needs to be morally accountable. Even though AI can't replace the role of clinical judgment completely, it can nonetheless aid in decision-making for clinicians. In many cases where there is a lack of medical knowledge and resources, AI can be utilized for screening and evaluation. AI decisions, unlike human decision-making, are always methodical due to the presence of algorithms [15]. It is observed by many groups that the fast speed development of AI in healthcare is an excellent strategy that might support healthcare practitioners. Nevertheless, despite the extensive potential and development of AI in the medical and healthcare sectors, this achievement has created additional challenges for medical ethics. We should be cautious because the disadvantages of it may outweigh the benefits. Professionals must consider morals and compassion when addressing this problem.

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5 Ethical Issues in Neurodisorder Diagnosis

Computational Intelligence toward Compassionate Psychiatric Treatment

Bhupinder Singh, Rishabha Malviya, and Christian Kaunert

5.1 INTRODUCTION

Computational intelligence (CI) advancements raise critical issues affecting privacy and data security. Diagnoses for neurodisorders usually indicate the most clinically sensitive aspects of a patient's mental and emotional well-being. Such advancements have transformed the neurodisorder diagnosis landscape, providing a new actionable avenue for more precise and individualized psychiatric therapy [1]. The overreliance on technology at times when humanistic perspectives might provide appropriate transparency and explainability and elicit informed consent presents issues constraining these systems, as complexity makes such processes extremely hard for healthcare providers to communicate to patients fully [2]. As CI is increasingly adopted in clinical psychiatry, it will be important to balance the embrace of systems capable of tracking and utilizing mental health information with a frontline stance that humanizes patient care – fostering engagement and observance while supporting autonomy and shared decision-making between patients and clinicians based on evidence-based management options, as well as facilitating active working alliance through psychoeducation targeting diverse aspects. Such ethical issues should be met for the responsible and ethical use of CI in neurodisorder diagnosis and therapy [3]. Figure 5.1 depicts the landscapes of introduction split sections.

5.2 OVERVIEW OF NEURODISORDERS

Neurologial disorders, or neurodisorders, are diseases of the central and peripheral nervous system [4]. Such disorders manifest with various symptoms, like cognitive impairment, motor deficits (ataxia), sensory loss, and emotional disturbances [5]. Progress in the field of CI may change a diagnosis and treatment for neurodisorders radically, including machine learning (ML) or artificial intelligence

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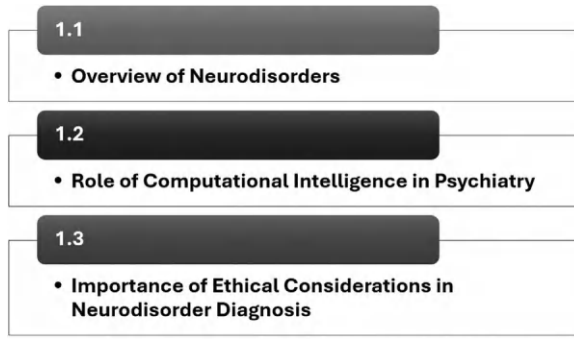

FIGURE 5.1 The landscapes of introduction split sections. (Source: Original.)

(AI) [6]. It is important to underscore potential ethical considerations associated with the integration of CI in psychiatric care [7]. Major ethical considerations include privacy concerns, algorithmic bias, and the risk of technology superseding human-based health practices [8]. As CI increasingly becomes a part of neurodisorder diagnosis and therapy, it is also vital to continue the advocacy for compassionate healthcare that honors patient autonomy while promoting shared decision-making [9].

5.3 ROLE OF COMPUTATIONAL INTELLIGENCE IN PSYCHIATRY

Fine-tuning image-based diagnosis and fostering creative treatment strategies for neurodisorders can be significantly enhanced through the application of Computational Intelligence, particularly the integration of Machine Learning and Artificial Intelligence techniques [10]. To change the future by improving diagnostic accuracy, allowing for unique tailored treatment plans and earlier intervention, Machine learning have the potential to help improve not only quality of life but ultimately increase the lifespan [11]. Yet, the inclusion of CI in mental healthcare provokes much needed ethical questions too [12]. Ethically, important issue in machine learning include algorithms bias that can entrench societal biases as well and creation of new discrimination against socially vulnerable populations [13]. It also raises questions about privacy, transparency, and the risk of overutilizing technology without human-centered care [14]. Overcoming these ethical hurdles is essential if the responsible and humanistic use of CI for diagnosing and treating neurodisorders is to be achieved [15].

5.4 IMPORTANCE OF ETHICAL CONSIDERATIONS IN NEURODISORDER DIAGNOSIS

Such applications are recommended even for examples of common neurodisorders (e.g., stroke, Parkinson's disease, dementia, attention deficit hyperactivity disorder [ADHD], and functional neurological disorder [FND]) [5]. These conditions can significantly affect an individual's quality of life and put a heavy financial weight on that person, as well as healthcare systems [16]. The increasing role of CO (e.g., ML

and AI) in the diagnosis, management, conducting of procedures, and treatment of neurodisorders puts an emphasis on maintaining a compassionate approach to clinical care that honors patient autonomy while also supporting shared decision-making [17]. Since the technologies are being used for life-threatening situations, it is very important to follow some ethical considerations [18]. Major ethical concerns are related to privacy, algorithmic bias, and overdigitization taking away the human responsibility from a part of care [19]. More generally, issues of being transparent and articulate are present in the description that must be given to patients before their decision concerning how data-hungry this method can get [20].

5.5 UNDERSTANDING NEURODISORDERS: DEFINITION AND TYPES OF NEURODISORDERS

These are a group of diseases referred to as neurodisorders, specialized conditions that affect our brain and spinal cord [21]. These range from cognitive through motor and sensory to emotional disorders. These disorders cover a broad range, affecting cognitive abilities, motor skills, sensory perception, and emotional well-being. More and more, experts are suggesting the use of cutting-edge technologies like AI and machine learning to help manage prevalent neurodisorders such as stroke, Parkinson's disease, dementia, ADHD, and Functional Neurological Disorder (FND) [22]. These conditions can deeply affect a person's quality of life and create a hefty financial strain on both those who are affected and the healthcare system as a whole [23].

5.6 PREVALENCE AND IMPACT ON SOCIETY

Neurodisorders such as stroke, Parkinson's disease, dementia, and ADHD are the leading causes of morbidity in some countries and can lead to poor quality of life and a burden on healthcare systems. This can manifest phenotypically in cognitive impairment, motor dysfunction, and deficits related to emotional processing. Gone Integrating CI (i.e., ML and AI) in the diagnosis and treatment of neurodisorders represents a promising approach to improving care for these patients [24].

5.7 SPECIFIC ETHICAL ISSUES AND DECISION-MAKING SCENARIOS IN CLINICAL PSYCHIATRY

Clinical psychiatry is where the ethical dilemma lies in a complexly woven web of patient autonomy, confidentiality, and beneficence [25]. Although keeping a patient's confidential information private is very important, there are circumstances where you might need to share such information with someone else, such as when a patient says they are going to hurt themselves or others. Psychiatrists have to appropriately assess the risk and see if breaching confidentiality falls within legal and ethical criteria [26].

5.8 COMPUTATIONAL INTELLIGENCE IN PSYCHIATRIC DIAGNOSIS

CI, including the use of ML and AI to diagnose and treat neurodisorders, has been widely looked at as an avenue with significant promise [27]. These technologies can help boost diagnosis accuracy, support personalized treatments, and promote early intervention. Psychiatry has very important ethical considerations when using CI to help treat patients [28].

5.9 APPLICATION OF CI IN DIAGNOSING NEURODISORDERS

There are also concerns over algorithmic bias, whereby the algorithms involved might reinforce social biases and further disadvantage already marginalized demographics [30]. The benefits of using CI for psychiatric diagnosis is depicted in Figure 5.2.

CI algorithms can learn from the vast amounts of patient data available with neuroimaging, genetics information, and clinical symptoms. It should be very capable of detecting patterns in such data, resulting in more accurate diagnosis [31]. This can allow for an earlier and honed treatment of tumors, for example, which may improve patient outcomes. Incorporation of CI, just like ML and AI in the field of diagnosis and treatment for neurodisorders, might be a great advancement [32]. These technologies can increase diagnostic precision, limit a course of treatment to the patient only, and support earlier intervention. The routine use of CI for psychiatric

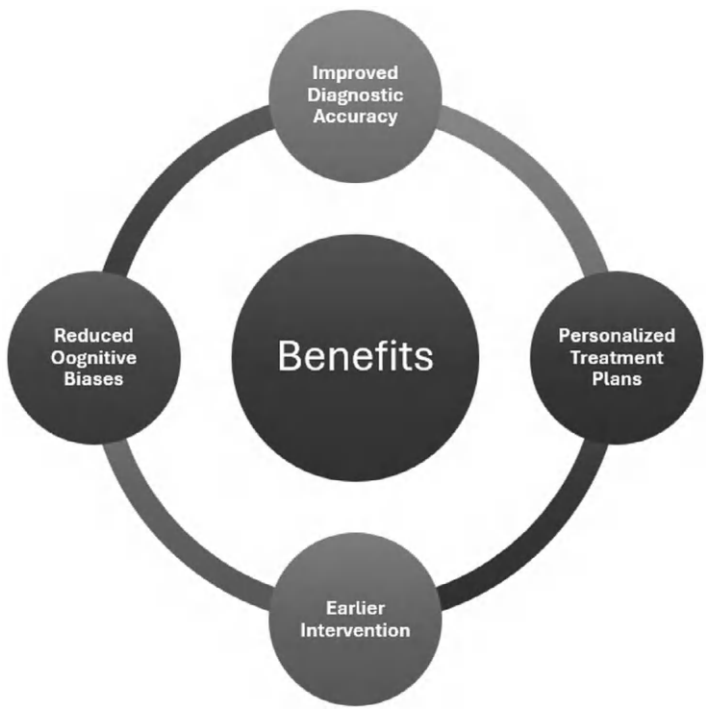

FIGURE 5.2 Benefits of using CI for psychiatric diagnosis. (Source: Original.)

diagnosis has the potential to be highly beneficial, as these technologies can increase diagnostic precision, tailor treatment plans to individual patients, and support earlier intervention [33].

Treatment strategies can be customized. CI can analyze data from individual patients to build personalized treatment plans that are more likely to reflect specific idiosyncrasies of each patient's condition, thus improving and even shortening treatment. CI algorithms can detect subtle neurodisorder signs and cognitive symptoms earlier than conventional diagnostic techniques [34]. This enables timely intervention that is essential in preventing or delaying onset of these disorders [35]. The influence of prejudices that may affect human judgment in psychiatric diagnosis can be reduced by CI algorithms. This can result in more impartial and repeatable diagnoses [36]. Yet, this implementation of CI in psychiatric care also has far-reaching ethical implications that deserve closer attention, including privacy risks, algorithmic bias, and the risk for technology to overpower human-centered approaches [37].

5.10 ETHICAL ISSUES IN NEURODISORDER DIAGNOSIS USING CI

The integration of CI including ML and AI in the diagnosis and treatment of neurodisorders raises several ethical challenges that need to be discussed, such as privacy, because CI algorithms usually act upon privacy-related patient data like neuroimaging, genetic, and clinical information [38]. Protecting the privacy and security of such data are paramount but not at the expense of patients being well informed about how their data will be used as part of connected care that benefits them [8]. To some extent, this is because CI can have the highly desirable effect of increasing diagnostic accuracy and personalizing treatment, but there are also concerns that physicians will come to rely on these technologies at the expense of human-centered care. It must balance harnessing the advantages offered by CI and a compassionate approach that keeps patient dignity at heart [39]. It is necessary to deal with these ethical dilemmas in order to ensure that CI is utilized responsibly and compassionately for the diagnosis and management of neurodisorders [40]. Continued collaboration among clinicians, researchers, ethicists, and patients is needed to guide the way through these knotty problems [41].

5.11 PRIVACY AND DATA SECURITY

Sobering concerns have also been raised in relation to neurodisorder diagnosis via CI, including ML and AI, which are nevertheless paramount as the process of data produced by mental processes [42]. Patient data collected and analyzed through these technologies include neuroimaging, genetics, as well as clinical information that is sensitive [43]. Maintaining the privacy and security of such data are paramount to preventing discrimination, stigmatization, and psychological harm for patients [5]. Patients have to completely understand what will be done with their data and how they are secured, and then their formal agreement reached in a clear manner. Data security measures like encryption, access controls, and regular security audits while

diagnosing neurodisorders through CI need to be adopted by the healthcare provider and researchers [44]. They also need to follow strict data governance rules that outline ownership, sharing, and retention defined data [45]. At the same time, in designing CI algorithms for neurodisorder diagnosis, it is necessary to follow privacy by design principles such as data minimization, purpose limitation, and storage limitation [46]. Remember that this can be a way to make sure that only the data needed for proper diagnosis and treatment are being collected and preserved. Focusing on ensuring patient privacy and data protection can help healthcare providers gain public support for CI-assisted neurodisorder diagnosis to benefit patients in a safe, ethical way [47].

5.12 BIAS AND FAIRNESS IN CI ALGORITHMS

Important concerns regarding fairness and bias can be brought up by the use of CI algorithms in the diagnosis of neurological diseases [9]. If these algorithms are not sufficiently built and verified, they could lead to the marginalization of people with disabilities and perpetuate social prejudices [48]. Several factors, including skewed training data, incorrect algorithms, or the naturally inherent preconceptions of the software developers, are susceptible to algorithmic bias. In this case, a CI algorithm may diagnose neurodisorders with lower precision in specific populations if trained on data that demographically underrepresent those groups [49]. It is essential to make sure that CI algorithms are created and evaluated using a variety of representative datasets in order to reduce the possibility of bias. Throughout the algorithm creation process, developers should watch for possible biases and take suitable measures to detect and address them [50].

5.13 TRANSPARENCY AND EXPLAINABILITY

An important ethical component to take into account when applying CI algorithms for diagnosing neurodisorders is the question of transparency and explainability [51]. Medical professionals may find it challenging to properly explain the decision-making process to patients due to the intricacy of these algorithms, which poses problems with informed consent [52]. Figure 5.3 specifies points on transparency and explainability.

The following are the salient features of the consent–autonomy relationship in the context of CI-based neurodisorder diagnosis. Informed consent is a means of safeguarding and promoting patient autonomy by ensuring they are aware of the suggested course of treatment and are able to make an informed choice [53]. Autonomy is regarded as an individual's ability to make free and rational choices about their healthcare. Informed permission is important for protecting patient autonomy when utilizing CI to diagnose neurodisorders [54]. This empowers patients to make independent decisions about accomplishing the CI-based diagnosing. Patients must have a complete understanding of how their data will be collected and used, the potential advantages and perils of the CI-based diagnosis, and any alternatives [55]. It may be challenging for medical professionals to thoroughly explain the decision-making process to patients due to the intricacy of CI algorithms employed in the diagnosis

FIGURE 5.3 Specifies the points on transparency and explainability. (Source: Original.)

of neurodisorders. In order to support informed consent and collaborative decision-making, efforts must be made to improve the explainability and transparency of these algorithms [56]. Encouraging beneficence, or acting in the patient's best interest, but still respecting their autonomy may conflict. In order to give the best care possible and make sure CI-based diagnoses respect autonomy, healthcare professionals need to carefully oversee this fine line [57].

5.14 CONSENT AND AUTONOMY

Few things are as central when it comes to use of CI for neurodisorder diagnosis than the matter of autonomy and consent. Autonomy is a patient's ability to make free and informed decisions regarding their own care, while informed consent helps safeguard this autonomy [58]. In the setting of CI-based diagnosis, patients must be given full disclosure as to how their data are used and may gain benefit or risk associated with any alternatives [59]. In this way, they can decide for themselves whether or not to go forward with the diagnostic process [60]. However, critical parts of the decision-making capacity may be impaired in some neurodisorder patients; having sound informed consent might become very difficult to achieve [61]. Individual autonomy must always be weighed against beneficence, the moral obligation to act in a way that benefits others. To allow informed consent and shared decision making, it is important to enhance the transparency and explainability of CI algorithms [62].

5.15 ENSURING INFORMED CONSENT IN CI-BASED DIAGNOSIS

One of the most important ethical issues is reasoning about how to obtain informed consent when analyzing neurodisease in using CI [63]. Patients need to get clear,

understandable information about the treatment process when using CI data and with whom and under which conditions this will or can be shared (a privacy statement) [64]. These individuals should also be informed of possible advantages, risks, and disadvantages of the technology [65]. The consent process should be continuous, with the patient having an opportunity to ask questions and withdraw consent at any time [66]. Providers may also be required to obtain consent from family members or legal guardians for patients with impaired decision-making capacity. Patient autonomy is paramount, and making well-informed decisions in their care respects transparency with shared decision-making [67].

5.16 BALANCING AUTOMATION AND PATIENT AUTONOMY

In the future, if it begins to be more common to use CI in neurodisorder diagnosis, then we may run into a problem of overautomating our diagnostics and taking away from patient autonomy [68]. However, we should not replace human intervention and the therapeutic alliance of the patient–provider relationship. Healthcare professionals need to find the right balance by taking advantage of CI while concurrently ensuring patient autonomy and promoting shared decision-making [69]. That could include, with regard to greater transparency over how the algorithms operate, getting patients involved in understanding results and keeping humans (clinicians) as part of the diagnostic process [70]. But the aim, in the end, is to enable patients to have information with which they can make decisions – not simply give up control so that automated systems take over [71].

5.17 CONCLUSION AND FUTURE SCOPE SMART SUSTAINABLE CITIES: A GUIDE TO TECHNOLOGY, DATA, AND URBAN TRANSFORMATION

The use of CI technologies in smart sustainable city development can provide a promising solution to promoting urban sustainability and enabling transformative changes [72]. But it must tread cautiously – while thoughtful application of AI holds the promise, the potential misuse and responsible use come with significant ethical considerations [73]. Ethical considerations include data privacy and security, algorithmic bias, transparency and explainability, and impact on vulnerable population. To inspire trust and guard against these risks, all AI regulation requires strong data frameworks combined with machine audit processes that are accompanied by a society-wide commitment to transparency.

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Part II

Neuroimaging and Diagnostic Techniques

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6 Improving Magnetic Resonance Imaging (MRI) for Better Understanding of Neurological Disorders

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6.1 INTRODUCTION

One of the most innovative medical imaging technologies is magnetic resonance imaging (MRI). The MRI equipment uses radio waves and a strong magnetic field to provide comprehensive images of the body's internal anatomy. These structures provide anatomical details that are helpful to diagnose various neurological disorders. However, the raw data of MRI images often contain some imperfections that inherently limit the imaging technology, such as patient movement during scanning and variations in tissue properties, and that cause the chance of artifacts (such as noise, motion artifacts, and intensity inhomogeneities) or poor image quality. So, preprocessing techniques are important to decrease the chances of artifacts and improve their image quality and reliability [1]. In this chapter, the various types of distortions and imperfections that can affect MRI image quality and the techniques used to mitigate these issues are discussed in detail.

6.2 BASICS OF MRI DATA

An MRI scanner produces images with the help of hydrogen atoms in the body. The human body is composed of approximately 60–70% water, and water molecules contain hydrogen atoms, which makes it possible to create MRI images. When a patient is placed inside the MRI machine, a strong magnetic field is produced by the magnet in the scanner, and the magnetic field affects the hydrogen atoms in the patient's body. Hydrogen atoms are particularly suitable for MRI because they have a single proton in their nucleus, and according to quantum physics, atoms with an odd number of protons are affected by magnetic fields. These protons behave like tiny magnets [2]. These protons align with the strong magnetic field in a manner like that of a compass needle aligning with the magnetic field of Earth. A radio frequency (RF) pulse is applied once the protons

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are positioned. Protons are deflected away from the magnetic field by this pulse, which throws them off alignment. A process called relaxation occurs when the RF pulse is stopped, causing the protons to move back toward their initial alignment. Radio waves are the signals that are released by the hydrogen nuclei when they realign [3]. Receiver coils in the MRI scanner pick up these signals. The signals that are released are dependent on the hydrogen atoms' surroundings, and this information gives specific details about the various body tissues. A computer processes the signals it has detected to produce digital images. Usually, these pictures are taken in slices that can be assembled to provide a three-dimensional picture of the scanned region. The little units that make up each slice are known as *voxels*, or volume pixels; these are the three-dimensional equivalents of pixels in a two-dimensional picture. Each voxel's intensity, which is connected to the signal given out by the hydrogen nuclei, depicts the properties of the underlying tissue [4].

The following factors can impact the quality of MRI images even with modern equipment:

Noise: Noise in MRI refers to undesired signals or interference that may obscure the original imaging data.

Motion artifacts: Motion artifacts are the unwanted blurring or distortion of the images potentially caused by several factors, such as patient movement or internal physiological movements. A motion artifact can produce images that are not clear to diagnose. Sometimes images are blurred, sometime distortion is produced in an image, and sometime ghosting artifacts are generated due to motion. Actually, the type of motion artifact depends on the degree and kind of motion.

Geometric distortions: A geometric distortion is produced due to the variation in the main magnetic field, and this produces local distortion in the frequency of spins. So, the frequency is affected, and also the image is affected.

Intensity inhomogeneities: This artifact is mainly in higher Tesla machines, like the 3 Tesla machine. Radio frequency waves are produced in a nonuniform manner so that the field excited due to the magnet can flip in an uneven manner across the image. This can obscure the true contrast of the tissue, making the image's interpretation very difficult.

Signal-to-noise ratio (SNR): This is the measure of quality of an MRI signal in relation with background signal. So the higher SNR is essential to produce better images and accurate interpretation of MRI images.

Artifacts: Artifacts are anomalies that are not present in normal anatomy or pathology. They are generated from various sources, like the patient's body, the MRI machine, or software. Artifacts may affect the image quality and lead to misinterpretation of images. In addition to motion artifacts, other sources of distortion may arise due to machine-related issues or acquisition inconsistencies. These machine and other artifacts include signal dropouts, hardware malfunctions, scanner calibration errors, and electronic interference.

6.3 IMPROVING IMAGE QUALITY

6.3.1 Noise Reduction Techniques

Noise reduction techniques are very important to improve the SNR. It is crucial to interpret images accurately. Many noise reduction techniques are used in MRI, such as spatial and frequency domain filtering, nonlocal means, anisotropic diffusion, adaptive filtering, and deep learning–based methods. Noise reduction techniques can be used to minimize noise while maintaining anatomical structure. Spatial filtering applies a direct spatial domain adjustment to the voxel intensities based on their neighbors. The three sources of noise – thermal, electronic, and physiological – are smoothed out of the MRI pictures using spatial filtering techniques, including mean, median, and Gaussian filtering. This filtering improves the clarity and quality of the images. Spatial filtering techniques can be divided into three main categories:

- Mean filtering: This technique replaces the intensity of each voxel with the average intensity of its neighboring voxels. It minimizes the noise artifact but can also affect the fine details and edges of the image and thus produce a blurry image.
- Median filtering: This technique is used mainly in MRI. It is used to minimize noise, such as salt and pepper noise. Unlike mean filtering, median filtering yields good quality edges and fine details.
- Gaussian filtering: This method increases the weight of surrounding voxels by transforming their brightness using a Gaussian function. A fair balance between edge preservation and noise reduction is achieved with the help of Gaussian filtering [5]

Several other filtering techniques are used:

- Frequency domain filtering: Frequency domain filtering is used to change the image back to its original form (spatial domain) and then transform it again into a new form (frequency domain).
- Fourier transform filtering: This technique is used in MRI for the noise reduction and better image reconstruction. It is a software that can convert the images into the frequency domain in the form of raw data. It is very important because k space naturally contains raw data or the frequency domain.
- Wavelet transform filtering: This is very sophisticated technique used to improve the image quality by reducing noise and suppressing artifacts. This software works by breaking the image in two different parts, that is, frequency and spatial components. This helps in improving image quality.
- Anisotropic diffusion filtering: This method is used in image processing to lower noise while maintaining important elements like edges. As opposed to isotropic diffusion, which uniformly blurs an image, anisotropic diffusion modifies the level of soothing by taking into account local gradients in the image. This preserves the edge sharpness while enabling a sizable

reduction in noise in homogeneous regions. Iteratively updating pixel values while striking a balance between noise reduction and feature preservation, the approach operates by solving partial differential equations [6].

- Nonlocal means (NLM) filtering: NLM filtering is an advanced technique that may be used to reduce noise. It cannot affect the structure of the image but can maintain the image's fine features. It also improves the SNR in functional MRI (fMRI) data. NLM filtering is used to determine the value of a pixel. The similarity between the local neighborhoods (patches) of the pixel under comparison determines the weights. By ensuring that the genuine underlying signal is taken into consideration during the averaging process, this method reduces noise without obscuring significant features [7].
- Deep learning–based noise reduction: This noise reduction model in MRI is a highly effective method that improves the image quality. The model can generate high-quality denoised images by learning to discriminate between noise and an actual signal. This is work during data collection in MRI. The dataset collected is both noisy images and their corresponding clean versions (which can be obtained through high-quality scans or simulations). This dataset is utilized to train a neural network. The network acquires the ability to map clean images to noisy ones. In order to minimize the difference between the predicted and actual clean images in the training set, the network's parameters are adjusted during this training process. After the network is trained once, it is used to denoise new MRI images. There are various neural network types that can be utilized for MRI noise reduction, but convolutional neural networks (CNNs) are the most widely used because of their superior image data handling capabilities [8].

6.4 TECHNIQUES FOR MOTION CORRECTION

Moving structures in an MRI, such as blood and cerebrospinal fluid (CSF), can cause phase changes that result in image ghosting and blurring. These artifacts arise from inconsistent MRI signals from moving tissues at the time of the image acquisition process. Motion artifacts may seriously affect the quality of MRI images, making it more challenging to correctly detect and understand neurological conditions [9]. Motion correction in MRI is important for obtaining high-quality images. Various techniques are used to eliminate the motion artifacts and improve image quality.

6.4.1 Gradient Moment Nulling (GMN)

GMN is an advanced technique in MRI which is used to reduce the effects of motion, particularly from periodic movements like blood flow and respiratory motion. Moving tissues encounter different magnetic fields when the MRI machine uses gradients to encode spatial information, which results in phase changes in the signals from those tissues. Over time, these adjustments compound to produce artifacts in

images. To compensate for motion-induced phase shifts, GMN alters the gradient waveforms. It primarily targets the gradient's initial moment, which is correlated with the motion of tissues. By nulling (or cancelling out) this particular time, GMN reduces the motion's effect on the image. In some cases, physiological processes such as blood flow and cerebrospinal fluid (CSF) movement can result in visible artifacts. These may include blood flow artifacts in the brain's veins and arteries during neuroimaging, CSF pulsation artifacts in spinal imaging, and motion-related distortions caused by blood flow to and from the heart. To reduce such artifacts, specific imaging techniques and sequence adjustments are often employed [10].

6.4.2 Motion-Insensitive Sequences

Motion-insensitive sequences in MRI are important for obtaining clear, high-quality images in situations where motion is unavoidable. Motion-insensitive sequences in MRI have been designed to reduce the artifacts caused by patient movement and internal body motions (e.g., breathing or heartbeats). They are particularly helpful in imaging patients who are unable to remain still, like children, or in obtaining images of naturally moving organs, such as the heart or lungs. Acquiring an MRI scan takes time. Any movement during this period may cause the images to become blurry, making it difficult to identify the small details. This is like attempting to take a clear picture with a camera when the subject is moving. To address this, certain MRI sequences have been developed to be less affected by motion. These sequences are designed to either capture images quickly or in a way that compensates for motion. Some main sequences are single-shot sequences, rapid imaging techniques, navigator echoes, and parallel imaging [11]:

- Single-shot sequences: These sequences minimize the possibility of motion affecting the image by capturing all the required information in a single shot or very quickly. One frequently utilized single-shot method is echo planar imaging (EPI).
- Rapid imaging techniques: These methods speed up the process of acquiring images. Patients need to stay still for shorter periods during faster scans, which minimizes motion artifacts. For example, compared to conventional spin echo sequences, fast spin echo (FSE) captures data more quickly. And similar to FSE, turbo spin echo (TSE) speeds up the process even more.
- Navigator echoes: These special echoes are collected along with the primary imaging data in order to track and adjust for mobility. The data can be adjusted and corrected by the scanner if it detects motion, as detected by the navigation. Clearer images are produced through real-time motion correction made possible by continuous monitoring.
- Parallel Imaging: This method effectively speeds up the scan by using multiple coils to record data at the same time. Motion artifacts are minimized when images are acquired more quickly because less time is available for motion to happen. Examples of such techniques include generalized autocalibrating partially parallel acquisitions (GRAPPA) and sensitivity encoding (SENSE) [12].

6.4.3 Breath-Hold Techniques

In MRI, breath-hold methods are used to reduce respiration-related motion artifacts. Breathing during an MRI scan can move the patient significantly, particularly in the chest and the abdomen. We can take images without respiratory motion interfering, which results in clearer, more accurate images, by asking patients to hold their breath. Breath-hold techniques are usually used along with fast imaging sequences in order to reduce the breath-hold duration. The scan sequences are designed to fit inside the breath-hold time, which is usually between ten and 20 seconds. Frequently used methods include gradient echo (GRE), EPI, and FSE [13]. Longer imaging sequences may be scanned in segments, with each segment acquired during a different breath-hold.

6.4.4 Physical Restraints

Motion can distort MRI scan results, making it challenging to obtain precise and clear results. This is particularly relevant for patients – such as children or individuals with mobility impairments – who may move during the scan. Techniques for physical restriction are employed to reduce this movement and enhance the quality of MRI images [14–16]. Restraints are used for many purposes, such as to take clear images, ensure patient safety, and minimize movement to avoid repeat scans and save time. There are various types of restraint techniques used in MRI. For example, pillow and cushions can be used to keep the patient comfortable and stay in the correct position. Foam pads can be used around the head, legs, and arms to minimize movement. And body straps are adjustable belts that are used to hold the head or neck during a scan and secure the patient's body on the table. In MRI, a head coil also works as a restraint as well as capturing the signals.

6.4.5 Prospective Motion Correction (PMC)

PMC is an advanced method used in MRI to instantly adjust for patient movement during scans. PMC operates by detecting and correcting motion as it occurs, in contrast to conventional techniques (retrospective correction) that attempt to fix motion artifacts after the scan. It reduces repeated scans and save times. In PMC, the initial step is to find the patient's movement. A variety of technologies can be used for this, like navigator echoes, external sensors, and in-bore sensors. They all are tracking the body movement [17].

6.4.6 Retrospective Motion Correction (RMC)

RMC is a technique that is used to adjust for patient motion after the scan is completed. As compared to PMC, which modifies for motion while the scan is happening, RMC processes the obtained images in order to eliminate or minimize motion artifacts. When motion is discovered after the scan, this method is quite helpful as it allows for image enhancements without repeating the scan.

Retrospective image correction saves time by minimizing the need for repeating scans. After the scan, motion is detected by analyzing the obtained images. There are various ways to achieve this such as comparison with reference images and image analysis algorithms; these two methods are commonly used to detect motion artifacts. After the detection of motion artifacts, some methods are used to correct the images, like filtering techniques, reconstruction methods, etc. RMC is frequently used in brain scans or neuroimaging, in which little motions can cause notable artifacts [18].

6.5 ADVANCED PREPROCESSING TECHNIQUES

In MRI, preprocessing is an advanced method that is important for increasing image quality, minimizing artifacts, and improving the accuracy of subsequent research. Clinicians and researchers can obtain more accurate and detailed images, improving diagnostic results and providing deeper insights into neurological and other disorders, by utilizing techniques like bias field correction, nonlocal means denoising, wavelet transform filtering, anisotropic diffusion filtering, and machine learning (ML)–based approaches [19].

6.5.1 fMRI Preprocessing

fMRI is a technique used for mapping and quantifying brain activity with the help of detection of blood flow. The preprocessing technique in fMRI is essential to provide clear and accurate data for analysis. Many software tools are available for fMRI preprocessing, including Analysis of Functional Neuro Images (AFNI), the FMRIB Software Library (FSL), and Statistical Parametric Mapping (SPM). Each software has some advantages and works well with particular kinds of analysis. Preprocessing techniques improve the quality and dependability of the data and produce more precise images and significant results by addressing problems such as head motion, slice timing, and artifacts and irregularities [20].

6.5.2 Diffusion MRI Preprocessing

Used to measure the diffusion of water molecules in brain tissues, this technique is generally applied in brain imaging for the mapping of white matter of the brain. The raw data of diffusion MRI sometimes contain various types of artifacts and distortion that must be eliminated or corrected before the data analysis. So, the preprocessing techniques are very important to maintain accuracy and better image quality [21].

6.6 MRI AND ARTIFICIAL INTELLIGENCE (AI)

Improvements to MRI technology helps patients and the medical facility by improving picture quality, shortening scan times, and creating a more comfortable environment. By utilizing less data to produce better images, AI allows for higher resolution and faster scan times. The data of MRI images may be used by

AI to build a 3D virtual reality training or diagnostic tool to improve the image quality. While AI is not yet widely used in the area of MRI, its application is anticipated to grow in the coming years as outdated equipment is replaced and a new generation of radiologists and technicians becomes more knowledgeable about its benefits. MRI is becoming an increasingly more dependable diagnostic tool because of the digitalization of technology and the introduction of AI, albeit it is still in its early stages for this application. A computed tomography (CT) scan and X-ray are often followed by an MRI as the last imaging modality that may provide the highest degree of information prior to surgery. With the extra advantage of just requiring one diagnostic procedure rather than three, cardiac MRIs may provide information not seen in other scan types or an angiography, including the ability to reveal the heart chambers, outflow pathways, and cardiac muscle degeneration from a variety of angles.

AI might be a welcome improvement over conventional MRI technology from the standpoint of the radiology MRI technician for a number of reasons. Without the presence of a cardiac specialist to ensure the scan's optimization, AI may design an MRI cardiac scan that is prepared by a skilled MRI technician, including four-chamber, two-chamber, left-ventricular outflow tract, right-ventricular outflow tract, and short axis views. AI can evaluate pictures and identify microscopic, early-stage malignant lumps or lesions, or it can quantify brain scans that identify and score diseases like dementia and Alzheimer's at levels that a human eye could miss. These abilities are used in radiologists' reports. AI is even capable of assigning a value or grade that facilitates diagnosis. For instance, a Gleason score—a scoring system for prostate conditions—could be used to determine the cancer stage based on an MRI of the prostate. Another reason to embrace AI is that it is more accurate than depending just on what the human eye can detect via examination. Shortening the learning curve for these processes, AI enables quicker 3D image scans and can also send pictures from an MRI scan to virtual reality (VR) software platforms. Before starting an invasive treatment, the surgeon may get greater information from VR-viewed brain scans, which can even help with a more successful game plan that includes a 3D trial surgery. The effect of surgery on organs or tissue may be minimized with the use of the information obtained from the MRI/VR technique before the operation. This usage of VR is made feasible by the Microsoft technology Apoqlar, which combines clinical procedures, medical education, and medical pictures (displayed in voxels, the units associated with 3D imaging) into a 3D mixed-reality environment. For this application, a cloud-based data platform is required. Using AI-gathered data from MRI scans, VR may be utilized not only to enhance presurgery preparation but also to further instruct medical students and surgical residents, reducing the requirement for cadaver training.

AI's capacity to convert coarsely sampled, faster MRI scans into higher-resolution images, minimize movement-related image degradation, and lessen patient discomfort from being in an enclosed, frequently cramped space offers additional advantages that help reduce scan times. Roomier MRI systems are the outcome of improved technology brought about by the stronger magnetic pulses produced and received during a scan. For example, cutting a 20-minute scan down

to a ten-minute one usually degrades that quality and presents new difficulties for the technician. Shorter scans may now have their resolution improved with the use of AI technology filters, stronger radio frequency coils, and improved software, producing picture quality that is closer to that of a conventional, lengthier MRI operation. One word of caution: investing entirely in AI for MRI scanning will also need hardware improvements, which will cost money for any imaging center or department.

Research from many universities, including Stanford University in California, demonstrates that using AI to MRI reconstruction may provide reliable pictures at half or even less of the time previously needed. The objective of reducing patient pain by cutting scan times without sacrificing picture quality is a constant throughout these experiments. Additionally, it allows independent imaging facilities and hospitals to see more patients in less time, which enhances productivity and potentially boosts revenue.

The Fast MRI blind test, which was conducted by Facebook AI Research (FAIR) and New York University (NYU), released its findings in 2020. Researchers discovered that there was no discernible difference in the way doctors participating in the blind test assessed conventionally generated MRIs and those produced with AI support utilizing much less (up to 75%) source data. Using both approaches, the patient's diseases or anomalies were found to be the same. It was found that, generally, the AI-generated pictures were of higher quality, and that five out of six radiologists were unable to identify which photos were produced with the use of AI enhancing methods. This, according to the NYU/Facebook research, is where ML and AI collide. By enhancing MRI picture quality, segmenting prostate scans to identify suspicious areas (foci) where cancer may be found, and separating cancer cells that may be deemed relevant from those that are not, AI may aid in the diagnosis of prostate cancer. After a lesion has been scanned, it may be graded (using Gleason scores, for example), which helps expedite the diagnosis and selection of the best course of action. Radiologists may use AI to see what's going on in the brain's sulcal spaces, or grooves and furrows, and gyral (gray matter). AI can precisely quantify scans with values and, using a prediction value built into the algorithm based on previous histories, can assist in determining the stage and early onset of dementia.

6.7 CONCLUSION

Preprocessing of MRI data is an essential first step to guarantee the quality, accuracy, and dependability of the final images, which are crucial for the diagnosis and understanding of neurological illnesses. Specific issues with MRI data, including noise, scanner distortion, and patient motion, are addressed by each of these methods. Preprocessing not only enhances image quality but also increases data consistency and comparability among various patients and research. Scientist and medical practitioners can improve diagnostic results and acquire a better knowledge of neurological disorders with the help of efficient preprocessing techniques to extract deeper insight from MRI data. Modern technologies like ML and AI may significantly change the way MRIs are preprocessed. Robotic and real-time preprocessing

techniques will eliminate the need for human intervention, increasing the accessibility and efficiency of MRI research. Motion correction, noise reduction, and artifact removal approaches will further improve the image quality, and standardization initiatives will guarantee that preprocessing techniques are dependable and repeatable in a variety of clinical and research scenarios for better quality.

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7 Advancements in Neuroimaging Techniques in Encephalopathy

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7.1 INTRODUCTION

Throughout history, scientists have worked to observe the brain and its system through the protective skull of a living human. Early civilizations, like the Egyptians and Greeks, had a basic understanding of the brain. The Edwin Smith Papyrus (approximately 1700 BCE) includes some of the oldest accounts of the brain and its injuries. The Greek philosopher Hippocrates (approximately 460–370 BCE) proposed that the brain was the seat of intellect, disputing the previously held idea that the heart was the center of thought and emotion. In the sixteenth century, Vesalius' meticulous anatomical drawings produced a more realistic portrayal of the brain organization, his treatise "De Humani Corporis Fabrica" (1543) cleared out many ancient fallacies [1]. Willis' "Cerebri Anatome" (1664), published in the seventeenth century, set the groundwork for contemporary neurology. He described the Circle of Willis, a crucial vascular circle near the base of the brain, and hypothesized that distinct brain areas performed specialized roles. Gall's phrenology, which proposed that the brain is made up of separate faculties, each corresponding to a different personality feature, was an early attempt to connect brain shape and function [1, 2]. Although eventually dismissed, it piqued curiosity in cerebral localization. In the 1860s, Broca discovered the region in the left frontal lobe involved in speech production, which is today known as Broca's area. Wernicke later identified Wernicke's region, which is located in the temporal lobe and is involved in language processing.

These insights were critical to understanding the localization of brain activities. In the late nineteenth and early twentieth century, Cajal employed the Golgi staining procedure to expose the complicated structure of neurons [3]. He proposed the neuron doctrine, which states that neurons are the fundamental units of the neurological system, and this transformed neuroscience. Significant milestones in the study and knowledge of the brain have occurred, ranging from early anatomical investigations to advanced imaging techniques. Each innovation has taken us closer to understanding the brain's intricacies and functions, paving the path for novel therapies and interventions for neurological and psychiatric illnesses. As technology advances, discoveries are expected to revolutionize

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our understanding of the brain and its enormous impact on human health and behavior. Despite significant advances in neuroimaging, diagnosing [4] encephalopathy syndrome in unusual patients remains difficult. Using modern imaging techniques can help clinicians rule out mimics and deliver a more accurate diagnosis at an earlier stage. Some of these methods can also help to understand the disease's complex pathophysiology [5]. In this article, we look at the function and findings of modern imaging techniques in the diagnosis of encephalopathy syndrome.

7.2 ADVANCED NEUROIMAGING ANALYSIS TECHNIQUES

Advanced artificial intelligence (AI) algorithms are making substantial advances in neuroimaging, with applications ranging from image processing to discovering new insights into brain activity. Some of the main techniques are discussed in this section.

7.2.1 Convolutional Neural Network (CNN)

CNNs are widely used to analyze neuroimaging data, such as magnetic resonance imaging (MRI). They can automatically recognize and segment brain structures, find patterns, and categorize various brain states or disorders [6, 7].

CNNs have transformed neuroimaging by offering strong tools for identifying and understanding neurological disorders. Here are some specific therapeutic applications and their implications:

- Brain tumor detection and classification: CNNs outperform standard approaches for detecting and classifying brain tumors using MRI data. This is critical for early detection and treatment planning. Accurate classification of tumor types (e.g., gliomas, meningiomas) aids in the development of personalized treatment strategies, ultimately improving patient outcomes.
- Alzheimer's disease detection: CNNs can detect tiny changes in brain structure that are characteristic of Alzheimer's disease, frequently before clinical symptoms occur. Early diagnosis enables early intervention and management. CNNs can track Alzheimer's progression by analyzing sequential MRI scans, allowing clinicians to change treatment strategies as needed [8].
- Multiple sclerosis (MS) lesion segmentation: CNNs can accurately segment MS lesions from MRI scans, offering consistent and trustworthy data that help to track disease progression. CNNs aid in the evaluation of therapy efficacy by quantifying lesion load and change over time.
- Epilepsy focus localization: The accurate localization of epileptic foci using CNNs from neuroimaging data aids surgical planning and improves surgical outcomes for epilepsy patients. CNNs provide a noninvasive way of detecting epileptic regions, which reduces the requirement for intrusive treatments.

- Stroke detection and outcome prediction: CNNs can detect acute strokes rapidly and reliably from CT and MRI scans, allowing for prompt intervention. Predicting outcomes and likely recovery trajectories using initial imaging aids clinical decision-making and patient counseling [9].

7.2.2 Generative Models

When real data are limited, techniques like generative adversarial networks (GANs) can produce synthetic neuroimaging data to aid in model training. They can also be used to enhance data and improve image quality. Generative models, notably GANs, have demonstrated great promise in the field of neuroscience. GANs are made up of two neural networks: a generator and a discriminator, which compete to enhance the quality of the generated data. Here's an in-depth look into how GANs function, their applications in neuroimaging, and their therapeutic implications:

Enhanced diagnostic accuracy: GANs increase the quality and quantity of training data, resulting in more accurate and robust diagnostic models. Better-trained models can detect and diagnose neurological diseases earlier and more accurately, resulting in better patient outcomes.

Reduced data acquisition costs: Using synthetic data eliminates the need for lengthy and costly neuroimaging examinations. Lowering prices makes advanced diagnostic procedures more accessible and allows for larger-scale studies.

Improved image quality for better study: Increasing image resolution and quality enables a more detailed and accurate study of brain structures and diseases. High-quality photos enable improved detection of small abnormalities, which aids in early diagnosis and treatment planning [10].

Standardization across investigations: Domain adaptation and data imputation standardize neuroimaging data, lowering variability and increasing reliability in multicenter investigations. Consistent data quality improves both the reproducibility of research findings and the dependability of clinical trials. GANs are effective methods for creating synthetic neuroimaging data, enhancing picture resolution, and addressing issues with data unpredictability and missing data. Their implementation in neuroimaging improves diagnostic accuracy, lowers expenses, and promotes improved clinical and research outcomes. GANs outperform traditional neuroimaging techniques by producing high-quality synthetic data, boosting picture resolution, imputing missing data, lowering costs, and increasing model robustness and generalization. These advantages make GANs an effective tool for improving neuroimaging analysis and clinical practice [11].

7.2.3 Multimodal Integration

AI may combine data from many imaging modalities (such as MRI, PET, and fMRI) to produce a more complete picture of brain function and anatomy. This can improve diagnostic accuracy and understanding of complex brain illnesses.

Enhanced diagnostic accuracy: Combining data from different imaging modalities lowers diagnostic ambiguity, resulting in more accurate and timely diagnosis. It also allows for more targeted therapies, which improves patient outcomes. Multimodal imaging offers extensive information about an individual's condition, allowing for tailored treatment options. It increases therapy efficacy while reducing side effects. Multimodal imaging enables complete monitoring of disease development and therapy response. It predicts disease outcomes and guides long-term care solutions. Multimodal imaging also provides a comprehensive perspective of the brain, making it easier to conduct research into the underlying causes of brain illnesses. It promotes the development of novel diagnostic tools and therapy techniques. Multimodal imaging identifies important brain areas that control sensory, motor, and cognitive functions, and reduces the possibility of injuring important areas during brain surgery, hence improving patient safety and outcomes [12]. Algorithms trained on multimodal data can forecast disease progression and treatment outcomes, which helps clinicians make informed judgments about patient care.

Enhanced understanding of brain function: Multimodal integration sheds light on the complex relationships among brain structure, function, and metabolism. It contributes to a more profound theoretical knowledge of brain function and disorders [13, 14].

7.2.4 Predictive Models

Machine learning (ML) algorithms can use neuroimaging data to predict disease progression, patient outcomes, and therapy responses. This is especially beneficial in personalized medical techniques. Predictive modeling uses ML algorithms to analyze neuroimaging data and forecast clinical outcomes such as disease progression, patient outcomes, and therapy responses. This technique is essential for personalized medicine, in which treatments and interventions can be tailored to specific patients based on predicted insights.

Enhanced diagnostic accuracy: Predictive models make it easier to discover neurological disorders early on, allowing for more prompt intervention and disease management. It improves the ability to differentiate between comparable neurological diseases, resulting in more exact diagnosis. They promote personalized medicine; by predicting individual reactions to treatments, healthcare providers can adapt interventions to maximize efficacy while minimizing negative effects and identify high-risk patients who may require more severe therapy or monitoring. Predictive models improved patient outcomes by assisting in designing optimized treatment regimens that are tailored to the patient's specific condition, resulting in better overall outcomes. This helps in continuously monitoring illness progression and changing treatment regimens in real time using predictive insights [15].

Resource allocation: Predictive models can determine which patients are most likely to benefit from specific treatments, ensuring that healthcare resources are spent wisely. They provides doctors with data-driven insights to help them make more educated decisions, hence improving patient care. These models aid in research

and development by helping discover new biomarkers for neurological illnesses by finding predictive patterns in neuroimaging data. They improve clinical trial design and efficacy by employing predictive models to choose appropriate participants and endpoints. Predictive modeling in neuroimaging uses ML to help improve patient care through early diagnosis, personalized therapy, and better results. These models give vital insights that help doctors make informed decisions, improving the efficacy and efficiency of neurological care [16].

7.2.5 Atlas-based Approaches

AI can improve brain atlases by incorporating fresh imaging data, boosting anatomical landmark precision, and assisting with the localization of brain regions of interest. Enhanced precision of anatomical landmarks incorporates fresh imaging data into brain atlases, enabling continual refining and enhanced accuracy and resulting in more exact localization of brain areas, which is critical for diagnostic accuracy and surgical planning.

Improved localization of brain areas: Refined atlases provide precise and accurate maps of brain areas, making it easier to identify small or obscure anatomical features. They improve localization and the correlation of anatomical abnormalities with functional deficiencies, resulting in a better knowledge of neurological diseases.

Guidance in surgical and therapeutic interventions: Accurate atlases help neurosurgeons plan and execute procedures, lowering the chance of injuring crucial brain areas. This helps to target specific brain regions for therapies like deep brain stimulation or tailored medication delivery [17].

Facilitation of research and education: Refined atlases are invaluable in neuroscientific research because they provide a consistent reference for comparing anatomical and functional data across studies. They serve as complete teaching resources for medical students and professionals, improving their understanding of brain anatomy and function.

7.2.6 High-dimensional Data Analysis

Tensor decomposition and manifold learning are useful techniques for handling and interpreting the high-dimensional data generated by neuroimaging investigations, allowing for a better understanding and visualization of complicated brain activity patterns. These techniques improve our understanding of the brain's structure and function, resulting in more accurate diagnostic tools and treatments for neurological diseases.

Enhanced data interpretation: Neuroimaging techniques generate massive amounts of high-dimensional data, which is difficult to analyze. Tensor decomposition and manifold learning are useful techniques for simplifying and analyzing such data, resulting in better insights into brain function and pathology.

Improved diagnostic accuracy: High-dimensional data analysis can reveal subtle patterns and abnormalities that regular analysis approaches may miss. Advanced pattern recognition enables the early diagnosis of neurological illnesses such as Alzheimer's, Parkinson's, and epilepsy [18].

Personalized medicine is the practice of tailoring treatment strategies to individual patients' unique high-dimensional data profiles. Such practice improves therapy efficacy by focusing on specific brain regions and functions uncovered through enhanced data analysis. Advanced research involves identifying novel biomarkers for a variety of neurological and mental diseases. Gaining better insights into the dynamic interactions of the brain will help to develop neuroscience [19].

7.3 OPTICAL IMAGING AND BRAIN-MACHINE INTERFACES

Optogenetics is a technique that uses light to regulate neurons that have been genetically engineered to be light-sensitive. It enables precise regulation of neural activity in animal models, revealing details about brain function and behavior.

Brain-machine interfaces (BMI) allow direct contact between the brain and external devices, which has the potential to restore function in paralyzed people while also enhancing our understanding of neural code.

Optical imaging techniques are generally noninvasive and repeatable, making them excellent for longitudinal research. Real-time monitoring of brain activity is useful for gaining insights into cerebral hemodynamics and oxygenation. Near-infrared spectroscopy (NIRS) techniques are portable and can be employed at the bedside, allowing for brain monitoring in critical care settings such as neonatal intensive care units. They allow for the imaging of brain activity, which is useful in cognitive neuroscience and studying brain function in both health and sickness [20].

BMIs can restore motor functions in paralyzed or limb-amputation patients by allowing them to control prosthetic limbs or external devices. BMIs can help people with severe motor disabilities communicate more effectively, improving their quality of life. They can be used in rehabilitation programs to retrain motor functions following a stroke. BMIs can also be used in neurofeedback therapy to help patients regulate brain activity, which may aid in the treatment of diseases such as attention deficit hyperactivity disorder (ADHD) or anxiety [21].

7.4 BENEFITS OF AI-RELATED ADVANCES IN NEUROIMAGING TECHNIQUES

CNNs provide significant advantages over standard neuroimaging techniques. These benefits include accuracy, efficiency, and the ability to handle complex data. Here are several significant advantages:

1. Automatic feature extraction, the traditional approach, identifies significant image properties mostly through handcrafted features and topic expertise. Manual feature extraction is time-consuming and subject to human mistakes. CNNs learn and extract hierarchical features from raw image data automatically, without the need for operator intervention. They capture intricate patterns and systems that may be invisible to human experts. CNNs adapt to fresh data and improve performance over time. Variability exists owing to differences in operators and subjective interpretations.

Automatic feature extraction is often less accurate at detecting subtle or minor anomalies [21].

2. CNNs produce consistent results by eliminating human variability from the equation. They can learn from enormous volumes of data and find minute patterns, allowing them to detect and classify problems with greater precision. CNNs outperform established methods for tumor identification, segmentation, and classification. Traditional neuroimaging struggles with high-dimensional data, necessitating dimensionality reduction approaches that may result in the loss of valuable information. Such neuroimaging has limited ability to handle multimodal data (for example, combining MRI, PET, and fMRI) [7, 22].
3. CNNs are capable of processing enormous amounts of high-dimensional data effectively. They integrate multimodal data to enable more thorough analysis, improving diagnostic accuracy and understanding of brain illnesses. CNNs use innovative architectures and layers to efficiently handle and comprehend complicated data structures.
4. Once trained, CNNs can swiftly analyze and interpret neuroimaging data, dramatically lowering diagnostic and analysis time. They enable real-time processing and decision-making, which is vital in healthcare applications where prompt intervention is required [9, 23].

7.5 EARLY DIAGNOSIS AND PROGNOSIS

Traditional neuroimaging may miss early symptoms of disorders that are difficult to identify using the human eye or traditional algorithms. Diagnosis is frequently based on obvious symptoms or severe disease stages. Such neuroimaging detects subtle changes and early indicators of neurological disorders, allowing for earlier diagnosis and treatment. Analyzing patterns and trends in imaging data over time can help predict disease progression and patient prognosis [5]. Performance varies substantially depending on the dataset and imaging settings. Traditional neuroimaging is frequently adapted to individual objectives, with insufficient generalization across varied applications. CNNs are good at generalizing across varied datasets and imaging circumstances because of their capacity to learn from diverse data sources. They provide reliable performance in a variety of neuroimaging tasks, including segmentation, classification, and detection [8, 24].

Traditional neuroimaging has had limited integration with new technologies like augmented reality (AR) and virtual reality (VR). CNNs are easily integrated with other cutting-edge technologies, improving visualization and interaction with neuroimaging data. They support sophisticated applications like surgical planning and navigation with AR and VR.

7.6 LIMITATIONS OF ADVANCED NEUROIMAGING TECHNIQUES

Advanced neuroimaging techniques, such as MRI and PET scans, have several restrictions, including cost and accessibility, technological constraints, invasiveness and safety concerns, interpretation difficulties, physiological limitations, and

ethical and privacy problems. These constraints can limit access for individuals and healthcare systems, particularly in low-income areas. Techniques such as fMRI and electroencephalogram (EEG) provide excellent spatial resolution but low temporal precision, whereas CT and PET require ionizing radiation. These limitations underline the importance of continued improvements and cautious consideration when using advanced neuroimaging techniques in both research and therapeutic contexts.

7.7 CONCLUSIONS

AI-based neuroimaging techniques, particularly those that use advanced models such as CNNs and GANs, provide dramatic advantages over traditional methods. These gains extend to data processing, analytical accuracy, and therapeutic applications, significantly improving the area of neuroimaging. AI approaches, like CNNs, automate the feature extraction process, minimizing the need for manual involvement and lowering the likelihood of human error. This automation improves accuracy in detecting and classifying neurological diseases, allowing for earlier and more reliable diagnoses than older techniques. GANs and other AI models can produce synthetic data to supplement existing datasets and overcome data scarcity constraints. This capacity guarantees more complete training datasets, resulting in the creation of more robust and generalizable models. As a result, AI-driven systems provide consistent performance across a wide range of datasets and imaging settings, outperforming traditional neuroimaging techniques. AI approaches, such as super-resolution GANs, improve the resolution and quality of neuroimaging data. This enhancement allows for the discovery of small anomalies and improved visualization of brain regions, resulting in more accurate and detailed studies that conventional approaches may struggle to achieve. AI-driven neuroimaging processes are far faster than traditional methods, allowing for real-time analysis and decision-making. This speed is significant in clinical applications that require prompt diagnosis and action, such as acute stroke detection and emergency treatment. The ability of AI models to generate high-quality synthetic data minimizes the need for large and costly neuroimaging experiments. This reduction in data-collecting costs makes advanced neuroimaging techniques more accessible, allowing for wider use in both research and clinical settings. AI approaches standardize data processing and analysis, which reduces variability caused by diverse imaging processes and equipment. This standardization improves the reliability and repeatability of neuroimaging studies, resulting in overall higher-quality research findings and clinical outcomes. Advanced applications enabled by AI approaches include early identification of Alzheimer's disease, precise localization of epileptic foci, and automated segmentation of brain tumors and MS lesions. These skills help with personalized treatment regimens, surgical outcomes, and patient management.

In conclusion, AI-based neuroimaging techniques outperform traditional methods in terms of accuracy, efficiency, and versatility. AI-driven techniques are transforming the field of neuroimaging by leveraging automated feature extraction, synthetic data production, higher picture resolution, and consistent

performance, resulting in better diagnostic tools, more effective treatments, and, ultimately, better patient care. The use of AI in neuroimaging is a paradigm change that offers the promise of propelling neurological research and clinical practice to new heights.

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8 Targeted Drug Delivery for Neurological Disorders

Bhupen Kalita

8.1 INTRODUCTION TO TARGETED DRUG DELIVERY IN NEUROLOGY

The nervous system is affected by varieties of neurological disorders ranging from degenerative diseases to acute injuries (Table 8.1). Central nervous system (CNS) disorders contribute up to 6.3% of all diseases worldwide [1]. Alzheimer's disease (AD) is a progressive neurodegenerative condition characterized by cognitive decline and memory loss, first defined by Alois Alzheimer in 1906 [2]. Genetic studies have identified risk factors associated with familial and sporadic forms of AD, influencing personalized medicine approaches [3]. Research findings designate the role of amyloid-beta and tau proteins in the pathogenesis of AD, leading to the development of novel biomarkers for early detection [4]. Parkinson's disease (PD) is a movement disorder and is characterized by motor symptoms like tremors and bradykinesia and generally seen later in life, attributed to the loss of dopaminergic neurons in the substantia nigra of the brain [5].

Stroke is an acute neurological disorders and leading cause of disability and mortality worldwide. Advances in antiplatelet therapy and endovascular procedures have contributed in acute stroke care [6]. Moreover, neuroimaging innovations like computed tomography (CT) angiogram and diffusion-weighted and susceptibility-weighted magnetic resonance imaging (MRI) have upgraded stroke diagnosis and prognosis [7]. Management of autoimmune diseases like amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) have benefited from genome-wide association studies (GWAS) and gene editing technologies, offering avenues for targeted therapies [8].

8.2 OVERVIEW OF CONVENTIONAL DRUG DELIVERY METHODS

The conventional drug delivery methods in neurological disorders aimed at effectively transporting therapeutic agents across the blood–brain barrier (BBB) to reach specific regions of the central nervous system (CNS).

8.2.1 Oral Administration

Oral drug delivery for brain disorders faces challenges due to poor BBB permeability and enzymatic degradation of the drug agent in the gastrointestinal tract (GI). Advances in formulation technologies aim to enhance drug bioavailability [9]. For chronic illness, oral drug administration offers greatest convenience in

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TABLE 8.1
Neurological Disorders and Their Symptoms, Pathophysiology, and Common Risk Factors

Neurological Disorders	Symptoms	Pathophysiological Mechanism	Risk Factors
Alzheimer's disease	Gradual decline of memory, reasoning, and handling of complex tasks, behavior, and personality.	Accumulation of abnormal neuritic plaques and neurofibrillary tangles in the brain leading to loss of neurons.	Aging, diabetes, stroke, heart problems, depression, genetic history, lifestyle.
Stroke	Trouble in speaking and understanding, confused, slur words; numbness, weakness or paralysis in the face, arm, or leg.	Ischemic stroke-deficient blood and oxygen supply to the brain; hemorrhagic stroke-bleeding or leaky blood vessels in the brain.	High blood pressure, heart disease, diabetes, smoking, high blood lipids, excessive alcohol use.
Parkinson's disease	Tremor in hands, arms, legs, jaw, or head; muscle stiffness, slowness of movement, impaired coordination.	Nerve cells in the basal ganglia become impaired leading to decreased secretion of dopamine that causes movement problems.	Advancing age, men are more likely to develop PD, genetics, environmental causes, brain trauma.
Epilepsy and seizures	Staring, jerking of the arms and legs, stiffening of the body, loss of consciousness, breathing problems.	Disrupted balance between excitatory and inhibitory neurotransmitters at the synaptic level can result in seizure activity.	Genetic factors, developmental brain abnormalities, infection, traumatic brain injury (TBI).
Multiple sclerosis	Numbness in one or more limbs, tingling, electric-shock sensations (Lhermitte sign), lack of coordination, unsteady gait or inability to walk, partial or complete loss of vision, usually in one eye at a time.	Formation of plaques in CNS along with inflammation, demyelination, axonal damage, and axonal loss. It is an autoimmune disease caused by autoreactive immune cells that traverse BBB and attack the CNS.	15–50 years of age, women are at more risk, North Europeans are at higher risk, those living at 40°C and above, family history, certain viral infections and autoimmune diseases.
Migraine	Intense throbbing or dull aching pain in head, stiff or tender neck, lightheadedness.	Imbalance in brain neurotransmitters, including serotonin, calcitonin gene-related peptide (CGRP).	Family history, hormonal changes in women, adolescence and younger age.

(*Continued*)

TABLE 8.1 (*Continued*)
Neurological Disorders and Their Symptoms, Pathophysiology, and Common Risk Factors

Neurological Disorders	Symptoms	Pathophysiological Mechanism	Risk Factors
Neuroinfections	Fever, pain, swelling, redness, impaired function. In the case of some viral infections, drowsiness, confusion, and convulsions may occur.	Occur if microorganisms invade the nervous system. Encephalitis, meningitis, HIV-AIDS, fungal infections, parasitic infections, prion diseases, bacterial infections such as Lyme disease, tuberculosis, syphilis, brain abscess.	Certain age groups, poor immune system, certain geographical locations, autoimmune disease, smoking, brain surgery.
Brain tumor	Headaches, seizures (fits), nausea and vomiting, drowsiness, mental or behavioral changes, such as memory problems.	Tumors can invade, infiltrate, or supplant normal parenchymal tissue, disrupting normal function, and can cause increased intracranial pressure.	Risk increases with age, genetics, and exposure to radiation.
Amiotrophic lateral sclerosis	Muscle twitches; muscle cramps; tight and stiff muscles (spasticity); muscle weakness affecting an arm, a leg, or the neck.	Degeneration of pyramidal Betz cells in the motor cortex, anterior horn cells of spinal cord, lower cranial motor nuclei of the brainstem.	Genetics, exposure to heavy metal, pesticides, head trauma, stroke, magnetic field, and hypertension.
Cerebral aneurysm	Headaches, eye pain, vision change.	Ballooning from wall of the blood vessels in the brain. If it expands and the blood vessel wall becomes too thin, the aneurysm will rupture and bleed.	Genetics, advancing age, alcohol consumption, atherosclerosis, cigarette smoking.

self-medication. Several lipids have been shown to affect the BBB and facilitate drug delivery into the brain after systemic circulation: oleic acid, triolein, alkylglycerols, and conjugates of linoleic and myristic acid [10]. These examples suggest exploring novel lipids for oral drug administration for neurodisorders.

8.2.2 Intravenous Injection

Intravenous administration is advantageous as it bypasses the GI tract and gives highest bioavailability. However, large molecular size and hydrophilicity often limit

BBB penetration. Strategies like use of viral vectors, nonviral vectors (nanoparticle, exosomes, etc.), prodrug design, or conjugation with BBB-shuttle peptides improve CNS uptake [1].

8.2.3 Intrathecal Injection

The intrathecal injection method has many important applications, such as treating meningitis or spinal cord injuries, spinal anesthesia, pain management, and chemotherapy. This injection method bypasses the BBB and delivers a drug directly into the CNS. The drug is injected into the cerebrospinal fluid (CSF) via lumbar puncture [11].

8.2.4 Intranasal Delivery

The drug is carried through the olfactory and trigeminal nerve pathways to the brain. This route, due to shorter physical distance, offers rapid delivery of drug into the brain. Also, the nose-to-brain lymphatic system has been proposed as a novel target for neurological disorders [12].

8.2.5 Intra-arterial Infusion

This method identifies the carotid or vertebral arteries supplying blood to the brain, to which drug is directly infused. It is particularly beneficial for acute stroke interventions. In recent decades, intra-arterial administration of anticancer drugs has been considered a suitable alternative drug delivery route to intravenous and oral administration [13].

8.3 IMPORTANCE OF TARGETED DRUG DELIVERY FOR NEUROLOGICAL DISORDERS

Targeted drug delivery into the brain has gained attention of researchers worldwide in the treatment of neurological disorders, addressing the challenges of BBB penetration, site-specific drug release, and minimizing systemic side effects (Table 8.2). The BBB is an important immunological feature of the CNS, which restricts most drugs from entering the brain [14]. Targeted delivery systems have demonstrated significant advantages over conventional therapies in neurological disorders like Alzheimer's disease and Parkinson's disease by encapsulating anti-inflammatory agents or neuroprotective compounds within nanoparticles to mitigate neuro-inflammation and oxidative stress [15]. A drug molecule must possess the required physicochemical properties for efficient permeation across the BBB. However, finding all these properties in drug molecules is a formidable task, and indeed most drugs fall away from these properties [16]. Nonpermeability is often an issue with macromolecular pharmaceuticals, including peptides, proteins, antibodies, and oligonucleotides [17]. There have been prodigious efforts to enhance drug diffusion into the brain parenchyma, including chemical modification of drugs, chemically or osmotically opening of tight junctions, physical disruption of the BBB layer,

TABLE 8.2
Comparison of Conventional versus Targeted Drug Delivery in Neurological Disorders

Parameters	Conventional Drug Delivery	Targeted Drug Delivery
BBB permeability of the drug	Poor	High
Amount of drug reaching the brain	Generally less	High
Site specificity	Less or nil	High
Enzymatic degradation of the drug	More	Less
Dose requirement	More	Less
Off-target effect	More	Less
Systemic side effect	More	Less
Peripheral exposure of the drug	More	Less
Patient convenience	Generally more with oral administration	Poor patient convenience in the invasive methods
Self-medication	Not possible with all drugs/methods	Not possible with all drugs/methods
Self-regulation	Not possible	Possible with programmable drug delivery methods
Protein and peptide delivery	Less efficient	Efficient
Economy	Less price	High price

and the use of specific carriers/transporters. Each method has its advantages and limitations. Chemical modification of a drug needs to go through the Investigational New Drug (IND) application, which is a very time-, effort-, and resource-consuming process [18]. Furthermore, the prodrug approach may exhibit altered pharmacokinetics, resulting in lower efficacy or toxicity in other organs. Disruption of the BBB by injecting a hyperosmolar substance or physically by ultrasound enhances drug transport but also enables paracellular transport of blood toxins into the brain [19]. This technique is limited mainly to small molecules.

8.4 CHALLENGES IN NEUROLOGICAL DRUG DELIVERY

8.4.1 BBB Penetration

The BBB is a highly selective membrane that restricts the passage of substances from the bloodstream into the brain parenchyma. This barrier is composed of endothelial cells with tight junctions, astrocytes, and pericytes, forming a strong defense mechanism against any solute, including blood-borne toxins and pathogens, which also limits the delivery of therapeutic agents [20]. BBB maintains brain homeostasis and prevents many potentially beneficial drugs from reaching their targets in the brain, making treatment of diseases like Alzheimer's, Parkinson's, and stroke very burdensome. Also, proteolytic enzymes capable of rupturing neuroactive blood-borne solutes and drugs in brain capillary endothelial cells (BCEC) form an additional

enzymatic barrier [21]. The systemic drug delivery to the brain is greatly hampered by the BBB, which rejects almost 98% of substances. Biopharmaceuticals such as recombinant proteins or monoclonal antibodies (mAb), which have emerged as a promising part of drug development, have failed in treating CNS diseases due to their poor access to the brain across the BBB. For instance, Bevacizumab (Avastin) and Natalizumab (Tysabri), which are FDA-approved monoclonal antibody-based therapeutics for treating brain cancer and multiple sclerosis, respectively, do not cross the BBB [22].

8.4.2 Physicochemical Properties

Some of the unfavorable physicochemical properties of drugs pose difficulties in drug delivery to the CNS. One of the major challenges arises from the size and molecular weight of drugs. Large molecules or those with high molecular weights face difficulty crossing the BBB due to its tight junctions and low permeability to hydrophilic and large molecules, whereas lipophilic drugs might penetrate the BBB more readily but can encounter issues with efficient transport mechanisms within the CNS once inside. Also, the degree of ionization of drugs at physiological pH decides the fate of the drug in membrane permeation. The unionized, lipophilic fraction of drugs can diffuse across membranes more easily, whereas ionized and hydrophilic drugs struggle due to their inability to pass through lipid-rich barriers like the BBB [21]. All pharmacokinetic calculations in drug delivery have dependence on the extent of plasma protein drug binding. Additionally, the presence of efflux transporters such as P-glycoprotein (Pgp), the multidrug resistance protein (MRP) family, and breast cancer resistance protein (BCRP) actively pumps drugs out of the brain endothelial cells, further limiting the central distribution of drugs that are beneficial to treat CNS diseases. Therefore, modulation of ATP-binding cassette (ABC) efflux transporters at the BBB forms a novel strategy to enhance the penetration of drugs into the brain [23].

8.4.3 Systemic and Other Off-Target Side Effects

Even after drugs successfully penetrate the BBB, they may still exhibit off-target effects. These effects can occur due to the nonspecific distribution of drugs in the brain, affecting unintended areas and leading to adverse reactions or diminished efficacy. Strategies to mitigate off-target effects include targeted drug delivery systems [21]. Moreover, the complexity of neurological diseases adds another layer of challenge. For example, Risperidone, which is used in the management of schizophrenia and bipolar disorder, has side effects like weight gain. In the treatment of Parkinson's disease, L-DOPA is a commonly prescribed drug. It is found to have side effects including dyskinesia, nausea, and orthostatic hypotension. Lamotrigine, which is a drug of choice in the treatment of epilepsy and bipolar disorder, causes skin rashes, headache, and dizziness. Attention deficit hyperactivity disorder is treated with Methylphenidate. It results in unwanted conditions like insomnia, decreased appetite, and increased heart rate. Clozapine is used in the management of treatment-resistant schizophrenia. Clozapine on chronic use causes agranulocytosis,

weight gain, and sedation [24]. These examples illustrate how medications used to treat neurodisorders often have significant side effects, suggesting scope for developing precisely targeted drug for neurodisorders.

8.5 NOVEL APPROACHES

The need for innovative technology in brain drug delivery was strongly felt in 1914 when Salvarsan, a drug for syphilis, did not enter the brain. For more than two decades afterward, researchers attempted to develop small molecular-sized high lipophilic drugs only. Then during 1980s, endogenous BBB carrier-mediated transport and receptor-mediated transport systems were identified and goals for drug design were guided by the identified transporters. A range of novel drug delivery approaches and devices has been developed to enhance efficiency of drugs for brain disorders since 1990s (Figure 8.1).

8.5.1 Nanoparticles for Drug Delivery across the BBB

Due to their unique properties, i.e., size and surface area, nanoparticles offer promising solutions to facilitate drug transport across the BBB. Polymeric nanoparticles can encapsulate drugs and protect them from enzymatic degradation, prolonging systemic circulation time and increasing the possibility of BBB permeation. Additionally, surface-modified nanoparticles tailored with ligands for targeting specific receptors on

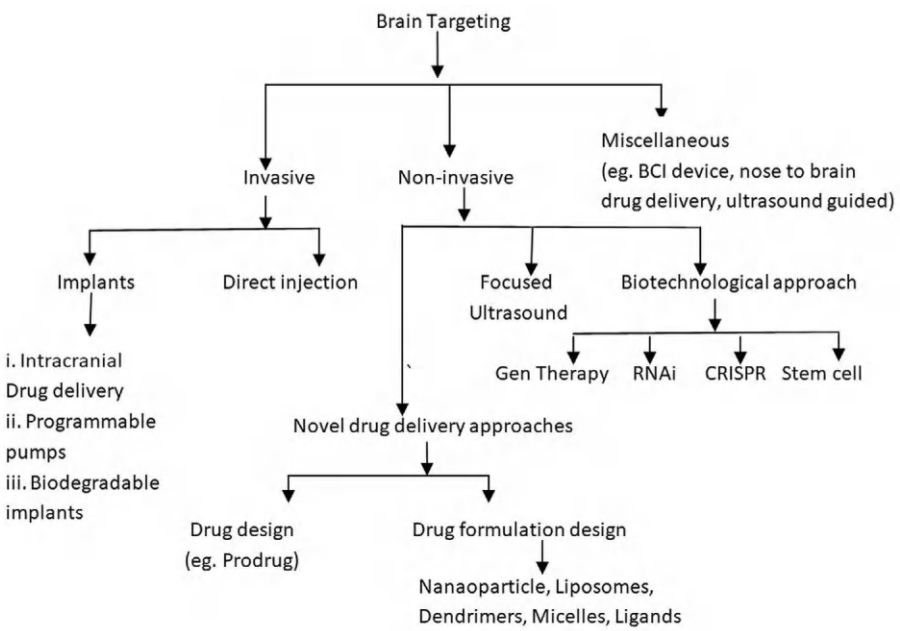

FIGURE 8.1 Flowchart showing various drug targeting approaches to the brain for site-specific, sustained, and controlled drug effect in the management of neurological disorders.

BBB endothelial cells can enhance their transport into the brain parenchyma. Also, various lipid-based nanoparticles have been proposed in recent research, such as liposomes and solid lipid nanoparticles, which facilitate their transport across the BBB, and they can encapsulate both hydrophilic and hydrophobic drugs [25].

8.5.2 Liposomes and Micelles as Drug Carriers

Both hydrophilic and hydrophobic drugs can be encapsulated in the liposomes and lipid-based vesicles with aqueous cores and lipoidal shells and thereby provide a stable environment ensuring enhanced drug permeation, solubility, and bioavailability. Their ability to traverse the BBB and additional advantage of biocompatibility make them ideal for brain targeting [26]. Liposomes functionalized with ligands like transferrin or antibodies have demonstrated significant BBB penetration and specific neurotargeting by virtue of their ability to bind with predefined receptors, thus reducing off-target effects [27]. Puri and coworkers reported that pH-sensitive liposomes release drugs selectively in response to the acidic microenvironment of neuroinflammatory sites, enhancing therapeutic efficacy [28]. Micelles are composed of amphiphilic molecules generally surfactant, which facilitate to solubilize hydrophobic drugs and enhance their delivery to target sites. Micelles have been shown to offer controlled release profiles and stability in biological fluids, which is advantageous for sustained drug delivery to neurons [29].

8.5.3 Dendrimers and Polymers for Targeted Delivery

Dendrimers are highly branched macromolecules that offer high drug entrapment, precise control of particle size, and surface functionality [30]. Their multifunctional nature allows for conjugation with targeting ligands and imaging agents, enhancing site-specific drug delivery [31]. Polymeric nanoparticles provide versatility in encapsulating both hydrophobic and hydrophilic drugs while stabilizing them against enzymatic degradation. Surface modification with ligands further improves their binding specificity [32]. Research in polymer science has succeeded in developing stimuli sensitive materials that enable controlled drug release within targeted brain regions [33].

8.5.4 Focused Ultrasound in Opening the BBB

Focused ultrasound (FUS) is a noninvasive technique for transiently opening the BBB, increasing permeability of drugs to the brain. By exploiting acoustic waves, FUS induces microbubble oscillation at the BBB site, leading to localized mechanical disruption and increased permeability. This approach allows therapeutic agents that are otherwise barred by the BBB [34]. Many studies have claimed the versatility of FUS in delivering a range of therapeutics, including chemotherapy agents and antibodies [35]. FUS offers spatial and temporal precision that minimizes systemic side effects and provide a safer alternative to invasive methods. Optimization of FUS parameters is very important for maximal BBB opening while ensuring tissue safety and uniform drug distribution within the brain parenchyma [36].

8.5.5 Advancements in Ultrasound-Guided Drug Delivery

Ultrasound-guided drug delivery for neurodisorders is a potential noninvasive approach to target brain tissues, offering precise and localized control of drug permeation. This approach not only minimizes systemic side effects but also enhances drug bioavailability in target areas. Many research attempts have demonstrated the potential of ultrasound-guided drug delivery in various neurodisorders. For example, FUS has been utilized to deliver chemotherapy agents and neuroprotective drugs for treating brain tumors and neurodegenerative diseases like Alzheimer's. Encouraging outcomes have been demonstrated in ultrasound guided delivery of the therapeutic agents oxygen, 1,3-bis(2-chloroethyl)-1-nitrosourea, triptolide, plasmid DNA, doxorubicin, muscimol, and propofol for various brain disorders [37].

8.6 NOSE-TO-BRAIN TARGETED DRUG DELIVERY

8.6.1 Anatomy of the Nasal Cavity and Its Relevance for Drug Delivery

The nasal epithelium comprises various cell types, including ciliated and nonciliated cells, tight junctions, and enzymes like cytochrome P450, which together influence drug metabolism and bioavailability [38]. The nasal cavity can serve as an entry point for drugs to reach the brain. Its highly vascularized mucosa and proximity to the brain via the olfactory and trigeminal nerves facilitate efficient drug transport directly into the CNS. Intranasal delivery provides a practical, noninvasive method of bypassing the BBB to deliver therapeutic agents to the brain and spinal cord. This technology allows drugs that do not cross the BBB to be delivered to the CNS within minutes. It also directly delivers drugs that do cross the BBB to the brain, eliminating the need for systemic administration and its potential side effects. This is possible because of the unique connections that the olfactory and trigeminal nerves provide between the brain and external environment [39].

8.6.2 Nasal Formulations for Neurological Disorders

Nasal formulations, generally liquid and semiliquid in nature, are applied as drops or spray that can be inhaled to the deeper regions of the nasal cavity. The nasal route offers advantages like noninvasive administration, ease of use, and potential for self-medication, particularly beneficial in chronic conditions requiring long-term treatment [38]. Various neurological conditions, including Alzheimer's disease, Parkinson's disease, and epilepsy, benefit from nasal formulations due to their ability to achieve rapid onset of action and improved patient compliance [40]. Recent advancements in formulation technologies, such as nanoemulsions, liposomes, and polymeric nanoparticles, have further enabled sustained drug release in the nasal mucosa, prolonging therapeutic effects [41]. Intranasal delivery has been used to target a wide variety of therapeutics to the CNS. For example, the following classes of therapeutics have successfully been intranasally delivered to the CNS: neurotrophins, neuropeptides, cytokines, polynucleotides, and small molecules (like chemotherapeutics and carbamazepine). Consequently, ability to deliver insulin by nose to

the CNS without altering blood glucose could provide an effective means to improve glucose uptake and utilization and reduce cognitive deficits in patients with memory disorders [39].

8.7 IMPLANTABLE DEVICES FOR TARGETED DRUG DELIVERY

8.7.1 Intracranial Drug Delivery Systems

Intracranial drug delivery systems represent those methods where the drug is directly injected to an identified location through the skull or implanted near the brain, aiming to precisely target drugs to the brain while minimizing systemic exposure and side effects. They encompass a range of approaches, including implantable devices, convection-enhanced delivery (CED), and direct intraparenchymal injections, each tailored to specific therapeutic goals [42]. Implantable devices, such as drug-eluting polymers and biodegradable wafers, provide sustained release of drugs directly to affected brain regions, enhancing therapeutic efficacy. CED utilizes pressure-driven infusion to distribute therapeutics into targeted brain areas, overcoming diffusion barriers and achieving homogeneous drug distribution [43].

8.7.2 Programmable Pumps for Precise Dosing

A programmable pump is a drug reservoir programmed as per the dosing need of the patient and represents a significant advancement in precision medicine, particularly in the context of targeting drugs to the brain and avoiding systemic side effects [44]. One prominent example is the use of programmable infusion pumps in treating Parkinson's disease, where precise dosing of levodopa can optimize therapeutic outcomes. These pumps enable continuous, intracerebral delivery of drugs, maintaining therapeutic levels within the brain while reducing fluctuations that often occur with oral administration [45]. In neuro-oncology also, programmable pumps have shown encouraging results. They facilitate localized delivery of chemotherapy agents directly into brain tumors [46].

8.7.3 Biodegradable Implants for Sustained Release

Biodegradable implants have been in use for achieving sustained drug release in brain targeting applications. These implants are designed to degrade over time, releasing therapeutic agents directly into the brain parenchyma and leaving less possibility of systemic side effects. Biodegradable wafers loaded with chemotherapeutic agents for the treatment of glioblastoma multiforme (GBM), a highly aggressive brain tumor. These wafers, such as Gliadel® (carmustine implant), are implanted at the surgical site following tumor resection. Over several weeks, the wafer gradually degrades, releasing carmustine directly into the tumor site, thus improving local drug concentration and reducing systemic exposure [47].

Advancements in polymer science have enabled the development of implants with modified degradation profiles and drug release kinetics. Polymers like poly(lactic-co-glycolic acid) (PLGA) are commonly used due to their biocompatibility and

ability to degrade into nontoxic byproducts, ensuring safety while delivering therapeutics effectively. Also, the use of chemically modified PLGA in delivery systems such as functionalizing PLGA to create surface modified particles has generated new ideas for targeted delivery. PLGA additionally provides a platform to develop external stimuli responsive drug delivery systems. Due to their versatile nature, they have been investigated for various neurological conditions beyond cancer, including neurodegenerative diseases and epilepsy, demonstrating potential for sustained release of neuroprotective agents [48].

8.8 GENE THERAPY AND RNA-BASED APPROACHES

8.8.1 Viral Vectors for Targeted Gene Delivery

Gene therapy has undergone many transitions in past 40 years. Viral vectors have been applied in targeted gene delivery to the brain. Viruses such as adenovirus, adeno-associated virus (AAV) and lentivirus are commonly employed due to their ability to transduce neurons and glial cells with high specificity and minimal immune response. These vectors are processed by recombinant technology to carry therapeutic genes that can correct genetic mutations, enhance neuroprotection, or modulate neuronal activity [49]. Clinical trials using AAV vectors have shown promising results in treating neurogenetic disorders like autosomal recessive genetic disorders, spinal muscular atrophy and certain types of inherited blindness. Lentiviral vectors, with their ability to integrate into the host genome, offer long-term gene expression, making them suitable for chronic neurological conditions. Despite these advancements, challenges such as immune responses to viral vectors and potential off-target effects necessitate ongoing research to refine vector design and delivery techniques. Nevertheless, viral vectors hold immense potential in advancing gene therapy in neurology, offering hope for treating previously incurable brain disorders [50].

8.8.2 RNA Interference (RNAi) in Neurological Disorders

RNA interference (RNAi) has emerged as a promising therapeutic approach for treating neurological disorders by selectively silencing disease-causing genes at the mRNA level. This mechanism involves delivering small interfering RNAs (siRNAs) or microRNAs (miRNAs) to target cells, where they bind to complementary mRNA sequences, leading to degradation or inhibition of translation. In neurology, RNAi holds potential for treating a spectrum of disorders including Parkinson's disease, ALS, spinocerebellar ataxia, neuropathic pain, neurodegenerative diseases like Alzheimer's and Huntington's diseases, as well as neurological conditions such as epilepsy and spinal muscular atrophy [51]. Clinical trials utilizing RNAi-based therapies have shown encouraging early results in conditions like amyloidosis and Huntington's disease [52].

8.8.3 CRISPR-Based Therapies for Genetic Neurological Disorders

Gene editing begins with identifying the defective gene causing the disorder, followed by disrupting the gene sequence using a very precise tool called CRISPR/Cas (clustered

regularly interspaced short palindromic sequences/CRISPR-associated). Cas comprises a family of nucleases synthetized by bacteria as part of their adaptive immunity against viruses, of which Cas9 (CRISPR-associated protein 9) is the most commonly utilized version for gene editing [53]. The CRISPR-Cas9 system allows precise editing of genetic sequences by inducing double-strand breaks, which can be repaired to introduce desired genetic changes or to disrupt faulty genes [54]. CRISPR presents hope for better treating conditions such as Duchenne muscular dystrophy, Rett syndrome, and Huntington's disease, where mutations in single genes contribute to disease pathology [55]. The application of CRISPR/Cas9 gene-editing technology is expanding to address etiological research, treatment, and intervention of neurodegenerative disorders such as Alzheimer's disease [56]. Many research attempts have focused on optimizing delivery methods, targeting disease-causing genes and associated factors in neurological disorders [57]. Early preclinical studies and clinical trials have demonstrated significant evidence for CRISPR-based therapies in correcting genetic defects [58].

8.9 INTEGRATION OF IT IN THE MANAGEMENT OF NEURODISORDERS

Brain–computer interfaces (BCIs) have been used to control prosthetic limbs, provide visual feedback, and improve cognitive functions such as attention and memory. A number of strategies have been used in the past to improve motor, somatosensory, and cognitive functions, as well as to assist with daily activities. Available literature indicates that BCI can provide a personalized and interactive therapeutic environment for neurological rehabilitation as well as monitoring treatment effectiveness [59]. Karageorgos and coworkers proposed HALO (Hardware Architecture for LOw-power BCIs), a general-purpose architecture for implantable BCIs. HALO enables tasks such as treatment of disorders (e.g., epilepsy, movement disorders) and records data for studies on the brain [60]. Recent advancements in virtual reality (VR) immersive technologies provide new tools for the development of novel and promising applications for neurological rehabilitation. This technique gives virtual tasks that encourage and facilitate the patient's empowerment and involvement in the rehabilitation process. Recently, VR has been applied in certain neurological conditions such as dementia, stroke, spinal cord injury, Parkinson's, and MS [61].

In the past two decades, several models have been developed based on machine learning and deep learning in healthcare data analysis, which can be used in the processing of a variety of data sets. Thomas et al. (2009) developed a new discriminative filter bank (FB) common spatial pattern algorithm to extract subject-specific FB for motor imagery (MI) classification [62]. Liu et al. attempted to enhance the detection of four-class motor imagery electroencephalogram (MI-EEG) signals through the utilization of a parallel spatial–temporal self-attention-based convolutional neural network (CNN) approach [63]. The use of MI-BCI has been observed to be advantageous in upper-limb stroke rehabilitation. BCIs offer avenues to treat neurological disorders, assist in understanding brain function, and interface the brain with the digital world. However, their wider adoption depends on achieving adequate real-time performance, meeting power constraints, and adhering to regulatory safety requirements for chronic implantation [59].

8.10 CLINICAL TRANSLATION AND FUTURE DIRECTIONS

8.10.1 Challenges in Transitioning from Preclinical to Clinical Studies

Despite years of efforts in CNS drug development, recent FDA approval of Zolgensma, viral-based gene therapy, is the first approved BBB-crossing biologics. In an era of biopharmaceuticals such as recombinant proteins being the most approved drugs for other diseases, their scope is greatly limited by poor delivery of such macromolecules across BBB, which reflects the poor rate of clinical translation (~8%) of CNS drugs. Transitioning from preclinical studies to clinical trials for brain-targeting therapies poses significant challenges, primarily due to the complex nature of the BBB and safety concerns [1, 64]. The absence of reliable and efficient in vitro BBB models resembling in vivo barrier properties is a major problem for researchers in developing successful therapy for CNS disorders. Moreover, preclinical models may not fully match human disease pathology or the dynamic BBB properties. Ethical considerations, patient heterogeneity, and regulatory requirements further complicate the transition, requiring vast preclinical data and complete safety profiles [65].

8.10.2 Regulatory Considerations for Targeted Neurological Therapies

The complex nature of brain-targeting therapies, which often involve cutting-edge technologies, necessitates clear regulatory pathways. Therefore, emphasis should be given to ensure safety, efficacy, and ethical standards throughout clinical trials and beyond. Regulatory agencies require data of preclinical observations demonstrating efficacy and robust safety profiles, particularly concerning potential off-target effects and long-term consequences [58]. Ethical considerations regarding informed consent, patient privacy, and the use of novel technologies in vulnerable populations are also paramount [38].

8.10.3 Future Prospects and Emerging Trends in the Field

Transformation from conventional to novel strategy is the future of drug targeting in neurodisorders. Recent biomedical research has made many steps forward that bring hope for brain drug targeting. All of the mechanisms behind the disease pathologies are still not very clear, and therefore a unique therapy does not seem to be the winning approach to solve the problem for all. One significant trend is the development of precision medicine approaches formulated to individual patient profiles [66]. Advancements in nanotechnology bring avenues for drug delivery innovations to cross the BBB [25]. Continued efforts are required in bringing innovations in nanoparticles tailored with ligands and overcoming the drug transport limitations due to efflux transporters. Engineering natural exosomes derived from mesenchymal stem cells (MSCs), dendritic cells (DCs), or macrophages to both deliver therapeutics and modulate the immune responses to tumors or in neurodegenerative disease (NDD) can allow for targeted personalized therapeutic approaches [67]. Clinical trials have shown initial success in correcting genetic

mutations responsible for conditions like spinal muscular atrophy and certain forms of inherited blindness, giving clues for broader applications. Nonetheless, precise genome-editing faces constraints such as modest efficiency, delivery challenges, and off-target effects [68]. Future research in neuro-drug delivery must consider addressing all these constraints. An interesting emerging trend is the integration of neuroimaging technologies with drug delivery systems, enabling real-time monitoring of drug distribution and therapeutic response in the brain [69]. There is scope of innovations in the development of biodegradable implantable devices and programmable pumps that allows controlled and sustained drug delivery directly into the CNS.

8.11 CONCLUSION

Brain-targeted drug delivery offers a transformative path forward in neurotherapeutics, particularly enhanced BBB transport, drug bioavailability, and patient compliance. It also offers immense potential for minimizing off-target effects within the brain and systemic side effects. There are research scopes in refining delivery technologies such as nano-drug delivery, gene therapy, implants, programmable pumps, noninvasive methods like nose-to-brain delivery, and ultrasound-assisted drug delivery to enhance the ability of therapeutics to traverse the BBB and achieve optimal therapeutic concentrations. Application of personalized medicine approaches, by capitalizing qualitative and quantitative details of biomarkers and genomic data, are expected to revolutionize neurological treatments. Furthermore, technological innovations and a growing understanding of disease mechanisms at the molecular level are supplementing development of novel drug delivery strategies for neurodisorders. BCI technologies have been advancing to meet the goals in treating neuro-impaired patients, particularly motor nerve functions. Although significant progress has been made, continued collaboration between researchers in academia and industry as well as regulatory agencies is highly appreciated to meet challenges and translate promising preclinical findings into clinically viable therapies. Regulatory bodies also need to evolve in their policies to accommodate novel technologies and ensure patient safety throughout the drug development process.

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9 Intelligent Deep Learning Algorithms for Autism Spectrum Disorder Diagnosis

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9.1 BACKGROUND

Neuroscience is a significant science field that covers study of the nervous system. The nervous system supports every activity of the human body and stimulates every action in the body. In ancient times, neurological disease identification and treatment for patients took more time and did not have much of a success rate. At the same time, many diseases were not identified and there was no knowledge of neurological disorders. In olden days, the trepanation method was used to open the skull, and around 5000 BCE the medicinal plant papyri was used for treatment. In 300–250 BCE, only medical practitioners had knowledge about ventricles, cerebrum, and cerebellum. Neuroscience experiments started during Greek civilization, and many of them showed interest to experiment and identify that the brain is basic for every action and that any problem in the brain affects normal human activity.

After many decades, Galen described clearly that sensation information was handled by the cerebrum, muscle actions were controlled by the cerebellum and a few muscles monitored by some special nerves. From 108 to 208 AD, physicians from China, Persia, and Arab countries performed the first brain operation. The invention of paper and the printing press shifted the medical world into the next stage by printing books to indicate diseases. In 1543, the first brain dissecting operation was carried out by Andrea's Vesalius, and drawings of all portions of the brain were printed as images. Following Vesalius, many researchers expanded his work and recorded various brain functions, including pineal glands.

In the eighteenth and nineteenth centuries, many experiments were performed in the field of neuroscience, and maximum people learned about neurological diseases. Table 9.1 shows the development stage of neurological disease diagnosis.

From the eighteenth to twentieth centuries, neurological disease diagnosis created awareness among people. Much research developed with respect to nerve cells, reflexes, and biochemical changes and electrical signals in neurons.

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TABLE 9.1
Neurological Disease Diagnosis

Author	Year	Disease Diagnosis Stages
Matthew Baillie & Jean Cryveilhier	1799 and 1829	Stroke lesions
Luigi Galvani	1737–1798	Nerve electricity
Charles Bell	1774–1842	Developed Bell-Magendie law
Francois Magendie	1783–1855	Developed Bell-Magendie law
Jean Perre Flourens	1820	Motricity, sensibility
Emil du Bois-Reymond, Johannes Peter Muller, & Hermann von Helmholtz	1820	Adjacent neurons of electrical state
J. E. Purkinje	1787–1869	Statement of neurons
John Martyn Harlow	1848	Study of cortex
Paul Broca	1824–1880	Experiment on cerebral cortex
Carl Wernicke	–	Brain function for language comprehension
Richard Caton	–	Rabbit & monkey cerebral hemispheres
Herman Munk	1878	Outstanding electricity in dogs & monkeys
Harvey Cushing	1909	Postcentral gyrus
Camillo Golgi & Santiago Ramony Cajal	1890	Nerve cells (Nobel Prize)
Eugen Bleuler	1911	Autism
James Parkinson	1817	Parkinson disease
Hippocrates	Fifth century BCE	Stroke
Galen	1550 BCE	Migrane

9.2 INTRODUCTION

In this digital world, everyone lives their life in scheduled way, and many of them do not give much thought to take care of their health. The environmental changes and unusual timings of food totally change human body activities, which results in more health issues. Autism is one such disease that seeks more diagnosis from researchers and medical practitioners. Normally it affects children and is identified during their development stage only. One with autism is not able to communicate, emotional imbalance arises, and weak interpersonal relationships result between the child and family and society. Mental health is basic for human well-being and supports normal activities. Brain activities regulate every neuron involvement and organ movement. In olden days, brain diseases were recorded manually, and patients' oral presentation was considered for disease diagnosis and treatment. Due to technological development, many new tools such as artificial intelligence techniques play a dominant role in disease diagnosis. This chapter analyzes and describes experiments using models such as convolution neural network (CNN), recurrent neural network (RNN), long short term memory (LSTM), visual geometry group-16 (VGG-16), and residual networks (ResNet-50) for autism detection.

9.3 RESEARCH OBJECTIVE

- The symptoms of ASD are the same as some other neurological diseases, but identifying those disease can be achieved by machine learning (ML) and deep learning (DL) algorithms.
- The research seeks to enhance accuracy and minimize processing time.
- Various ML and DL algorithms with optimization techniques will improve the performance of the model.

9.4 TYPES OF NEUROLOGICAL DISORDERS

The problems in the central nervous system produce neurological disorders. They can happen to people of any age group. Figure 9.1 shows the types of neurological disorders.

Alzheimer's disease: It affects the portion of brain responsible for thinking, memorizing, learning, and intellectual activity. It can be treated by regular physiotherapy and regular stimulation of brain thinking activities.

Acute spinal cord injury: The spine, or vertebrae, is a building block of bones. The spinal cord is a collection of nerves that transfer messages between brain and other parts of body. These messages are related to movement and sensation. Acute spinal cord injury is a result of bruises in the core that tears the portion of core or completely tears it. Accidents or falls may result in such injury. As result, this injury may result in permanent disability or death for a child or adult.

Parkinson's disease: It slow down the body movement and occurs mostly to older people. It results loss of smell, excess salivation, mood disorder, constipation, insomnia, depression, and loss of cognition and is a leading disease around the world. It is also considered a palsy disorder.

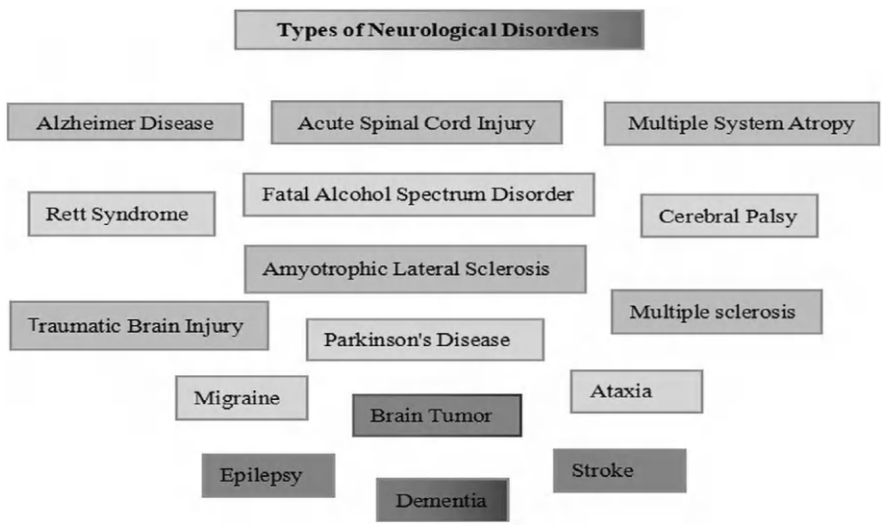

FIGURE 9.1 Types of neurological disorders.

Multiple system atropy: It damages the nerve cells in the brain and occurs rarely for humans. It affects movement, balance, breath control, bladder control, and low blood pressure. It usually afflicts those ages 30 to 60.

Rett syndrome: It occurs due to genetic mutation and is a progressive neurodevelopment disorder. People with this syndrome cannot respond quickly, have lower cognitive abilities, and are slower in communication. Verbal communication takes long time for children with Rett syndrome.

Fetal alcohol spectrum disorder: Alcohol consumption in pregnancy affects the fetus, resulting in fetal alcohol spectrum disorder. It creates severe effects in face forming, skeleton and bone development, and cardiac development. It is a lifelong disorder.

Cerebral palsy: It mainly affects the fetus brain and is a combination of multiple disorders. Cerebral palsy mainly disturbs motor activities, cognitive abilities, sensations, and results in pressure ulcers, seizures, and problems with feeding, listening, hearing, vision, etc.

Traumatic brain injury: The World Health Organization declared that around 60 million people have been affected by traumatic brain injury annually. It happens in two ways: damaged and nondamaged brain injury. Damaged brain injury occurs by falls, accidents, assaults, child abuse, domestic violence, etc., and nondamaged brain injury occurs by seizure, tumors, metabolic disorder, drug overdose, etc.

Amyotrophic lateral sclerosis: This fatal neurological disorder affects motor movements. Also termed Motor Neurons Disease, it results in paralysis. It appears in the age group from 54 to 67 years.

Multiple sclerosis: This disease affects the central nervous system (CNS) when the body produces abnormal activities against CNS. Hence it affects brain, spinal cord, and optic nerves.

Migraine: Disorders in the brain and cord result in migraine, which creates pain in blood vessels and nerves. It is also called neurovascular pain syndrome and is followed by depression, irritability, cyclical vomiting, and loss of appetite.

Brain tumor: Brain tumors may be cancerous, noncancerous, or benign. They grow slowly and affect the normal life cycle of the brain. Sometimes, they result death for benign patients. Malignant tumors grow rapidly and create the most severe problem for patients, requiring immediate attention from a medical practitioner. In the United States, 5,000 children become affected by brain tumors with different types gliomas, medulloblastomas, and ependymomas.

Ataxia: This disease affects the voluntary muscle movement and causes cerebellar dysfunction. The disorder destroys the activities of cerebellum, spinal cord, brain stem, cortex, and basal ganglia.

Epilepsy: This neurological disease creates metabolic disorders, cerebral trauma, stroke, and tumors. It affects the signals in the brain.

Stroke: This condition creates damage to the brain and disturbs cerebral function, which leads to brain attack. Based on severity and causes in the human body, the type of stroke is decided. Interruption in blood flow creates ischemic stroke, which destroys nearly two million neurons, bursting blood vessels and leading to hemorrhagic stroke or acute stroke.

Dementia: This disease is caused by decline of brain activity and results in overthinking, decline in normal performance of human activity, memory loss, and unawareness about the patient's own problems. Vascular and fronto-temporal are two types of dementia. Alzheimer's disease patients can suffer dementia.

9.5 AUTISM SPECTRUM DISORDER

A brain is continuously growing organ to some age limit. This growth involves normal motor activities, muscular activities, and cognitive skill development. The physical processing stage is different for every child, but ASD children's life activities differ from others, and they miss actual milestones in their life.

- They do not stand alone and walk properly.
- They do not show facial expressions or make eye contact.
- They repeatedly do few actions inappropriate for their age like clapping, waving, pointing some direction, etc.
- They are more obsessive with their objects and easily get upset by changes in regular activities.
- They are more sensitive to smell, taste, etc.
- They are unable to learn and grow the way that non-ASD children do.
- They are unaware of social interaction and environment.
- At the same time, they are intelligent in some skills compared to other children.

Applied behavior analysis helps them to interact with society and improve communication skills.

Early intensive behavioral intervention was developed particularly for kids below five years of age.

Cognitive behavior therapy provides real-time skills to manage particular situations and help them to identify their own strengths and weaknesses. According to law 108-177, education and school-based therapies allow autistic children to learn freely at school and gives more interaction among others.

Nutritional therapy allows children to get more bone development foods and easily digestive foods.

Medication treatment can control autism behavior by changing children's focus on some other skills and allows for antipsychotic drug intake.

Parent-mediated therapy groups children with their parents to do some activities to improve communication skills, attention therapy, and behavioral therapy, thereby improving the nature of autistic kids.

Occupational therapy helps in identifying children's own interests and abilities and encourages them to pursue those.

Physical therapy helps them to sit, stand, walk properly, and rectify movement problems.

Social skills training allows for communication, effective conversation, handling bullying behaviors, etc.

Speech language therapy improves interaction and communication among other skills.

Farooq et al. (2023) utilized support vector machine and logistic regression to classify the ASD factors and detection of ASD. Four different datasets were analyzed for children, for which the proposed model achieves 98% accuracy, and for adults, for which 81% accuracy as achieved [1].

Al-disbat et al. (2018) experimented with fuzzy data mining algorithms for ASD kids for classification in the University of California, Irvine Machine Learning (UCIML) repository dataset. The researchers evaluated various models of FUZZY and found the FURIA model produced better results than others [2]. Thabath et al. (2020) proposed rules in the machine leaning (ML) model for classification and showed the actual cause for this disease. The researchers used this model in experiments with children, adolescents, and adults datasets with boosting, bagging, decision trees, and rule induction algorithms and produced higher accuracy [3]. Wingfield et al. (2020) developed an ML embedded mobile application to monitor autism detection and identified that the random forest algorithm AUCROC produced accuracy of 98%, and this application helps in many ways to identify ASD [4]. Leroy et al. (2024) analyzed the ML model, three deep learning (DL) models, and various ensemble models for ASD detection and found that majority voting with BiLSTM Ml achieved 100% precision, 91% accuracy, 100% specificity, and a 0.91 F1 score [5]. Reddy et al. (2023) used a facial image dataset for CNN, VGG16, VGG19, and the EfficientNet BO classification and attained accuracy of 84.66%, 98.50%, and 87.9% for each algorithm [6].

Alsaade et al. (2022) developed a model with web application and DL algorithms such as CNN, Xception, VGG19, and NASNETMobile to classify the facila autism image dataset and attained accuracy of 78% for NASNETMobile, 80% accuracy for VGG19, and 91% accuracy for the Xception model [7]. Khosla et al. (2021) proposed a DL model to classify facial images of healthy and autistic children and removed the duplicate images. The Mobile net model attained the accuracy of 87% in classification [8].

Research gaps include the following:

- Identification and treatment of ASD takes more time, which leads to proper medical practice.
- Many researchers experiment with DL and ML for ASD analysis, yet they struggle to attain high accuracy.
- Many researchers experiment with feature datasets instead of image datasets.

9.6 METHODOLOGY

The failure of ML technique was the basic reason to develop a DL algorithm. DL is an advanced technology of ML and artificial intelligence (AI). It can handle large sets of data and doesn't need external feature extraction techniques. It contains multiple layers of neural networks and hidden layers, and every process is carried out promptly. This architecture can process large data in accurate manner within short

time. DL algorithms play a significant role in the medical field due to its efficient and timely analysis [9]. Every algorithm performs its role in unique way due to its interconnected neurons and ability to learn from the given data [10]. DL models have an ability to capture dominant features and works in an end-to-end fashion. It plays a dominant role in classification, object detection, segmentation, speech recognition, sentiment analysis, medical analysis, predictive analysis, fraud detection, recommender systems, etc. [11, 12]. This research analyzed DL techniques such as CNN, RNN-CNN, LSTM-CNN, VGG-16, and ResNet-50 for autism detection.

9.6.1 Datasets

The facial dataset for ASD is picked from the Kaggle dataset, and it contains 1,468 autism files and 1,468 nonautism files. The training folder contains 1,628 for autism and 1,628 for nonautism. At the same time, the test folder contains 150 for autism and 150 for nonautism images. The validation folder contains 50 autism and 50 nonautism images. A total of 5,874 images were experimented with for this study. Figure 9.2 shows the autism and nonautism images in the dataset. Image resizing is carried out for image preprocessing.

Figure 9.3 shows the overall methodology of the ASD classification.

9.6.2 CNN

This network was developed to execute grid information and mainly used for image analysis. Convolution layer, activation function, stride, padding, pooling layer, batch normalization, flattening, and fully connected layers are the basic operations and building layers for CNN. Convolution layers works with input and filters by dot product and produce feature maps by capturing dominant features. Pooling layers are utilized to reduce the dimensionality of feature maps and can be either max pooling or average pooling. Figure 9.4 shows the layers and architecture of CNN [13].

FIGURE 9.2 Autism and nonautism images.

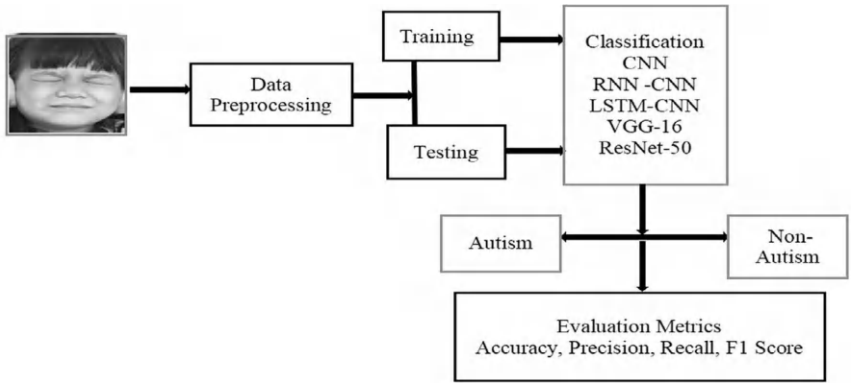

FIGURE 9.3 Schematic model of workflow.

The max pooling fetches the maximum value from the feature map by filtering, and average pooling considers the average value from the feature map region. This research utilized the concept of max pooling. The activation function helps to identify the nonlinearity in the model and learned complex features. Every layer used the concept of the same padding to protect the edge features by adding zero. Fully

```
Model: "sequential_1"
_________________________________________________________________
 Layer (type)                Output Shape              Param #
=================================================================
 conv2d_3 (Conv2D)           (None, 62, 62, 32)        896

 max_pooling2d_3 (MaxPoolin  (None, 31, 31, 32)        0
 g2D)

 conv2d_4 (Conv2D)           (None, 29, 29, 64)        18496

 max_pooling2d_4 (MaxPoolin  (None, 14, 14, 64)        0
 g2D)

 conv2d_5 (Conv2D)           (None, 12, 12, 128)       73856

 max_pooling2d_5 (MaxPoolin  (None, 6, 6, 128)         0
 g2D)

 flatten_1 (Flatten)         (None, 4608)              0

  dense_2 (Dense)            (None, 128)               589952

  dropout_1 (Dropout)        (None, 128)               0

  dense_3 (Dense)            (None, 10)                1290

=================================================================
Total params: 684490 (2.61 MB)
Trainable params: 684490 (2.61 MB)
Non-trainable params: 0 (0.00 Byte)
_________________________________________________________________
```

FIGURE 9.4 CNN layer architecture.

connected layers work as same as dense layers in ML and fetch the final feature maps with dominant patterns. The activation function sigmoid produces binary output for classification.

9.6.3 RNN

This network processes sequential and temporal data (see Figure 9.5). Hidden layers in RNN capture data from a previous sequence with the help of hidden layers. It works similar to CNN, and it also has memory to capture previous data. The output depends on previous data. The important property of RNN is the hidden state or memory state, which reduces the complexity of parameters.

The recurrent unit is the basic unit, and it keeps the hidden state. The hidden state holds the knowledge of previous time step and is updated as per the following formula. The current state can be calculated by $H_t = f(H_{t-1}, x_t)$., where H_t is the present state, H_{t-1} is the previous state, and x_t is the initial setup. The activation function performs as follows:

$$H_t = tanh\left(W_{hh}\ H_{t-1}\ + W_{xh}\ x_t\ \right)$$

where W_{hh} is recurrent neuron weight and W_{xh} is the input neuron weight. The output layer is computed as $y_t = W_{hy}$, H_t, where y_t is output and W_{hy} is the output layer weight.

Back propagation helps to update these parameters. This process is repeated until the calculation is made for output. The final output is compared with actual output, and bias is propagated back to the network for changing the weight. Hence it remembers every detail of the process. RNN combined with CNN performs image classification based on image features [14, 15].

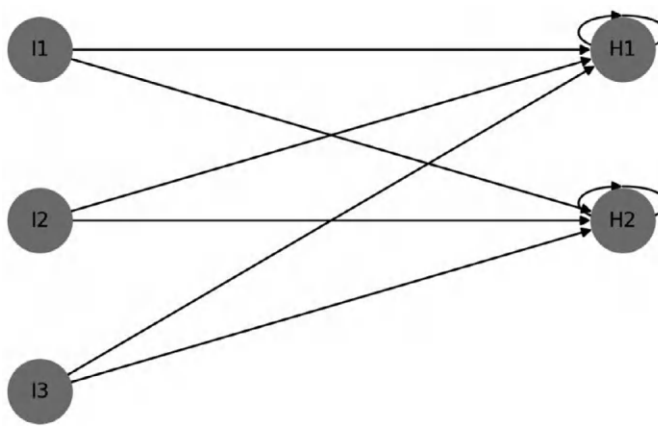

FIGURE 9.5 RNN

9.6.4 LSTM

LSTM utilized the concept of RNN, and it has a structure to maintain read, write, and forget states. It reads and writes significant information and forgets unnecessary information. Developed by Hochreiter and Schmidhuber, the process overcame the problem of vanishing gradient from RNN. It maintains long-term dependencies and consists of three gates: the forget gate, the input gate, and the output gate. The forget gate simply forgets the unwanted information, the input gate captures new information, and the output gate carries and passes the present time stamp information to the next state. This full process is called single time stamp. Figure 9.6 presents the single time stamp of LSTM.

LSTM networks works on sequential data so that image features were extracted first and combined architecture of LSTM with CNN attained the desired classification.

9.6.5 VGG-16

This DL model is based on the CNN architecture and has 16 convolution layers and is made up of the basic constructive layers of CNN. A. Zisserman and K. Simonyan are the developers of VGG-16.

VGG-16 has one input layer, 13 convolution layers, five pooling layers, three fully connected layers, and one output layer.

9.6.6 ResNet-50

ResNet-50 is a combination of CNN architecture with residual blocks. The residual blocks help to recover the degradation problem. ResNet-50 allows the direct delivery of data through skip connections. It acts next to the convolution and batch normalization layer. ResNet-50 captures positive values, thereby learning critical patterns of data. The bottleneck convolution layer is special structure of ResNet and is a collection of three convolution layers, the batch normalization layer, and the Relu activation function. These convolution layers use 1×1, 3×3, and 1×1 filters, prevent information loss, and extract dominant features from the data, and the final filter helps to restore the information. Skip Connections allows unchanged input to the convolution layer output. All information is securely transferred to the next layer without any loss. Hence it performs the deeper learning of networks.

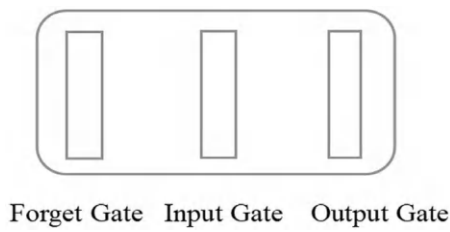

FIGURE 9.6 LSTM gates.

9.7 RESULT AND DISCUSSION

This section summarizes the performance of experimented DL algorithms with proper evaluation metrics. The evaluation metrics accuracy, recall, F1 score, and precision are utilized to discuss the outcome of the framework.

Accuracy: It assess the true prediction from the overall given prediction.

$$\text{Accuracy} = \frac{TruePositive + TrueNegative}{TruePositive + TrueNegative + FalsePositive + FalseNegative} \quad (9.1)$$

Precision: It shows the correctly predicted positive instances from overall positive classes.

$$\text{Precision} = \frac{True\ \ Positive}{True\ \ Positive + False\ \ Positive} \quad (9.2)$$

Recall: It measures the correct prediction of actual positive classes.

$$\text{Recall} = \frac{True\ \ Positive}{True\ \ Positive + False\ \ Negative} \quad (9.3)$$

F1 score: This determines the harmonic mean between precision and recall and also shows distribution of unequal classes.

$$\text{F1score} = 2 * \frac{Precision * Recall}{Precision + Recall} \quad (9.4)$$

Table 9.2 and Figure 9.7 show the performance of deep experimented models in percentage.

Figure 9.8–9.12 demonstrate the accuracy and loss for each classification model.

Using information from Figures 9.8 to 9.12, Figure 9.13 shows the DL model classification performance.

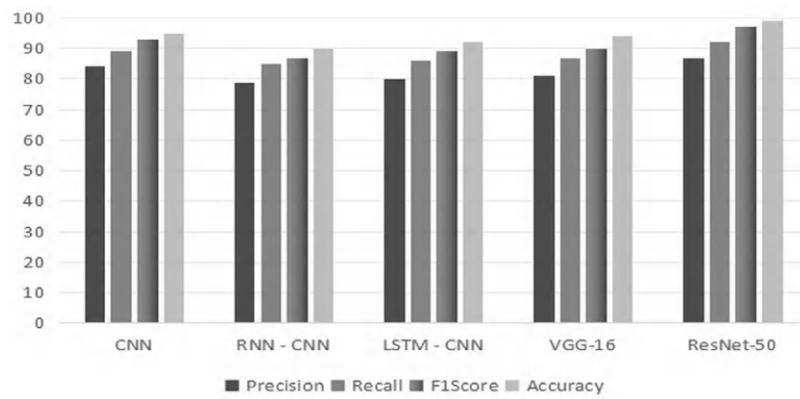

FIGURE 9.7 Performance of deep experimented models.

TABLE 9.2
Performance of Deep Experimented Models

Models	Precision	Recall	F1 Score	Accuracy	Loss
CNN	84	89	93	95	1.63
RNN-CNN	79	85	87	90	1.67
LSTM-CNN	80	86	89	92	1.59
VGG-16	81	87	90	94	1.54
ResNet-50	87	92	97	99	1.47

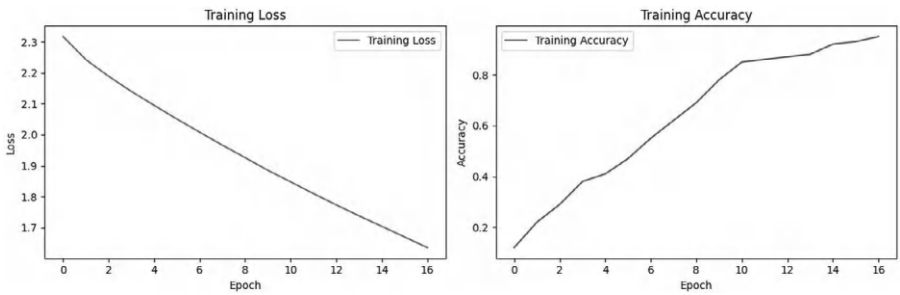

FIGURE 9.8 CNN classification.

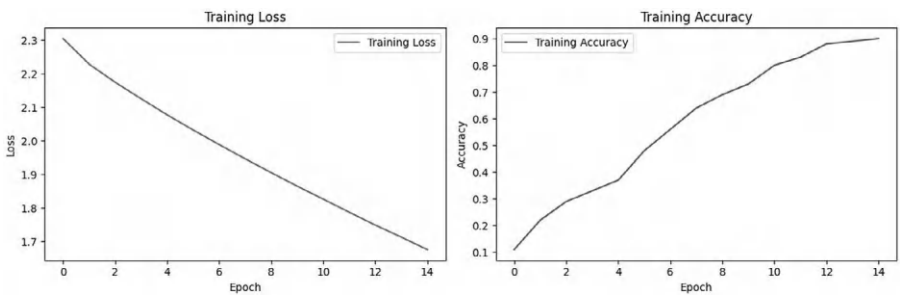

FIGURE 9.9 RNN-CNN classification.

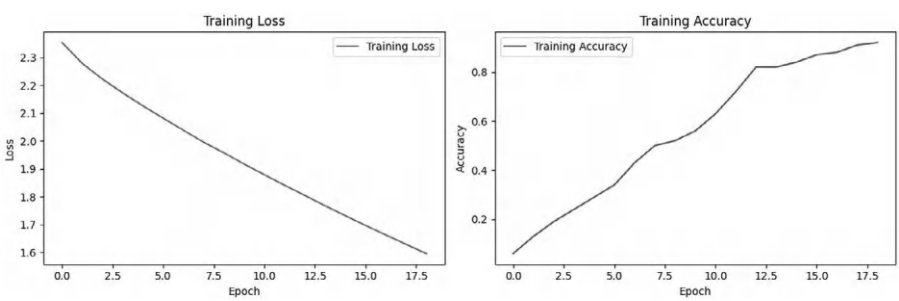

FIGURE 9.10 LSTM-CNN classification.

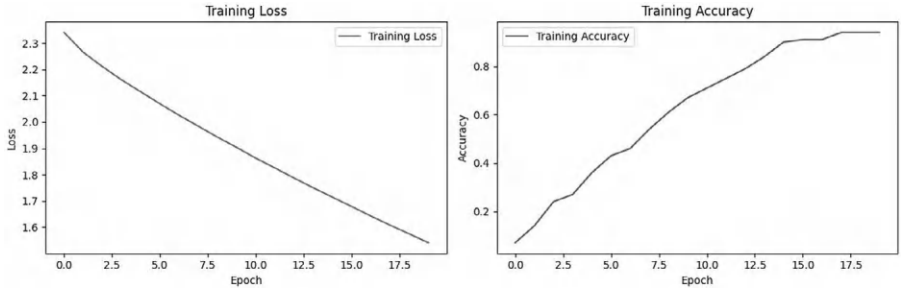

FIGURE 9.11 VGG-16 classification.

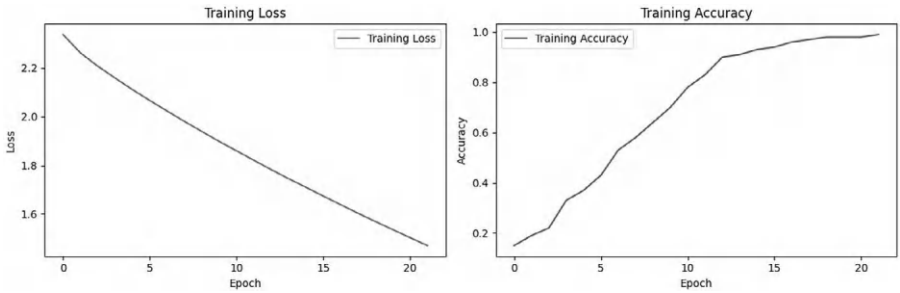

FIGURE 9.12 ResNet-50 classification.

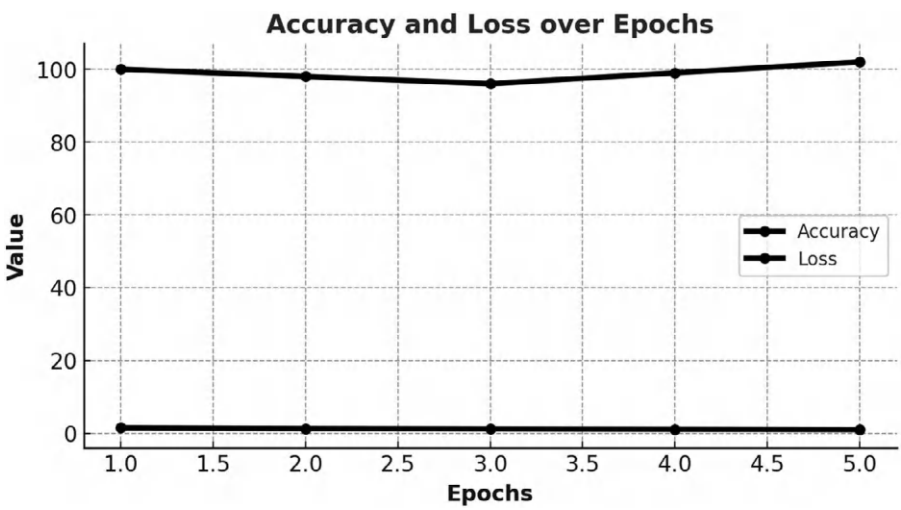

FIGURE 9.13 Accuracy and loss for DL models

9.8 CONCLUSION

ASD is a silent disease that gets worse with the long-run growth of afflicted children. It totally affects the social behavior, understanding, communication, and physical activities of the children. Early identification may control the severeness of the ASD [16–18]. This chapter tries to identify the better classification algorithm for ASD facial image recognition for autistic and nonautistic children. It proposes five DL models for autism detection, which include CNN, RNN-CNN, LSTM-CNN, VGG-16, and ResNet-50. The CNN model achieves an accuracy of 95%, RNN-CNN attains an accuracy of 90%, 92% accuracy for LSTM-CNN, 94% for VGG-16, and 99% for ResNet-50. As a result ResNet-50 attains the highest result for ASD classification. This chapter finds that every model performs well in classification, and differences between them are very minor, but ResNet outperformed the other models. Hence this chapter provides a solution to identify autistic children at low-cost implementation.

9.9 FUTURE ENHANCEMENT

For ASD detection, a golden metric dataset is not available for public usage. Upcoming researchers need a proper dataset for ASD detection. It will create a gateway to analyze various advanced architectures with AI integration.

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10 Advanced Neuroimaging with Generative Adversarial Networks

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10.1 INTRODUCTION

With the recent strides in medical science, computer science stretching has started showing promising results since it can foresee the advancements required for medical science in many ways. Computational intelligence is one of the arms of artificial intelligence (AI) that has changed the face of medical imaging. More specifically, it changes human decision-making processes with complex algorithms and data-driven approaches. The application of computational intelligence techniques in medical imaging has been very instrumental in sharpening image resolution, facilitating diagnosis with accuracy, and therefore smoothening operations to yield highly improved outcomes for patients. These technologies extend all the way from traditional machine learning (ML) models to state-of-the-art deep learning (DL) networks for establishing fully automated systems to analyze images with an accuracy that matches, and at times goes beyond, human experts.

In sharp contrast, a technology among them, called generative adversarial networks (GANs), was first invented in 2014 by Ian Goodfellow and his fellow colleagues with an aim to raise the quality level of image generation, videos, and voice recordings. One way of putting this proposal was to develop a system in which two neural networks, a generator and a discriminator, would work in a competing way. It means the generator tries to produce data that cannot be distinguished from real-world data, while a discriminator tries to correctly classify the generator's output versus real data. The mechanism of this competition is what enables both networks to learn and improve over time. Initial applications for GANs are directed toward improving image processing and computer graphics, having broader implications for other areas such as semisupervised learning, domain adaptation, and data augmentation [1]. GANs are therefore one of the advancements in the field of AI, more specifically in the domain of medical imaging. GANs involve two neural networks – the generator and the discriminator – engaging in a continuous contest that improves the quality and utility of generated images over time. In neuroimaging, GANs have become quite useful. They not only improve image quality but also generate synthetic yet very real images of the human brain that have proved very useful in the training of medical professionals without having to compromise the

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privacy of patients. It is an important capability in a domain where high-quality, annotated datasets are few and the concerns for privacy are of high priority.

GANs provide improved quality, availability, and utility of imaging data, making them very critical in accurate diagnostics and research. The developments made to date in the application of GANs in neuroimaging are in some critical areas, including GANs that have transformed neuroimaging through the improvement of the quality of images, augmentation of data, anomaly detection, and automation in segmentation. They take low-resolution images and transform them into high-resolution outputs, hence enabling doctors and researchers to see small details in the image for the diagnosis of brain tumors, vascular anomalies, degenerative diseases, and so on. Also, GANs generate artificial neuroimaging data to enlarge datasets and give a richer basis for the training of diagnostic algorithms without breaching patient confidentiality. They can also learn the distribution of normal anatomic structures and identify abnormalities at an early stage of disease detection. Besides, they provide automated segmentation of brain structures, which is complex, reducing the time and potential human error involved in a clinical setting. Such models are designed with privacy in consideration by synthesizing de-identified images, considering various privacy laws and ethical guidelines. GANs contribute to research and training by generating very realistic-looking pictures for educational purposes. Further development is accelerated by improvements in technology and demands coming from the clinics themselves [2].

This chapter aims to delve into the sophisticated realm of GANs and their transformative impact on neuroimaging. The primary objectives are to:

1. Establish the relevance
2. Describe the technology
3. Showcase applications
4. Discuss challenges and ethics
5. Explore future prospects

Through these objectives, the chapter will provide a thorough introduction to the significant role that GANs play in advancing neuroimaging, setting the stage for a detailed discussion of their applications and implications in the subsequent sections. To fulfill these objectives, this whole chapter is further divided into eight sections, namely "Introduction," "Literature Review," "Foundational Principle of GANs," "GANs in Neuroimaging: Enhancing Diagnostic Imaging," "Practical Applications of GANs in Neurology, Ethical Considerations and Challenges," Future Directions," and Conclusion.

10.2 LITERATURE REVIEW

GANs have been used in neuroimaging just after a span of their discovery. GANs are being used by various researchers in various domains of medical sciences to make them more useful and effective. Among so many of them, Kossen et al. (2021) and Wang et al. (2023) worked on the subjects of applications of GANs in neuroimaging and clinical neuroscience. Kossen et al. applied GANs to generate synthetic time-of-flight magnetic resonance angiography (TOF-MRA) patches at the

vessel segmentation of the brain for increased data privacy and thus facilitating large labeled datasets [3]. Wang et al. (2023) indicated that GANs open up the path to the generation of realistic data for disease diagnosis, anomaly detection, and modeling of disease progression [2]. Seeliger et al. (2018) explore how GANs can be applied to reconstruct natural images from brain activity recorded with functional magnetic resonance imaging (fMRI) [4]. Dar et al. (2020) introduced a new approach that can substantially accelerate multicontrast MRI acquisition using GANs called reconstructing-synthesizing GANs (rsGAN) [5]. Song et al. (2020) proposed a technique for the smallest set of smallest rings (SSSR) in positron emission tomography (PET) images using dual GANs. This approach avoids paired low- and high-resolution training data; it improved the image quality metrics to a large extent. Advanced deep-learning techniques are linked in a clinical setting within this study [6].

Moazami et al. (2024) proposed a probabilistic approach for MRI brain extraction by conditional generative adversarial networks (cGANs)to solve the problem of brain part segmentation from MRIs. This approach uses the cGAN model to generate a set of probable brain images, conditioned on an input head MRI, from which a pixel-wise mean image can be created as an estimate of an extracted brain and a standard deviation image, and for quantifying prediction uncertainty. This facilitates getting more accurate segmentation, leading to valuable uncertainty estimates attached to the segmentations, hence ensuring fuller reliability in the neuroimaging analysis course [7]. In that regard, Logan et al. 2021 review DL methodologies, more specifically convolutional neural networks (CNNs) and GANs, for Alzheimer's disease (AD) classification in neuroimaging data. The authors have found that CNNs extract highly complex features from imaging data, enhancing greatly the accuracy of AD diagnosis. Integration of Ensemble Learning with CNNs, and the use of GANs for generating synthetic imaging data to overcome issues related to data scarcity, can aid in the early and accurate diagnosis of AD and improve management and treatment [8].

Gao et al. 2022 proposed a DL framework for the imputation and classification of multimodal brain images in AD. In particular, the TPA-GAN integrates pyramid convolution, attention modules, and disease classification tasks to generate missing PET data from MRI, ensuring that generated images retain details of the disease. A pathwise transfer dense convolution network (PT-DCN) exploits full multimodal images to extract and fuse features from both MRI and PET for accurate classification of diseases [9]. Jung et al. (2022) proposed a conditional GAN with a 3D discriminator to generate high-quality 3D MRI images for the prediction of AD progression. The architecture of the cGAN model itself embeds an attention-based 2D generator, a 2D discriminator, and a 3D discriminator. In that way, it will be smooth when transitioning through slices and maintain high-quality 3D structural consistency [10]. Schlaeger et al. (2023) explored the worth of artificial T2-weighted fat-saturated images generated by a generative adversarial network in the reduction of spine imaging scan times. The results indicated that synthetic T2-w fat-saturated (fs) images were not different in apparent Signal-to-Noise Ratio and apparent Contrast-to-Noise Ratio from actual T2-w fs images [11].

Bouman et al. (2023) investigated the accuracy of AI-generated double inversion recovery (DIR) and phase-sensitive inversion recovery (PSIR) images in detecting

cortical and juxtacortical lesions in multiple sclerosis (MS) patients. A temporal recurrent generative adversarial network (TR-GAN) has been proposed to deal with the challenge of incomplete longitudinal MRI datasets in AD progression analysis [12]. Table 10.1 is a detailed tabular comparison of the related papers based on key factors such as focus, methodology, key findings, dataset, and evaluation metrics.

The table is extremely systematic in laying out the key points of each study, so there is no problem in seeing exactly how each contribution fits into the broader context of neuroimaging and GAN applications.

TABLE 10.1
GAN-Based Neuroimaging Studies Comparison

Focus	Methodology	Key Findings	Dataset	Evaluation Metrics
Synthetic TOF-MRA patches for brain vessel segmentation [3]	GANs (DCGAN, WGAN-GP, WGAN-SN)	High similarity and predictive properties in synthetic data	Custom dataset	Dice coefficient, Hausdorff distance
GANs in neuroimaging for disease diagnosis and progression modeling [2]	Various GAN architectures	GANs improve diagnosis and prediction accuracy	Multiple neuroimaging datasets	PSNR, SSIM, accuracy
Natural image reconstruction from brain activity via GANs [4]	DCGAN	Reconstructed images resemble the original stimuli	fMRI data	Behavioral tests (image identification)
Accelerated multicontrast MRI using GANs [5]	rsGAN	Improved MRI quality and scan efficiency	ADNI dataset	PSNR, SSIM, MSE
PET image super-resolution using GANs [6]	SSSR with dual GANs	Enhanced PET image resolution and diagnostic accuracy	Clinical neuroimaging datasets	PSNR, SSIM, NRMSE
Probabilistic brain extraction via cGANs [7]	cGAN	Improved segmentation accuracy and uncertainty estimation	Multiple neuroimaging datasets	Accuracy, uncertainty estimation
DL for AD classification using MRI [8]	CNNs, GANs, ensemble learning	Improved AD classification accuracy	ADNI dataset	Accuracy, balanced accuracy
Multimodal brain image imputation and classification in AD [9]	TPA-GAN, PT-DCN	Enhanced image quality and diagnostic accuracy	ADNI dataset	Accuracy, PSNR, SSIM

(*Continued*)

TABLE 10.1 (*Continued*)
GAN-Based Neuroimaging Studies Comparison

Focus	Methodology	Key Findings	Dataset	Evaluation Metrics
Synthetic T2-w fs images for spine imaging [11]	GAN-generated synthetic images	Improved image quality and diagnostic accuracy for spine imaging	Multicenter spine imaging dataset	PSNR, SSIM, aSNR, aCNR
AI-generated DIR and PSIR for MS lesion detection [12]	AI-generated images	Higher lesion detection accuracy and reliability	Multicenter MS dataset	Lesion detection accuracy, ICC
Simulating EEG data using GANs [13]	GANs	Realistic EEG data simulation	Clinical EEG datasets	PSNR, SSIM
Group difference testing using GAN-generated data [14]	GANs with spectral graph theory	GAN-generated data can be used for reliable group difference testing	ADNI dataset	ICC for reliability
Short scan time amyloid PET image restoration using GANs [15]	GAN-based restoration	Comparable quality to true images with reduced scan times	Clinical amyloid PET datasets	PSNR, SSIM, diagnostic accuracy
Tensorizing GAN for AD assessment [16]	Tensorizing GAN with high-order pooling	Improved AD classification with fewer labeled samples	ADNI dataset	Classification accuracy, PSNR, SSIM
Multisession future MRI prediction with TR-GAN [17]	TR-GAN with recurrent connections	Enhanced prediction accuracy and dataset completeness	ADNI dataset	MSE, MS-SSIM, PSNR, balanced accuracy

10.3 FOUNDATIONAL PRINCIPLES OF GANs

GANs are complex mathematical constructs applied to the concepts of computer science and are made of two separate neural networks in dynamic rivalry: a generator and a discriminator. A generator is used to create images that seem real; hence, it serves with the meaning of "faking" data as real as possible. On the other side, the discriminator acts as the critic that checks whether the received data are a part of the real dataset or were generated by the generator artificially. The setup puts the networks in a competitive environment in which the improvement of one network forces the other to do better as well, hence improving its functionality with time. As shown in Figure 10.1, the neural networks, discriminator (represented by D), and generator (represented by G), are training adversely to attain a state where the generator can

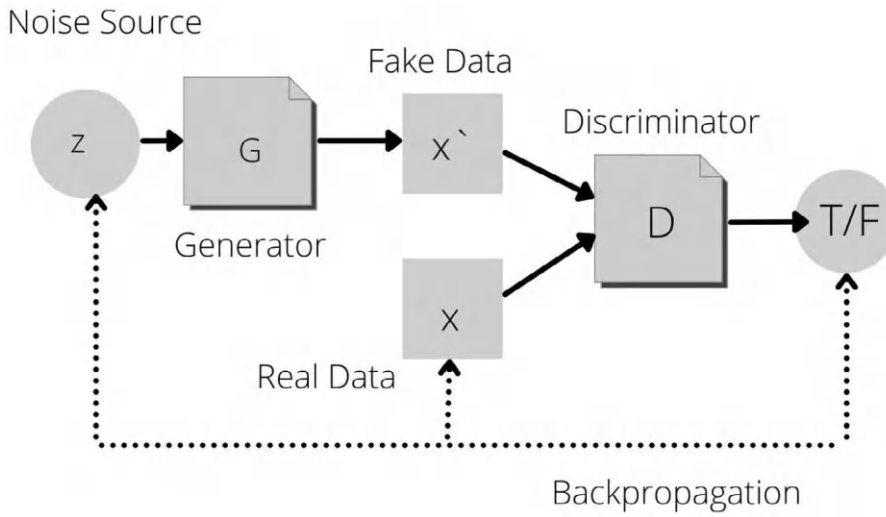

FIGURE 10.1 Working of generative adversarial neural networks.

generate real data from random noise. In the initial training phase, the discriminator discriminates the data bits as real or fake, which helps the generator learn to generate real data, as discussed previously. Discriminator training is a part of the very initial phase of the setup, as it can learn to differentiate.

In contrast, the arrangement works to contend between the two networks in a zero-sum game, where Generator G is trying to amplify the probability and Discriminator D is trying to reduce that. GANs are a class of ML frameworks designed to generate new data samples that are similar to a given dataset. To understand the mathematical formulation of GANs, one must understand the mathematics of its working components. As mentioned previously in this section, the GAN consists of two neural networks, a generator (G) and a discriminator (D), which are trained simultaneously in a game-theoretic setting where one network's gain is the other's loss. This process is formulated as a minimax optimization problem. Here, Generator (G) is a neural network that takes a random noise vector z∼pz(z) (usually drawn from a simple distribution like Gaussian or uniform) as input and maps it to a data space to produce a synthetic data sample G(z). Also, the other part of the set discriminator (D) is a neural network that takes a data sample as input (either from the real dataset x∼pdata(x) or from the generator G(z)) and outputs a scalar representing the probability that the input data are real (from the training data) rather than fake (generated by G).

The GAN framework aims to train G and D in a two-player minimax game. The discriminator D is optimized to maximize the probability of correctly classifying real and fake data samples, while the generator G is trained to minimize the likelihood that D correctly distinguishes between real and fake samples. The objective function for GANs can be formulated as:

$$min_G max_D \; V(D,G) = E_{x\sim p_{data}(x)}\left[logD(x)\right] + E_{z\sim p(z)}\left[log\left(1-D\left(G(z)\right)\right)\right]$$

Here, $E_{x\sim p_{data}(x)}$ represents the expectation of the log probability that the discriminator correctly identifies real samples from the data distribution $p_{data}(x)$, and $E_{z\sim p_{(z)}}\left[log\left(1-D\left(G(z)\right)\right)\right]$ represents the expectation of the log probability that the discriminator correctly identifies fake samples generated by G(*z*) as not coming from the real data distribution.

The training process involves the two alternating steps:

1. *Discriminator update*: Given a batch of real samples from the data distribution and a batch of fake samples G(*z*) generated by the generator, the discriminator is updated to maximize its ability to distinguish between real and fake samples. This is done by maximizing the objective function V(*D,G*) with respect to D.
2. *Generator update*: After updating the discriminator, the generator is updated to minimize its success in fooling the discriminator. This is achieved by minimizing V(*D,G*) with respect to G.

The optimization is typically performed using stochastic gradient descent (SGD) or its variants (like Adam), with updates alternating between D and G. The update rules for the discriminator are evaluated as:

$$\theta_D \leftarrow \theta_D + \eta\theta_{\theta_D}\left(\frac{1}{m}\sum_{i=1}^{m}\left[logD\left(x^{(i)} + log\left(1-D\left(G\left(z^{(i)}\right)\right)\right)\right)\right]\right)$$

where θ_D represents the parameters of the discriminator, η\etaη is the learning rate, and mmm is the batch size.

The generator update is evaluated as:

$$\theta_G \leftarrow \theta_G + \eta\theta_{\theta_G}\left(\frac{1}{m}\sum_{i=1}^{m}\left[log\left(1-D\left(G\left(z^{(i)}\right)\right)\right)\right]\right)$$

where θ_G represents the parameters of the generator.

The training process is designed to reach a Nash equilibrium, where the generator produces samples that are indistinguishable from the real data (i.e., D(G(*z*)) = 0.5), meaning that the discriminator cannot differentiate between real and fake samples better than random guessing.

The GAN objective is closely related to minimizing the Jensen–Shannon (JS) divergence between the real data distribution $p_{data}(x)$ and the generator's distribution $p_g(x)$. The optimal discriminator, given a fixed generator, is:

$$D*(x) = \frac{P_{data}(x)}{P_{data}(x)+P_g(x)}$$

Ideally, as the training progresses, the generator's distribution $p_g(x)$ converges to the real data distribution $p_{data}(x)$, minimizing the JS divergence to zero [1].

There are several GAN variants that modify the original objective function or architecture to improve stability, convergence, or performance for specific tasks that have a wide spectrum of applicability in medical imaging. Examples include Wasserstein GANs (WGAN), least squares GANs (LSGAN), conditional GANs (cGAN), CycleGAN, and StyleGAN, among others. GANs have been remarkably successful in multimedia processing tasks. They can create entirely new images and videos or enhance the quality of existing multimedia data. GANs can even generate images of people or places that are completely fictitious. Recently, GANs have found applications in security fields. Given their effectiveness, GANs are being explored to predict security threats and analyze systems for vulnerabilities. This method of vulnerability prediction has the potential to create more robust and efficient security systems, proactively addressing security attacks [18]. The following is a high-level pseudocode that outlines how GANs can be implemented for this purpose:

Initialize:
- Generator network G with parameters theta_g
- Discriminator network D with parameters theta_d
- Set the number of training epochs and batch size
- Load real neuroimaging dataset

For each epoch:
For each batch in the dataset:
// Train the Discriminator
1. Generate noise samples from a random distribution (e.g., Gaussian)
2. Use Generator G to create fake images from noise
3. Sample real images from the actual neuroimaging dataset
4. Feed both real and fake images to Discriminator D
5. Calculate discriminator loss:
   – Loss on real images (D should output 1)
   – Loss on fake images (D should output 0)
6. Update the discriminator parameters (theta_d) to minimize the loss

//Train the Generator
7. Generate new noise samples
8. Use Generator G to create fake images from noise
9. Feed fake images to Discriminator D
10. Calculate generator loss:
    – Loss based on D's output (G wants D to output 1 for fake images)
11. Update generator parameters (theta_g) to minimize the loss

// Optionally, evaluate the performance on the validation set
// The networks are trained until the specified epochs are completed or until convergence criteria are met
// Optionally, further refine or adjust models based on specific imaging modalities or analysis needs

This pseudocode provides a template for how GANs can be structured for the task of generating and refining synthetic medical neuroimages. In practice, the specifics

of the network architecture, loss functions, and training details (like learning rates, optimizer choices, and handling of training stability issues) would need to be tailored to the specific characteristics of the neuroimaging data and the goals of the research or application. The practically applied GAN for enhanced neuroimaging will be discussed in the upcoming sections. Training a GAN involves a delicate balance where the generator learns to produce more realistic images while the discriminator becomes better at detecting fakes. This process is iterated through numerous cycles, with the generator trying to maximize the errors of the discriminator by producing increasingly convincing outputs, and the discriminator learning to minimize its mistakes. Optimized techniques often used include backpropagation and gradient descent, which modify the internal parameters of both networks based on their performance in every iteration. The quality of this training process is very critical, as it dictates how well a GAN would be able to come up with new data for application in real-life scenarios [19].

The framework of GAN theory maps particularly well onto the challenges of medical imaging. It speaks for itself to the core challenges in medical imaging: the availability of a few large, annotated medical datasets is only what is available to train GANs for generating high-quality synthetic images. Further, GANs may be trained for creating images that capture the variability of pathological features across different patients, which can itself be of value in training and testing diagnostic algorithms. Applications of GANs in medical imaging improve both quality and quantity, obeying privacy regulations through the generation of de-identified images. This means that the relevant pathological information is preserved in the images while keeping the corresponding personal data safe [20].

Understanding only the basics of GANs, one cannot but help relate to the fact that these networks are going to drastically change medical imaging, more so neuroimaging. This section tries to explain as much as possible in simple language while avoiding jargon so that technical and nontechnical readers can engage fully with how advanced tools work and their potential to really change medical diagnostics. It sets the scene for an understanding of how GANs may be put into practical applications to improve the accuracy and efficiency of neuroimaging, explored in-depth throughout the rest of the chapter.

10.4 GANs IN NEUROIMAGING: ENHANCING DIAGNOSTIC IMAGING

One of the most important challenges in neuroimaging is that high-quality and diverse datasets are not commonly available, especially considering the rare neurological conditions. GANs aid in this by synthesizing quality images that could be used for the augmentation of existing datasets. Such creation of synthetic data is especially useful in training and increasing the precision of other AI-driven diagnostic tools, which require volumes of data for learning effectiveness. The GANs generate images that mirror the variability present in real patients, providing a way to build more robust and complete datasets to train from, making the diagnosis models more predictive [21].

There are various techniques and methodologies associated with ML and AI that are being used in several advanced medical imaging applications in neurology and other relevant medical applications; it is quite a task to decide which is needed to be chosen for the required task. Hence, Table 10.2 compares various techniques used in advanced neuroimaging, alongside their applications, and their respective advantages and disadvantages compared to GANs.

TABLE 10.2
Other AI and ML Techniques with Advantages and Disadvantages over GANs

Technique	Application in Neuroimaging	Advantages over GANs	Disadvantages Compared to GANs
Variational autoencoders (VAEs)	Data augmentation, disease progression modeling	The probabilistic approach allows for better data understanding and can model the distribution of input data.	Often produce less sharp, blurrier images than GANs.
Convolutional neural networks (CNNs)	Tumor detection, lesion segmentation, anatomical analysis	Highly effective for classification and segmentation with stable training processes.	Not generative; mainly used for supervised tasks requiring extensive labeled data.
U-Net	High-precision segmentation of complex structures	Specialized architecture provides excellent segmentation accuracy, especially in layered structures like the brain.	Mainly for segmentation; it does not generate new images.
Deep belief networks (DBNs)	Feature extraction, image classification	Good at unsupervised learning and feature extraction; robust to overfitting due to greedy layer-wise training.	Generally produces lower-quality images; complex training process.
Sparse Coding	Image reconstruction, noise reduction, data compression	Excellent at reconstructing high-quality images from noisy data; enhances signal quality.	Not inherently generative and computationally demanding.
Transfer Learning	Enhancing model performance with pretrained networks	Can leverage existing neural network architectures trained on large datasets to improve performance and training speed.	Performance is highly dependent on the relevance of the source model to the target task; it may not capture all task-specific nuances.

This comparison table offers a comprehensive view of the various computational techniques used in neuroimaging alongside GANs.

- *Applications:* All of these methods have particular applications in neuroimaging. For example, VAE and GAN are mostly used for generating new images, which can become very useful during training when limited data are available. On the other hand, CNN and U-Net are very efficient in the segmentation and classification of images, which are very common analyses within medical imaging.
- *Advantages over GANs:* Techniques like VAEs offer a probabilistic understanding of the data, which can be advantageous in tasks where modeling the underlying distribution of data points is crucial, such as in simulating disease progression. CNNs and U-Nets provide high accuracy in segmentation, making them indispensable in clinical settings.
- *Disadvantages Compared to GANs*: Despite their strengths, some of these techniques have limitations when compared to GANs, particularly in image generation. For example, VAEs tend to produce blurrier images compared to the often sharp outputs from GANs. Moreover, methods like CNNs and U-Net are not designed for generative tasks, focusing instead on analysis and segmentation [22].

Overall, the choice of technique heavily depends on the specific requirements of the neuroimaging task, such as whether the priority is on generating new data, enhancing image quality, or extracting meaningful features for diagnostic purposes. GANs are neural networks used for generating synthetic data, particularly in advanced neuroimaging. They are basically made of generators (G) and discriminators (D), which can be used together to come up with excellent medically realistic images. Truly, this is learning a better representation of real data by the generator. Figure 10.2 presents a

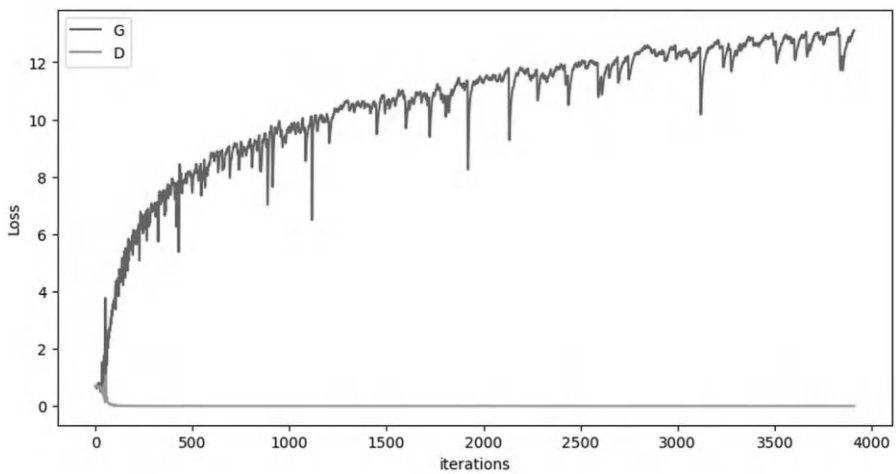

FIGURE 10.2 Generator and discriminator loss during training.

graph that shows the trend in losses for both the generator and discriminator during such training. Fast convergence of the discriminator's loss may be an indicative case for being too strong compared to the generator, hence a clear indication of overfitting. The generator's loss goes down initially, then increases again, hence a hint that it is struggling to produce plausible examples. This will have implications for advanced neuroimaging; the high accuracy by the discriminator drastically limits the learning potential of the generator and might provide images lacking some essential details [23]. One such GAN is trained and used for the purpose of this study of GANs in advanced neuroimaging for upgrading the image resolution, and the generator and discriminator are trained with the pseudocode shown in the previous section with the losses shown in Figure 10.2.

The graph in Figure 10.2 shows the loss curves for both the Generator (G) and the Discriminator (D) over a number of iterations during the training process of a GAN.

1. *Discriminator loss (D)*: The discriminator loss quickly converges to a value close to zero and remains relatively flat for most of the training. This suggests that the discriminator quickly learns to distinguish between real and fake images effectively, to the point where it almost perfectly identifies fake images generated by the generator.
2. *Generator loss (G)*: The generator loss initially decreases but then starts increasing and stabilizes around a higher value. This increase and stabilization indicate that the generator is struggling more to fool the discriminator as the training progresses.

For applications in advanced neuroimaging, these training dynamics have specific implications:

- *Rapid discriminator convergence*: The fact that the discriminator loss drops and remains low could be a sign that the discriminator is too powerful compared to the generator. In neuroimaging, where nuances in the image can be critical for accurate diagnosis or analysis, a discriminator that outperforms the generator might lead to the generator producing less realistic or overly smooth images, missing important details.
- *Generator performance*: The pattern of the generator loss suggests that it has difficulty generating images that are convincing to the discriminator. For neuroimaging applications, this could mean that synthetic images generated by the GAN might not be of high enough quality for clinical use, lack necessary details, or introduce nonrealistic artifacts.

The GAN model that is trained and the training results are shown in the graph in Figure 10.2. The CIFAR-10 dataset is used for training the GAN model. The CIFAR-10 is a public dataset similar to the MNIST dataset, widely used in ML and computer vision. It is formed of 60,000 color images of aggrandized 32×32 pixel resolution, delineated across ten classes, each proffering 6,000 images. The classes depict objects and animals like airplanes, cars, birds, cats, deer, dogs, frogs, horses,

TABLE 10.3
Details of the Dataset Used to Train GAN

Attribute	Details
Total images	60,000
Image size	32 × 32 pixels
Color channels	3 (RGB)
Classes	10
Images per class	6,000
Training set size	50,000 images
Test set size	10,000 images
Usage	Object recognition, computer vision, ML

ships, and trucks. Here the total number of images is 60,000 and out of them, 50,000 images are used for training, and the remaining 10,000 images for testing. More to the point, this dataset is particularly suitable for training GANs because it is sufficiently complex and diverse compared to the manageable number of images. It sets a relatively difficult but realistic standard for training generative models. Various details concerning the CIFAR-10 dataset are provided in Table 10.3.

For GAN training, as can be observed in Table 10.3, the CIFAR-10 dataset provides a diverse and colorful set of images that help the generative model learn to produce a wide range of small-scale images. Training a GAN with CIFAR-10 involves using real images from the dataset to train the discriminator to identify real and fake images accurately, while the generator tries to produce images that are indistinguishable from the actual dataset images. While CIFAR-10 is not specifically designed for neuroimaging and doesn't include medical images, the principles learned from training GANs on CIFAR-10 can be applied to more specialized datasets in neuroimaging. For neuroimaging-specific applications, researchers typically use medical imaging datasets, such as those from the Alzheimer's Disease Neuroimaging Initiative (ADNI), Brain Tumor Segmentation (BraTS) Challenge, or the Human Connectome Project. When transitioning to neuroimaging applications, it is crucial to train the GAN on relevant medical datasets that contain MRI scans, computed tomography (CT) scans, or other medical images to ensure the model can generate realistic and clinically relevant synthetic images. The choice of the dataset will depend on the specific application, such as disease modeling, anomaly detection, or image enhancement in medical contexts. Hence, for a practical application where GANs are being used in some real-life applications of advanced neuroimaging, the following are some recommendations for improved training of GANs:

- Balance the networks.
- Advanced regularization techniques.
- More realistic training data and more variability.
- Domain-specific adjustments [24].

Advanced neuroimaging requires a balance during training between the generator and discriminator for improved synthetic image quality, a factor that is critical in medical applications. In that respect, techniques such as network balancing, advanced techniques, and fitting a generator for neuroimaging data are encouraged. The ability to generate high-quality synthetic images that can be applied clinically depends on achieving a balance in the training dynamics between the generator and discriminator. GANs have been successful in enhancing the resolution of images through super-resolution: reconstructing high-resolution images from their lower-resolution versions by learning data mappings of low to high detail. Since the resolutions are enhanced, clinicians and researchers will identify fine details in neuroimages to improve diagnosis accuracy [25].

First of all, it concerns the privacy of patients in healthcare since this is the number one concern of the industry, more so on the application of medical images in research and training. GANs make a big difference in this respect by making very realistic but completely synthetic neuroimaging data, which can be used without violation of privacy laws. These images do not correspond to any real patient but retain essential anatomical and pathological features necessary for effective training of diagnostic tools. This capability is thus not only useful in scaling up the development of neuroimaging techniques but also in adhering to strict data protection regulations.

Complex and clinically very useful GANs in neuroimaging require a diversity of high-quality datasets to guarantee the robustness and generalizability of the trained models. Here are some of the most widely used neuroimaging datasets that one can use to train GANs:

1. *Alzheimer's Disease Neuroimaging Initiative (ADNI)*
   - *Content*: MRI and PET images, genetic, cognitive, cerebrospinal, and other biological markers.
   - *Use*: Ideal for studies on Alzheimer's disease progression and aging, including tasks like predicting disease progression and generating synthetic images of disease stages [26].
2. *Brain Tumor Segmentation (BraTS) Challenge datasets*
   - *Content*: Multi-institutional preoperative MRI scans of glioblastoma and lower-grade glioma, with annotations for tumor and tumor subregions.
   - *Use*: Useful for training GANs to synthesize brain tumor images or to enhance tumor segmentation capabilities [27].
3. *Human Connectome Project (HCP)*
   - *Content*: High-resolution 3T MRI scans from healthy adult subjects, including structural and functional MRI data.
   - *Use*: Provides a baseline for normal anatomical and functional brain imaging, valuable for generating control images in studies or enhancing functional MRI analysis [28].
4. *Open Access Series of Imaging Studies (OASIS)*
   - *Content*: Cross-sectional MRI data from young, middle-aged, nondemented, and demented older adults.
   - *Use*: Facilitates the study of normal aging and cognitive decline, ideal for GANs aimed at generating or augmenting aging brain datasets [29].

5. *Pediatric Imaging, Neurocognition, and Genetics (PING) dataset*
   - *Content*: MRI data and a variety of clinical and cognitive scores from a pediatric population.
   - *Use*: Helps in generating pediatric brain images for studies focusing on early development and neurodevelopmental disorders [30].
6. *UK Biobank Imaging Study*
   - *Content*: Extensive imaging data including brain MRI, alongside rich genetic and health information from a large-scale cohort.
   - *Use*: It offers a comprehensive resource for training GANs in a diverse adult population, and it is ideal for broad applications in disease prediction and aging [31].
7. *LONI Probabilistic Brain Atlas (LPBA40)*
   - *Content*: Brain atlases derived from 40 MRI volumes with segmented brain structures.
   - *Use*: Useful for tasks requiring precise anatomical segmentation and for generating anatomically accurate synthetic brain images [32].
8. *Cam-CAN*
   - *Content*: Contains MRI and other modalities from a large range of ages across the adult lifespan.
   - *Use*: Useful for understanding changes in brain structure and function across the lifespan, and for synthesizing age-varied brain images [33].

These datasets include a wide and deep range of data that would be very useful for GAN training applied to various neuroimaging applications. Each of the associated datasets has various strengths, including high-resolution annotations, large sample sizes, diversity in populations, and inclusion of healthy/pathological subjects. It should, however, be appreciated that each of these datasets has an agreement to use and share, with accompanying ethics on the confidentiality of the patients and permission to make use of their data.

GANs in neuroimaging can help alleviate some of the most pressing concerns of this domain: data scarcity, image resolution, and privacy. Specifically, GANs synthesize high-quality images to enhance the resolution of the images and generate de-identified synthetic data, thereby enhancing the quantity and quality of the data for neuroimaging applications. The techniques are strongly impacting neurology and leading to more accurate and earlier diagnoses of neurological disorders. The next sections will introduce concrete applications and case studies that further realize the benefits of GANs in neuroimaging.

10.5 PRACTICAL APPLICATIONS OF GANs IN NEUROLOGY

There are several practical applications of GANs through which they can particularly be considered useful in neurology and neuroimaging. Apart from a spectrum of applications, some of the most relevant and most developed recent applications are listed below for reference. However, the studies and research on its applications are

being conducted continuously, which makes them a continuously evolving technology with continuous advancements.

1. *Data augmentation*
   a. Addressing the scarcity of annotated neuroimaging data
   b. Techniques for synthetic data generation [34]
2. *Image reconstruction*
   a. Enhancing clarity and detail in neuroimages
   b. Case studies demonstrating improved diagnostic utility [35]
3. *Automatic segmentation*
   a. Techniques for segmenting complex brain images
   b. Impact on the speed and precision of diagnoses [36]
4. *Anomaly detection*
   a. Identifying subtle signs of neurological disorders [37]
   b. Comparative analysis with traditional diagnostic methods [10]

GANs have become vital in advanced neuroimaging because of the impressive way in which they generate and manipulate images. Their applications range from data augmentation to image synthesis, reconstruction of images, and the detection of anomalies. Table 10.4 presents some of the uses of GANs in advanced neuroimaging that were developed first, summarizing their applications, advantages, and challenges as a quick preview of the applications of GANs in advanced neuroimaging.

Table 10.4 shows the practical applications of GANs in neuroimaging, complemented by real examples of cases where those technologies have been tested or applied. That increases credibility and gives insight into what their potential is:

- One study discusses how GAN-based data augmentation can be applied to improve the performance of ML models within medical image classification tasks [34].
- Another case illustrates how, in quite a crucial setting, where one kind of imaging may be formally contraindicated or unavailable, GANs could take a key role in synthesizing medical images across modalities [35].
- One research project represents an example of how GANs reconstruct high-quality images from already existing MRI data, which is quite important in neurology, where image clarity might critically determine diagnosis [38].
- An example of the usage of GANs in detecting anomalies in retinal imaging is a pertinent transferable concept to neuroimaging for the identification and diagnosis of various brain anomalies [39].
- The study gives insight into how GANs can model disease progression – an area emerging to revolutionize how neurological diseases are studied and treated [40].

The area of neuroimaging is already unparalleled, in nearly all aspects, by GANs – tending from improved diagnostic capabilities to developing new ways of studying and better understanding neurological conditions. Each of these studies or applications has its challenges, most especially accuracy issues and ethics of AI-generated

TABLE 10.4
Practical Applications of GANs in Advanced Neuroimaging

Application	Description	Benefits	Challenges	Case Study Reference
Data augmentation	Generating synthetic neuroimaging data to augment datasets.	Enhances model training with limited real data and improves robustness.	Risk of synthetic data not accurately representing real patient variations.	A study used GANs to augment data for liver lesion classification in CT images, significantly improving classification performance [34].
Image synthesis	Converting images from one modality to another (e.g., MRI to CT).	Useful when certain modalities are unavailable; supports comprehensive diagnostic evaluations.	Synthesized images may miss subtle yet critical features present in actual scans.	Another study in 2017 demonstrated the synthesis of cardiac MR images into CT images, aiding in multimodal studies and treatments [35].
Image reconstruction	Enhancing the quality of images from lower-resolution inputs.	Produces higher resolution images, corrects artifacts, and improves diagnostic accuracy.	Requires careful calibration to avoid introducing artificial features that could mislead clinicians.	Conduction of one research used GANs to reconstruct high-quality 7T-like MR images from 3T MR images, enhancing the image quality for better diagnosis [38].
Anomaly detection	Identifying and highlighting abnormalities in brain images.	Facilitates early detection and diagnosis of tumors, lesions, and other anomalies.	Dependence on the diversity and quality of training data to avoid false positives or negatives.	One such study in 2017 utilized GANs for detecting retinal diseases from optical coherence tomography images, showcasing the potential for early diagnostic applications [39].
Simulating disease progression	Generating images that show the progression of neurological diseases.	Aids in understanding disease trajectories and planning treatment strategies.	Ethical concerns and accuracy in predicting future disease states need rigorous validation.	Another study simulated the progression of white matter lesions in brain MRIs, providing valuable insights into disease progression and potential therapeutic effects [40].

images, which calls for further research and development. GANs have most neurological applications, which show the potential for GANs to prove transformative in this field. From data augmentation, image reconstruction, and automatic segmentation to even anomaly detection, GANs-augmented neuroimaging technologies are giving way to more accurate, efficient, and comprehensive diagnoses. Further innovations to such technologies likely see clinical integration growing, further revolutionizing diagnosis and treatment related to neurological disorders.

10.6 ETHICAL CONSIDERATIONS AND CHALLENGES

Employing synthetically created images in neuroimaging through GANs presents several ethical considerations. As accurately mentioned, there are numerous challenges in achieving high accuracy and reliability of the synthetic data, while these datasets may not mimic the real human pathology in certain ways and can result in inaccuracies of the diagnostic tools trained on such data. Also, there is an ethical imperative to make sure that synthetic data that are used in any research or clinical training does not prejudice or lead to wrong practices in case they will have unfortunate consequences for the patients. Another ethical concern, as with synthetic data, is informed consent; since identifying details are removed, the distinction between patient privacy and consent is not distinct. This can indeed shield the privacy of patients, but it also brings up important legal concerns as to the defined medicolegal jurisdiction of consent regarding ensuing data or data procured from the unique imaging of a patient. There is a concern thus being raised about whether such bias would be reflected in the generated images and thus cause disparities in healthcare delivery and diagnostic accuracy between different populations that are represented differently in the training set for the GAN.

Mitigating these sources of bias entails appropriate selection and flavor of the populations from which data for GANs are drawn. Also, adjustments to the current AI models are required to prevent such biases as the models continue to be applied in varied aspects of healthcare operations. As a result, there a several steps that are difficult in the validation and clinical acceptance of GAN technologies:

1. The aspects of validation and clinical acceptance of GAN technologies are the main difficulties. Firstly, there is no consistent set of rules that establish how synthetic data and AI-generated results should be validated due to the fact that the regulations for AI in the healthcare sector are still rather ambiguous. The law has certain expectations from its accredited organizations, and since the nature of algorithms is dynamic and self-learning, the authorities may find it hard to accept results and call for hard evidence of efficacy and safety.
2. It is also seen clinically that establishing trust in AI systems is another key issue. The public may have low confidence in diagnostic tools that are based on synthetic data, especially if they do not understand how the tools work. Accuracy and reliability, as evidenced by validation studies, are axiomatic when it comes to the use of GANs, but training and awareness of GAN simulations among healthcare practitioners are critical as well.

3. Moreover, many factors make it difficult to integrate GAN technologies into current clinical workflows. They have to accommodate very diverse infrastructures in hardware and software in healthcare settings while accommodating many such fine details and exceptions – very common in medical practice during execution.

Technical, regulatory, and ethical challenges with using GANs in neuroimaging are multidimensional. Such concerns must be raised together by developers, researchers, ethicists, and regulatory bodies to ensure that these powerful tools remain in empowered hands to serve responsibly for the betterment of patients and not to promote unethical practices or foster already existing biases. Looking ahead, bringing together the collaborative development of frameworks for the ethical use and validation of synthetic data and AI technologies in healthcare will be central to their successful integration and acceptance in clinical practice.

10.7 FUTURE DIRECTIONS

The neuroimaging field is still dynamic, where GANs are at the forefront of steering the industry forward. Multimodal GANs are able to combine information from various imaging techniques, which results in the usage of synthesized images for better understanding neurological disorders and making accurate diagnoses. They are also being used for projecting longitudinal data simulation and the development of neurological diseases such as AD or MS at different phases in life. Mitigation of deficits and the combination of GANs with other AI technologies, including CNNs and reinforcement learning (RL), improve diagnostics' accuracy and time. CNNs get training data from GANs and then are employed for the specific segmentation, analysis, and diagnosis of an image. Obviously, with the help of RL, the combinations of diagnostic strategies can be made dynamic and adjusted depending on the results' feedback, making treatment flexible and individualized.

It might be useful to integrate GANs with natural language processing (NLP) technologies, which should bring a significant change in diagnostics reports generation and analysis, making them more accurate and available for clinicians. This could make a better link between image analysis and reaching clinical decisions as far as the flow of information among several medical teams is concerned. GANs will be applied in predictive diagnostic procedures and individualized approaches where simulation of individual patient outcomes for various potential treatments will be possible. With the increases in the development of GAN technology, GAN becomes work in clinical practice, which can help standardization of diagnostic procedures, decrease the possibility of error in diagnosing, and contribute to stabilization of the treatment process. This could also decrease the management load of medical professionals since most of the repetitive tasks could be automated. Based on these findings, the prognosis for GANs in neuroimaging is positive; there has been a plethora of advancements in detecting, managing, and treating neurological disorders. Thus, the protocols of ethical behavior and legislation are crucial to prevent new developments from becoming a tool for doctors' profit and preserving the quality of treatment for all patients.

Despite the aforementioned context, GANs for advanced neuroimaging can be extended further in some other possible ways:

1. *Development of multimodal GANs*: Other studies that conducted in the future could develop different GAN models using combined data from MRI, PET, and fMRI. Such an approach would prove to be more efficient since each imaging modality has its merits that can be harnessed for the betterment of neurological disorders diagnosis.
2. *Explainable GANs for neuroimaging*: Further, researchers need to come up with virtual machine (VM) parameters to reveal details of synthesized images and data to clinicians, explaining how synthetic data are created and which aspects of patients' images are most beneficial in diagnosing disease at different stages. This increase in transparency could improve the confidence of clinicians in GAN-based tools when used for patient diagnosis or treatment.
3. *Improving GAN robustness and reliability*: More work needs to be done to investigate GANs' stability in terms of patient cohorts, scanners, and clinical settings, making certain that GANs can hold acceptable image quality regardless of conditions that affect the input data or the scanners.
4. *GANs for early disease detection and prediction*: Research can be made directed toward whether GANs are capable of detecting initial biomarkers or symptoms of neurological disorders, including but not limited to AD or Parkinson's, which usually are not easily done by humans and can lead to better prevention and treatment.
5. *Optimizing GANs for low-resource settings*: It is also necessary to consider the possibilities of developing GAN models considering the conditions of working with low-quality images and insufficient amounts of material. This adaptation would therefore assist in spreading the gains of the advanced neuroimaging tools to these groups of people.
6. *Hybrid GANs with other AI techniques*: Further studies can be conducted to investigate the integration of GANs with other AI techniques like RL so as to work even better in areas like anomaly detection or image segmentation to improve on the current models.
7. *Real-time GAN applications in neuroimaging*: Studying new architectures of GAN to enable their use in real-time while performing imaging could give on-the-spot feedback to clinicians and aid in quicker decision-making that could possibly help better the quality of patient care.
8. *GANs for rare neurological conditions*: Researchers should therefore employ GANs in the construction of synthetic datasets, especially in ailments such as neurological diseases where data acquisition is a challenge. Such synthetic data could enhance the diagnostic performances of such disorders and provide clinical insights into these disorders.
9. *Personalized medicine and patient-specific modeling*: This would mean that creating models that use actual data about a patient, like their genetic makeup and past diseases, is possible and valuable when it comes to designing GANs.

10. *Ethical and privacy-preserving GAN models*: There is a need to design GANs that will be able to generate synthetic data in such a manner that patients' identities will not be available to third parties, to ensure confidentiality while data sharing and collaboration among researchers.
11. *Benchmarking and standardization of GANs in neuroimaging*: Guidelines and standards for assessing the quality of GAN models would go a long way toward creating consistent benchmarks and validation standards that are needed for the field to achieve better levels of credibility in order to promote more cooperation as well as openness.
12. *Clinical trials and real-world testing*: It is imperative to have a post-facto assessment to evaluate the clinical performance of GAN-based methods through clinical trials and real-world studies in order to generate quantifiable benchmarks for its applicability and adoption in clinical use.
13. *GANs for longitudinal studies and disease monitoring*: The creation of GANs that have the potential to synthesize realistic images and forecast alterations in the evolution of brain structures might enhance the diagnostic capabilities of condition evolution and the utility of treatments in follow-up examinations.

When cultivating these directions, researchers are likely to make incremental improvements on GANs' application to neuroimaging while also improving the technology and the lives of their patients.

10.8 CONCLUSION

GANs have brought significant change in neuroimaging by removing the need for high-quality synthetic data, making it easier to generate annotated datasets, addressing the need for high image resolution, and also tackling the issue of patient privacy. Some of the applications are data augmentation, image reconstruction, automated segmentation, and anomaly detection, which ensure that the diagnostic procedures are enhanced and research on neurological disorders. The adoption of GANs in clinical practice may become one of the key factors that will change the nature of medicine, offering accurate and fast diagnosis. However, integration of AI in healthcare cannot be successful unless there is a technological update, medical personnel are trained on AI, trust in AI outputs is established, and, moreover, sound ethical and legal structures are in place. There is a wide and open field to expand and investigate the utilization of GANs in neuroimaging and other areas of science. Different fields, namely AI professionals, neurologists, ethicists, and policymakers should come together to work on GANs to the maximum capacity they possess. The investment in basic research and applied clinical studies shall guarantee that the discoveries progress in a scientifically proper manner and respond to patient care necessities.

All in all, GANs in neuroimaging are depicted as a future where technology and healthcare coalesce to produce better, more efficient, and feasible medical practice. The use of GANs in neurology is still in its initial phase, and its development will inevitably change the paradigm of instantiating and addressing neurological diseases to improve the patient's quality of life across the globe.

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11 Machine Learning Strategy with Decision Trees for Parkinson's Detection by Analyzing the Energy of the Acoustic Data

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11.1 INTRODUCTION

Parkinson's disease (PD) is a progressive neurological disorder characterized by a variety of motor and nonmotor symptoms that significantly affect the quality of life. It affects more than 10 million people worldwide, with an annual death rate of approximately 100,000, according to recent surveys by the World Health Organization (WHO) [1]. Early detection of PD is crucial for effective management and can significantly slow the progression of the disease. One of the notable motor symptoms includes changes in speech patterns, making acoustic analysis a valuable tool for early detection and monitoring of the disease [2]. The articulation of specific vowels, such as "a" and "i," often exhibits distinctive energy variations in individuals with PD, which can serve as reliable biomarkers. Automated analysis through signal processing strategies enables precise extraction and evaluation of these acoustic features, facilitating accurate diagnosis and monitoring. This chapter introduces a decision tree–based approach to classify and detect PD, offering a noninvasive, cost-effective method that enhances diagnostic accuracy. By focusing on the energy levels of sound recordings of the vowels "a" and "i," the aim is to establish a robust framework for identifying PD with improved precision and efficiency.

Few methods dealing with the detection and characterization of PD are available in the literature. Abdullah et al. [3] used a publicly available dataset called Newhand containing voice recordings to detect PD by employing optimized feature selection and deep transfer learning techniques, focusing on acoustic features such as pitch, jitter, shimmer, and Mel-frequency cepstral coefficients (MFCCs). The approach also used pretrained convolutional neural networks (CNNs) for feature extraction.

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They reported an accuracy of 95%, a precision rate of 98%, and loss value of 0.12. A custom-built robotic platform to analyze sensorimotor integration in PD patients has been set up by Tamilselvam et al. [4]. They utilized a dataset comprising 60 participants and focused on features such as reaction time, movement accuracy, coordination metrics, tremor frequency, and grip force dynamics. Machine learning (ML) techniques, specifically support vector machines (SVM), were used for classification and achieved an accuracy of 95%.

Khan et al. [5] utilized the Parkinson's Disease Data Set from the University of California, Irvine (UCI) Machine Learning Repository, which includes voice recordings and clinical data from PD patients and healthy individuals. The key features analyzed comprise the acoustic characteristics, clinical symptoms, and patient history. The system employed a multilearning trick strategy, integrating CNNs and recurrent neural networks (RNNs) and achieved a classification accuracy of 96.2%. A weakly supervised learning approach to detect tremors has been proposed by Zhang et al. [6]. They used the Pa Data Set from the UCI Machine Learning Repository, which includes sensor data capturing tremor activity from PD patients. Key features analyzed were tremor frequency, amplitude, and duration. The method applied weakly supervised learning techniques to train models with limited labeled data, leveraging additional unlabeled data to improve detection accuracy. They reported accuracy of 94.5%.

Sabo et al. [7] examined the effectiveness of combining Zeno Instrumented Walkway with video-based gait analysis. They utilized gait data from adults with PD, collected using the Zeno Walkway, which offers precise measurements of gait time domain parameters such as stride length, gait speed, and variability, and was complemented by video recordings for visual gait analysis. They compared the two methods like quantitative measurements from the Walkway and qualitative observations from video by analyzing stride length, gait speed, and variability, finding a strong correlation with a coefficient of 0.89. In [8], the feasibility of detecting PD using phonemes recorded via smartphones in everyday settings. They utilized a dataset of phoneme recordings collected from PD patients and healthy controls using standard smartphone microphones. The frequency domain acoustic features such as pitch, formants, and speech rate were applied to SVM and random forests (RF) to classify and obtained an accuracy of 92.3%.

Aljalal et al. [9] exploited the time-frequency domain features extracted via Discrete Wavelet Transform (DWT) and entropy measures such as approximate entropy (ApEn) and sample entropy (SampEn) from the EEG Dataset available from the UCI Machine Learning Repository. These features were given as input to SVM and RF and obtained a classification accuracy of 94.8%. Xu et al. [10] investigated brain network differences between PD patients and healthy controls using edge functional connectivity of the functional magnetic resonance imaging (fMRI). Features analyzed included edge functional connectivity metrics within the frequency domain, where they constructed functional connectivity graphs with nodes representing brain regions and edges indicating connection strength. The analysis employed graph theory metrics such as degree centrality, betweenness centrality, and clustering coefficient to characterize network properties, and statistical tests like permutation tests and group comparisons to identify significant differences.

Most of these studies predominantly focused on frequency-domain and time-frequency domain features, such as pitch, formants, and tremor characteristics; while such features are informative, they may overlook the potential of fundamental time-domain metrics like the energy of specific phonemes. This focus suggests a gap in exploring how time-domain features alone could enhance detection capabilities. Furthermore, the literature indicates a diverse application of methodologies and datasets – ranging from voice recordings to gait analysis and electroencephalogram (EEG) signals – without a standardized approach or comparative analysis, which could constrain the generalizability of findings. Additionally, statistical and feature separability measures, including histogram and Kolmogorov–Smirnov (KS) tests, are underutilized in current research. Incorporating these methods may provide more refined understandings of feature distributions and separability, thereby enhancing the precision of diagnostic evaluations.

Incorporating time-domain features, specifically the energy of vowels such as "a" and "i," provides a direct measurement of acoustic signals, simplifying the analysis process without requiring complex transformations. These features are sensitive to subtle changes in speech patterns, potentially aiding in early detection of PD. Moreover, time-domain features enhance interpretability by establishing clear correlations between acoustic data and clinical symptoms, thereby improving the overall performance of diagnostic methodologies. Addressing these gaps and leveraging the merits of time-domain analysis can significantly advance the accuracy and effectiveness of PD detection frameworks. The rest of the chapter is structured as follows. A thorough description of the investigation, the dataset used, and the mathematical derivation of the features is provided in Section 11.2. Section 11.3 delves deeply into the statistical significance and separability that the characteristic offers in terms of distinguishing between different kinds of speech input followed by the ML strategy employed. Section 11.4 includes the conclusion and possible directions for further development, followed by the references.

11.2 METHODOLOGY

This chapter presents a decision tree–based methodology for the classification and detection of PD, providing a noninvasive and cost-effective approach that may improve diagnostic accuracy. By analyzing the energy levels of acoustic recordings of the vowels "a" and "i," the chapter aims to develop a robust framework that enhances the precision and efficiency of PD identification. The publicly available dataset called Figshare [11] is used in this work. This comprises the artificially synthesized renditions of sustained vowel sounds, specifically the vowels "a" and "i" produced by individuals across various demographic categories, including healthy individuals and those diagnosed with PD, multiple system atrophy, and progressive supranuclear palsy [12]. The wave pattern of a sample record of healthy and PD cases for the vowels "a" and "i" is shown in Figure 11.1(a) and (b).

As shown in Figure 11.1, the waveform pattern of the sound recordings exhibits distinct differences between the two situations, particularly in amplitude and random features.

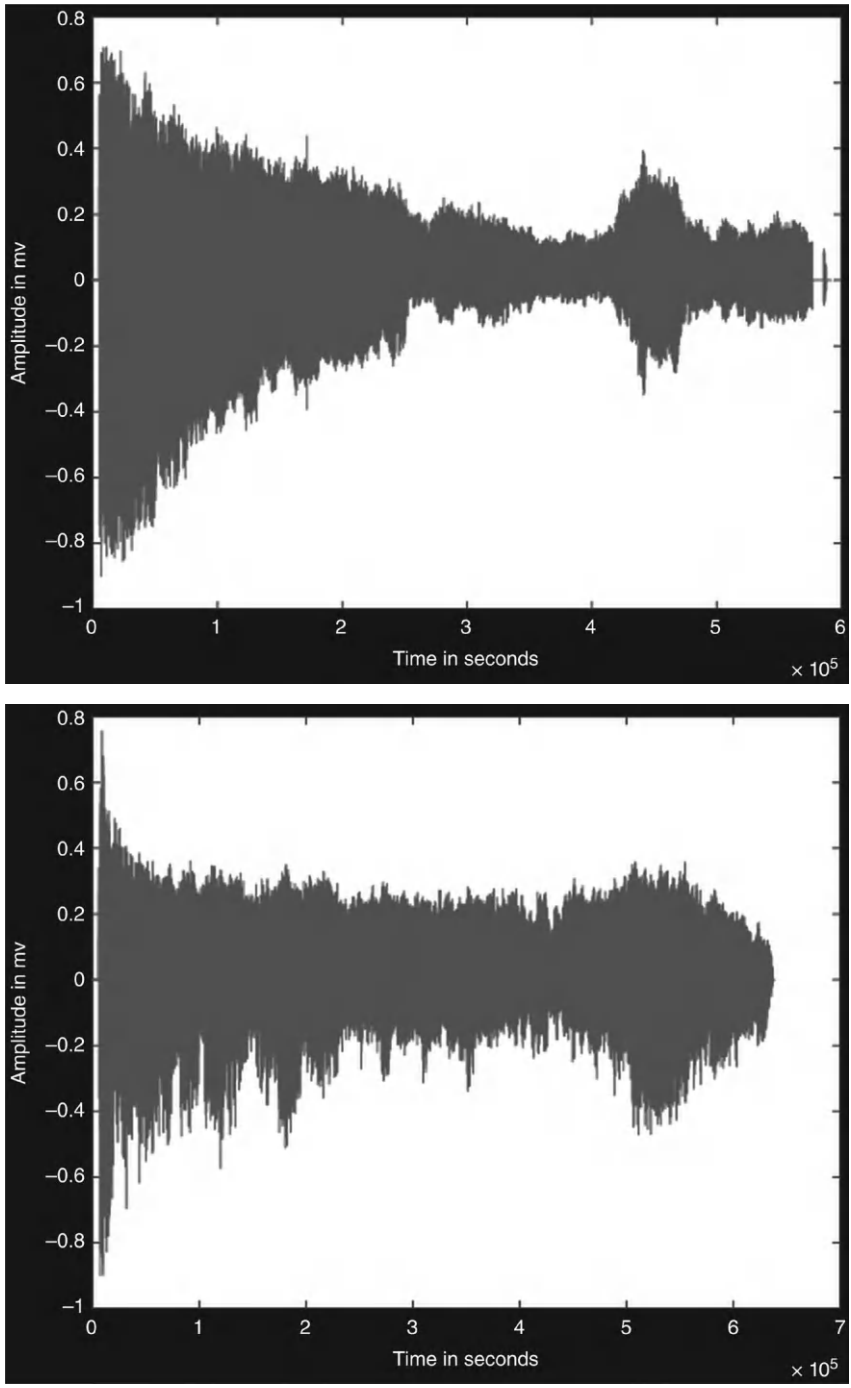

FIGURE 11.1 Wave pattern of sample record of vowel "a" and vowel "i" cases: (a) Vowel "a" normal; (b) vowel "a" PD; (c) vowel "i" normal; and (d) vowel "i" PD. (*Continued*)

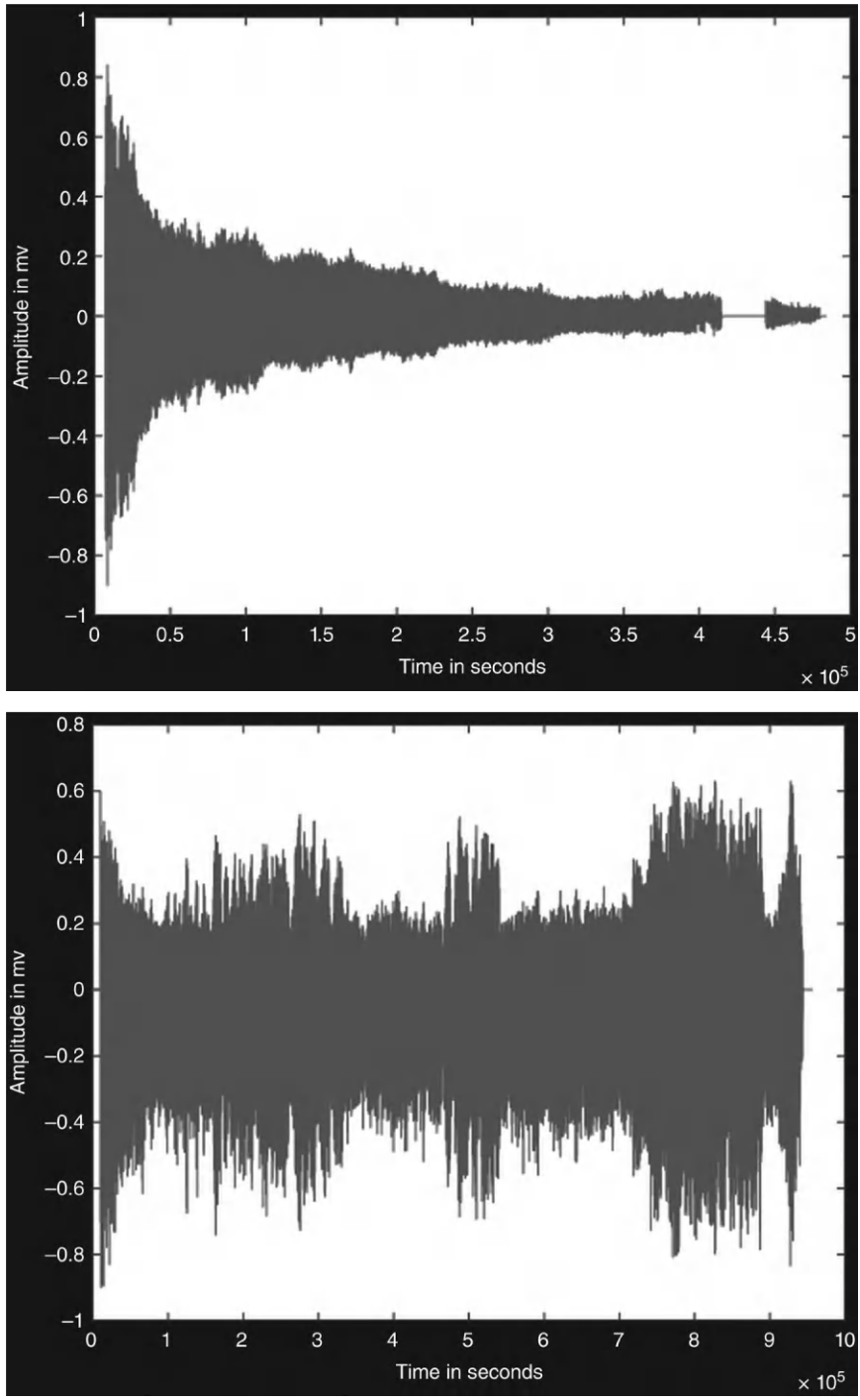

FIGURE 11.1 (Continued)

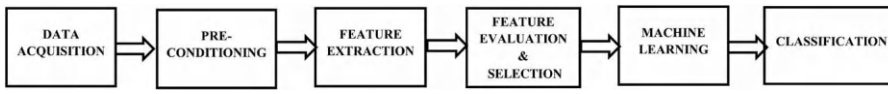

FIGURE 11.2 Schematic of the steps involved.

The proposed method for classifying PD cases involves a block diagram consisting of six key steps, as shown in Figure 11.2. They are data acquisition, preprocessing, feature extraction, feature evaluation and selection, ML, and classification. Data acquisition begins with collecting audio recordings from the publicly available dataset Figshare, which includes recordings of the vowels "a" and "i" from both healthy individuals and PD patients. The preprocessing stage is crucial for preparing the raw audio data, where noise reduction techniques are applied to minimize background interference and ensure clarity. Subsequently, the audio data are normalized to a range between +1 and −1, reducing amplitude variations and providing a uniform basis for comparison and analysis.

Feature extraction focuses on calculating the feature called energy of the acoustic signals. This feature is then evaluated for its significance in distinguishing between healthy and PD cases, ensuring that only the most pertinent features are selected for further analysis. In the ML stage, various decision tree models, including coarse, fine, and medium decision trees, are employed to handle complex decision-making by creating branches based on feature values. The final classification step involves using these decision tree models to categorize data into healthy or PD-affected based on learned patterns. The stochastic signal $X_i(t)$ after normalization is given as [11]:

$$X_n(t) = \frac{X_i(t)}{\max|X_i(t)|} \tag{11.1}$$

The energy of the of the stochastic signal "$X_n(t)$" given by [12]:

$$\text{Energy} = \frac{\left[\sum_{t=1}^{N}\sqrt{|(X_n(t))|}\right]^2}{N} \tag{11.2}$$

where N is the total number of samples.

11.3 RESULTS AND DISCUSSIONS

The energy of the voice record "a" and "i" of healthy as well as PD cases is statistically tested for the ability to distinguish between healthy and PD cases using the KS test. Histogram plots are also used to qualitatively assess feature separability. Matlab® is employed for all mathematical formulations, feature extraction, statistical evaluation, and ML processes.

The range and numerical values of different audio data for healthy and PD cases are presented in Table 11.1.

TABLE 11.1
Range and Numerical Values

Audio Data	Parameter	Healthy	PD
Vowel "A"	Range	0.00399–0.06595	0.00926–0.10269
Vowel "I"		0.01433–0.11883	0.02496–0.12989
Vowel "A"	Numerical values	0.02304 ± 0.01646	0.03824 ± 0.02469
Vowel "I"		0.05463 ± 0.03266	0.07647 ± 0.03188

As per the data presented in Table 11.1, the range of energy values for vowel "a" in healthy individuals is 0.00399 to 0.06595, while in PD patients, it ranges from 0.00926 to 0.10269. For vowel "i," healthy individuals show a range of 0.01433 to 0.11883, whereas PD patients exhibit a range from 0.02496 to 0.12989.

The absolute deviation values, which indicate the spread of energy values around the mean, also reveal notable differences. For vowel "a," healthy individuals have an absolute deviation of 0.02304 ± 0.01646, compared to 0.03824 ± 0.02469 in PD patients. For vowel "i," the absolute deviation is 0.05463 ± 0.03266 for healthy individuals, while it is 0.07647 ± 0.03188 for PD patients. These findings, detailed in Table 11.1, emphasize the variations in both the range and absolute deviation of energy values between healthy and PD cases, potentially reflecting the vocal changes associated with Parkinson's disease. The KS test results for the audio recordings are detailed in Table 11.2, assessing the statistical significance of the differences between healthy and PD cases.

Both vowels "a" and "i" have Chi-square values of 0, indicating no observed difference in feature distribution. However, the probability values show that neither vowel demonstrates significant statistical differentiation between healthy and PD cases. Thus, based on this analysis, neither vowel "a" nor vowel "i" appears to be highly effective in distinguishing between the two conditions. Despite the lack of significant differentiation for both vowels, vowel "a" shows a probability value closer to the significance threshold. Therefore, vowel "a" might be slightly better for potential differentiation between healthy and PD cases compared to vowel "i." The histogram of the energy of both the voice records pertaining to healthy and PD cases is shown in Figure 11.3.

The histograms reveal that the speech input for the vowel "i" demonstrates greater feature separability [13] in the feature space than the vowel "a." The performance

TABLE 11.2
KS Test Values

Type of Audio Records	Chi-square Value	Probability Value
Vowel "A"	0	0.0591
Vowel "I"	0	0.4255

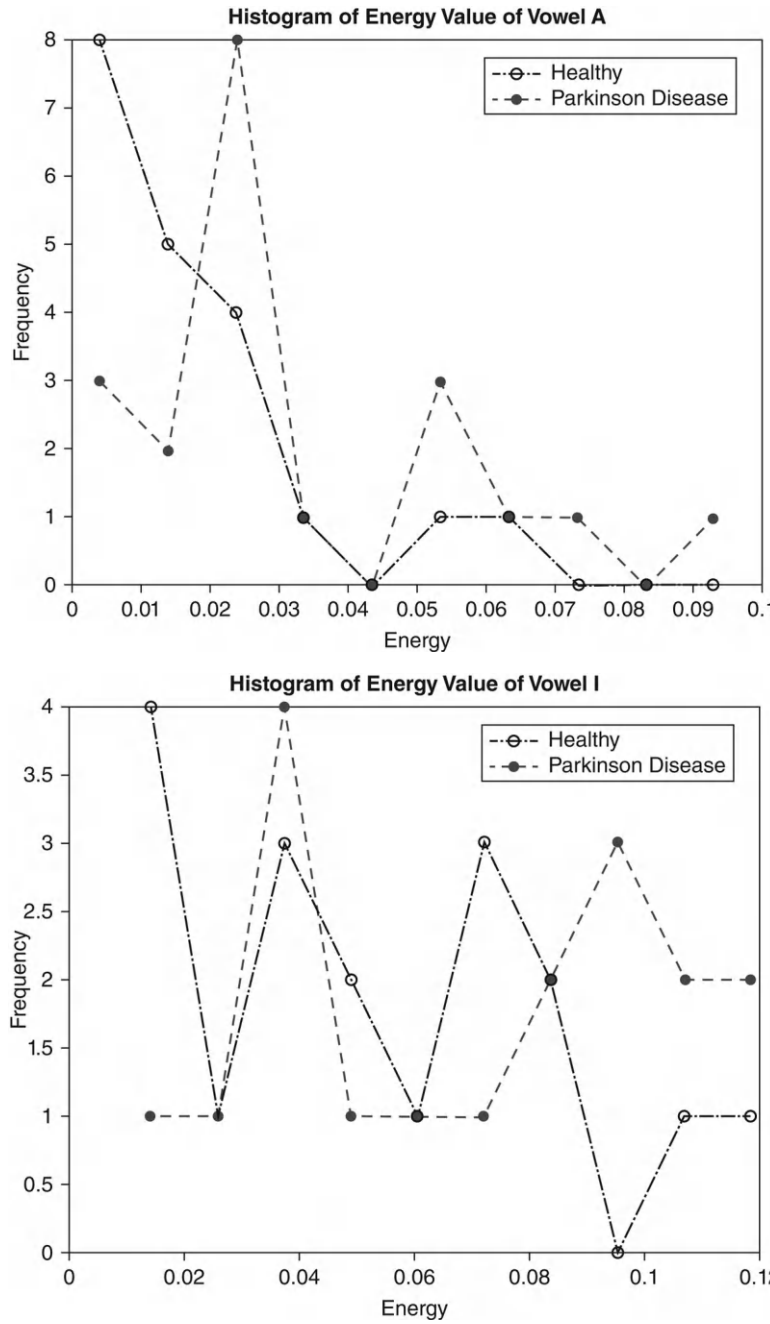

FIGURE 11.3 The histogram of the energy of both the voice records: (a) vowel "a"; (b) vowel "i."

TABLE 11.3
Performance Metrics

No.	Record	Sens. (%)	Spec. (%)	Acc. (%)
1	Vowel "A"	75.00	65.00	70.00
2	Vowel "I"	50.00	77.78	63.89

parameters of the sound record to distinguish healthy and PD cases are presented in Table 11.3.

Bit is inferred from Table 11.3 that vowel "a" demonstrates superior sensitivity (75.00%) compared to vowel "i" (50.00%), indicating that vowel "a" is more effective in correctly identifying PD cases. However, vowel "i" shows higher specificity (77.78%) than vowel "a" (65.00%), suggesting it is better at correctly identifying healthy cases. Despite vowel "a" having higher overall accuracy (70.00%) compared to vowel "i" (63.89%), the higher sensitivity of vowel "a" makes it more suitable for distinguishing PD cases. While both vowels have their strengths, vowel "a" is preferable for its better sensitivity, making it more effective in identifying PD among the two vowels analyzed.

11.4 PERFORMANCE OF DECISION TREES

From the analysis done in the preceding sessions, it is evident that the energy values from the vowel "a" sound record exhibit superior performance in distinguishing between PD and healthy conditions compared to other sound records. Consequently, this feature has been selected for further analysis and used as input for various decision tree models, including fine tree, medium tree, and coarse tree [14]. Figure 11.4 present the confusion matrices for these decision trees, illustrating the effectiveness of the vowel "A" energy feature in differentiating between PD and healthy conditions.

For both fine and medium trees given in Figure 11.4(a) and (b), the confusion matrices show that 14 healthy samples were correctly classified, and six were misclassified as PD. For PD cases, 12 were correctly classified, and eight were misclassified as healthy. This results in a positive predictive value (PPV) of 60% for PD cases and 70% for healthy cases for both fine and medium trees. For the coarse tree (Figure 11.4(c)), out of 20 samples of healthy cases, 14 were correctly classified as healthy, and six were misclassified as PD. For PD cases, 11 were correctly identified, and nine were misclassified as healthy. This results in a PPV of 55% for PD cases and 70% for healthy cases.

Given their superior performance in distinguishing PD cases while maintaining consistent accuracy for healthy cases, the fine and medium trees are preferable over the coarse tree for this classification task. The performance indices of various decision trees during training and testing are presented in Table 11.4.

Table 11.4 compares the performance of fine, medium, and coarse trees in classifying vowel "a," focusing on validation accuracy, prediction speed, training time,

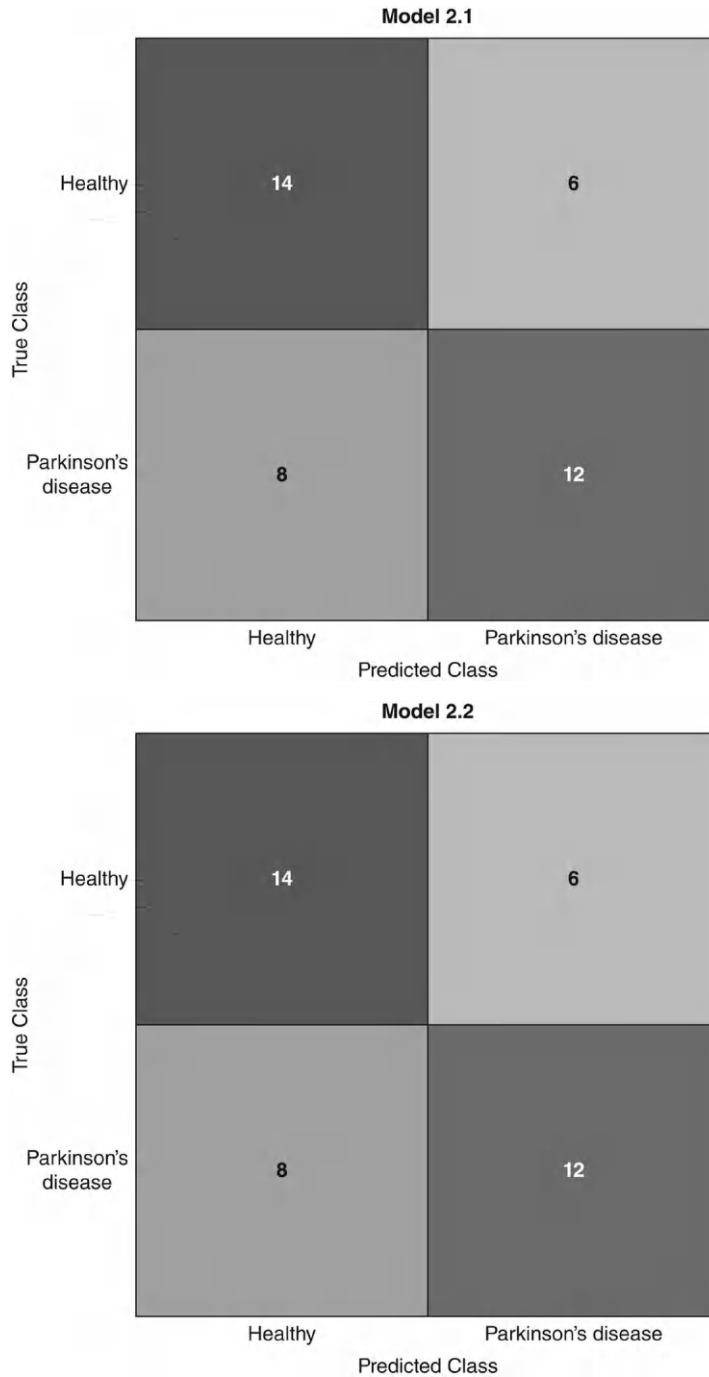

FIGURE 11.4 Confusion matrix of vowel "a" of various decision trees in predicting different cases: (a) fine tree; (b) medium tree; and (c) coarse tree. (*Continued*)

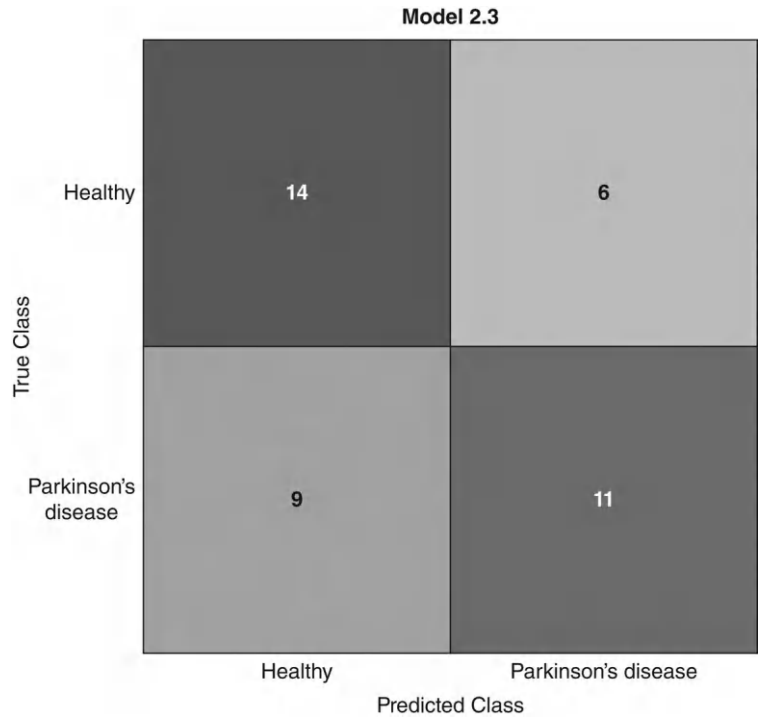

FIGURE 11.4 (Continued)

and test accuracy [15]. Both the fine and medium trees have a validation accuracy of 65% and a high test accuracy of 85%, with the medium tree significantly outperforming the fine tree in prediction speed (640.65 observations/sec vs 152.66 observations/sec) and having a shorter training time (14.70 sec vs 16.37 sec). The coarse tree, although it has the fastest in prediction speed (761.73 observations/sec) and with the shortest training time (14.12 sec), shows a lower validation accuracy of 62.5% and a reduced test accuracy of 70%. This suggests that although the coarse tree excels in prediction speed, the fine and medium trees deliver superior overall accuracy. Among them, the medium tree achieves the optimal balance between speed and accuracy.

TABLE 11.4
Performance Indicators of Different Decision Trees

Tree	Accuracy (Validation) (%)	Prediction Speed (Obs/Sec)	Training Time (Sec)	Accuracy (Test) (%)
Fine	65	152.66	16.37	85
Medium	65	640.65	14.70	85
Coarse	62.5	761.73	14.12	70

11.5 CONCLUSIONS AND FUTURE SCOPE

This chapter presented a noninvasive approach for detecting PD using ML techniques, specifically decision trees, with acoustic energy features from vowel sounds. The analysis indicated that energy features from vowel "a" outperformed those from vowel "i" in distinguishing between healthy and PD cases. The KS test revealed that vowel "a" exhibited better feature separability with a p-value of 0.0591 compared to 0.4255 for vowel "i." The separability offered by the feature to differentiate both cases has been also evaluated. The performance metrics showed that the energy of vowel "a" achieved an accuracy of 70%, sensitivity of 75%, and specificity of 65% in identifying PD cases. The chapter observed that the fine and medium trees offer better accuracy of 85% for classifying, with the medium tree balancing speed and accuracy, while the coarse tree excels in speed of 761.73 obs/sec but has lower accuracy of 70%. Future work could enhance PD detection by integrating advanced ML techniques, such as ensemble methods or combining decision trees with other algorithms like neural networks. Expanding the dataset to include diverse speech samples and additional biomarkers could improve model accuracy and robustness. Additionally, optimizing feature extraction methods and using cross-validation to fine-tune model parameters would be beneficial. Testing these models in real-world clinical settings could help refine their performance and applicability.

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12 Adaptive Convolution Neural Network-Based Brain Tumor Detection from MR Images

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12.1 INTRODUCTION

Cancer is a crucial health subject in the modern world, being the second most common reason for death globally after heart disease [1]. Brain tumors are among the deadliest forms of cancer due to their dangerous nature, heterogeneity, and poor prognosis [2]. They can vary significantly in shape, texture, and location, each type having its own characteristics [3]. Clinical data indicate that 45% of all brain tumors are gliomas, 15% are meningiomas, and 16% are pituitary tumors [4]. A brain tumor is an abnormal development of cells in or around the brain or skull, which can significantly impact a person's quality of life [5]. Brain tumors occur when brain tissue grows uncontrollably [6], leading to increased intracranial pressure and disruption of normal brain function. Benign tumors do not spread cancer, while malignant tumors do. Malignant tumors can proliferate, damaging healthy tissues and potentially spreading to other parts of the body [7]. Brain tumors are classified into two main types: primary and secondary. High-grade tumors grow more quickly, whereas low-grade tumors grow more slowly but can eventually transform into high-grade tumors [8]. Secondary tumors, also known as brain metastases or metastatic cancer, originate from cancers in other body parts, such as the breast, colon, or lungs, and spread to the brain [9, 10].

The brain is a crucial organ that requires protection from damage and disorders [11]. A patient's prognosis and treatment options can be determined based on the type of tumor. Doctors may choose from various approaches, including a "watch and wait" strategy that avoids invasive procedures [12]. Tumor grading is critical in medication and ongoing management [13]. However, radiologists often spend a significant amount of time analyzing images of brain tumors [14]. The ability of modern radiologists to detect and interpret these images depends on their expertise and subjective judgment [15]. Magnetic resonance imaging (MRI) is frequently used in neurology because it allows for a comprehensive evaluation of the brain and skull [16]. MRI's capabilities for axial, coronal, and sagittal imaging provide enhanced assessment [17]. One of the advantages of MRI is that it does not involve radiation

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and produces high-resolution images with excellent contrast [18]. This noninvasive imaging technology can detect many types of brain cancer [19]. MRI is a transparent, painless medical imaging technique that provides 2D and 3D views of human organs. However, detecting cancer cells from MRI images is a time-consuming, error-prone, and specialized assignment that heavily depends on the radiologist's knowledge.

An image may not have enough noticeable features to accurately judge the tumor's shape. Consequently, it can be challenging for humans to make precise diagnoses. An additional concern is that an incorrect diagnosis of a brain tumor type could jeopardize a patient's survival. In contrast, an accurate diagnosis allows for prompt initiation of treatment, significantly extending the patient's life expectancy. Artificial intelligence (AI) subfields, such as deep learning (DL) and machine learning (ML), have revolutionized neuropathology. These techniques involve several phases: data preprocessing, feature extraction, feature selection, feature elimination, and classification. This chapter proposes an adaptive convolution neural network brain tumor detection (ACNN-BTD) framework. The following are the framework's main contributions:

- ACNN-BTD uses a bilateral filter to reduce noise and shrink the image, which is the first step in the preprocessing stage.
- When applied to the training dataset, data segmentation involves normalizing the obtained data and performing operations such as translation, rotation, and scaling.
- ACNN is used to identify the visual features. All input photos are fed through a network of fully connected artificial convolutional neural networks (ACNNs), with the training and testing images sourced from the Kaggle dataset.
- According to the results of the experiments, ACNN-BTD outperforms all other approaches in accuracy.

Section 12.2 describes the rest of the manuscript, including the related study; Section 12.3 elaborates on the complete process of ACNN-BTD; Section 12.4 is based on the results and discussion; and Section 12.5 concludes the methodology.

12.2 RELATED STUDY

Various studies have been conducted to classify tumor cells from normal brain tissues using MRI scans. Research in this area has primarily focused on developing secure and effective strategies for tumor cell classification. The literature often emphasizes preprocessing techniques and the classification of normal versus abnormal brain cells. Mahesh T R et al. [20] developed gradient-weighted class activation mapping (Grad-CAM) imaging to highlight critical regions in the MRI images affecting the categorization results. The EfficientNetB0 architecture, in conjunction with explainable AI, approaches to make this study more accurate and easier to understand. The accuracy of brain tumor classification is improved to 98.72%, providing precise visual information into the decision-making mechanism.

Muneeb A. Khan et al. [21] introduced a convolutional-block-based architecture for multiclass brain tumor diagnosis utilizing MRI data. By capitalizing on convolutional neural networks (CNNs), our suggested system efficiently and robustly differentiates between various types of tumors. The accuracy is about 97.52%, highlighted by extensive assessments of three varied datasets. Javeria Amin et al. [22] suggested an unsupervised clustering method for tumor segmentation. In addition, a fused feature vector, a combination of features from section-based fractal texture analysis (SFTA), is employed. The proposal's apparent superiority is shown by its encouraging detection efficiency.

Palani Thanaraj Krishnan et al. [23] developed a rotation invariant vision transformer (RViT) DL model for brain tumor categorization using MRI scans. RViT improves the precision of brain tumor detection by including rotating patch integration. The Matthews Correlation Coefficient (MCC) was 0.972, demonstrating RViT's exceptional performance. Pendela Kanchanamala et al. [24] introduced a practical detection approach called exponential deer hunting optimization-based Shepard convolutional neural network (ExpDHO-based ShCNN) to identify brain tumors. The classification accuracy is about 0.91. Mohammad Zafer Khaliki et al. [25] developed CNN-based EfficientNetB4, VGG19, and transfer learning techniques to identify several brain malignancies, including gliomas, meningiomas, and pituitary tumors. The prototypes were assessed using F-score, recall, imprinting, and Accuracy. The most impressive accuracy result was achieved by VGG16, which stood at 97%. The same transfer learning model also achieved 97% F-score, 97% area under the curve (AUC), 98% recall, and 98% precision. To quickly diagnose and cure these diseases, CNN architecture and transfer learning models based on CNNs are crucial to human health. From the preceding literature survey discussion, the accuracy of tumor classification varies according to different methods. The ACNN-BTD method is compared in the preprocessing and classification stages.

12.3 ADAPTIVE CONVOLUTION NEURAL NETWORK–BASED BRAIN TUMOR DETECTION (ACNN-BTD) FRAMEWORK

An ACNN-BTD framework distinguishes between tumor cells and normal brain tissues in MRI scans. The first step is preprocessing, which involves resizing the image and removing noise using a bilateral filter. It undergoes normalization before applying the segmented data to the training dataset, which entails translation, rotation, and scaling. Using the Kaggle dataset for training and testing, the input photos are processed using a network of kernels, a pooling layer, and a fully connected ACNN. The performance evaluation in accuracy, sensitivity, and specificity is obtained by the classification process and the preprocessing stage, as shown in Figure 12.1.

12.3.1 Preprocessing

The images are collected from the dataset; the initial stage of the framework is noise reduction. A bilateral filter is an image-normalizing filter that is unpredictable, preserves edges, and reduces noise. It takes a mean of the intensities of surrounding pixels and uses that as a replacement for each pixel's strength. A Gaussian range can

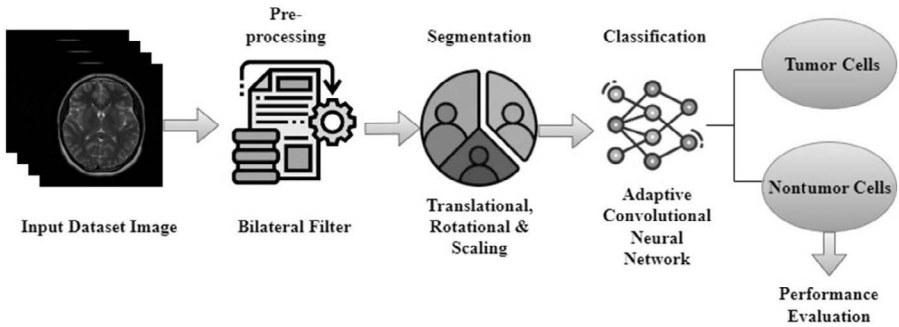

FIGURE 12.1 Architecture of adaptive convolution neural network–based brain tumor detection framework.

be used to determine this weight. The weights depend on the physical discrepancies and the average length between pixels. The filtering of noise is obtained from Equation (12.1).

$$J^{(f)}(a) = \frac{1}{v_q} \sum_{a_x \in \phi} J(a_x) g_k(|J(a_x) - J(a)|\, h_l(a_x - a) \tag{12.1}$$

Here, $J^{(f)}(a)$ represent the noise-removed image, J denotes the actual image that needs to be denoised, and a represents the matching ratio of the pixel to be filtered. v_q represents the average length between pixels ϕ and denotes the weight of each pixel. a_x represents the Gaussian range to preserve edges. h_l denotes the intensity values of the pixel. The standardization of the equation is shown in Equation (12.2):

$$wh_x = \sum_{a_x \in \phi} g_k(J(a_x - J(a) h_l(a_x - a) \tag{12.2}$$

J denotes the actual image that needs to be denoised; a represents the matching ratio of the pixel to be filtered. v_q represents the average length between pixels ϕ and denotes the weight of each pixel. a_x represents the Gaussian range to preserve edges. h_l denotes the intensity values of the pixel. The stages in preprocessing are shown in Figure 12.2. The bilateral filter obtains the normalization of the image. The filtering process is concentrated on the intensities of surrounding pixels. The Gaussian range is fixed around the surrounding pixel values, and the filtered image is obtained.

12.3.2 Segmentation

There are a lot of approaches that work well for segmenting MRI pictures, but picking just one or two is not enough for every image. Because of its adaptability and

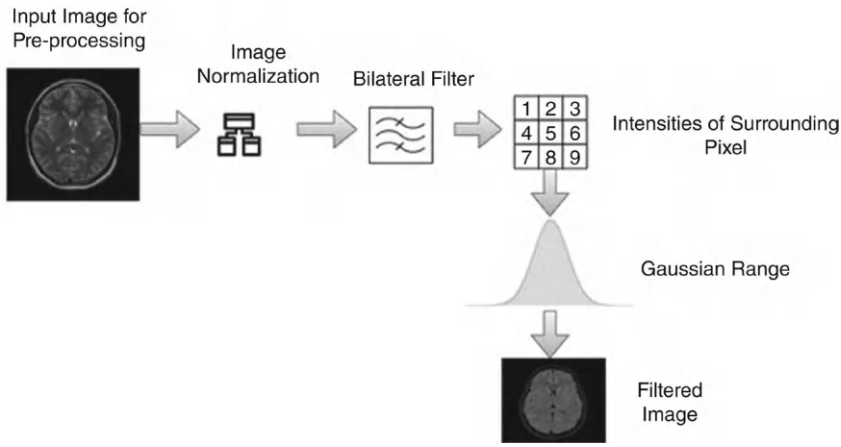

FIGURE 12.2 The stages in preprocessing.

ability to handle the high complexity of MRI images, the suggested framework uses the adaptive thresholding method, as shown in Equation (12.3):

$$h(a,b) = \begin{cases} 1, \; if \; (a,b) > A \\ 0, \; if \; (a,b) \geq A \end{cases} \tag{12.3}$$

The selection of intensity values is based on the threshold value A; the MRI image with the pixel values is represented as (a,b). Depending on condition 1 0, the histogram and a variation of intensity values can be used to choose a threshold value (A). Over the whole picture $h(a,b)$, the threshold value shouldn't change. This step's output identified the precise locations of the tumor areas. The range of threshold values 0,1 obtains the location of tumor cells. The accurate location of tumor cells is shown in Figure 12.3.

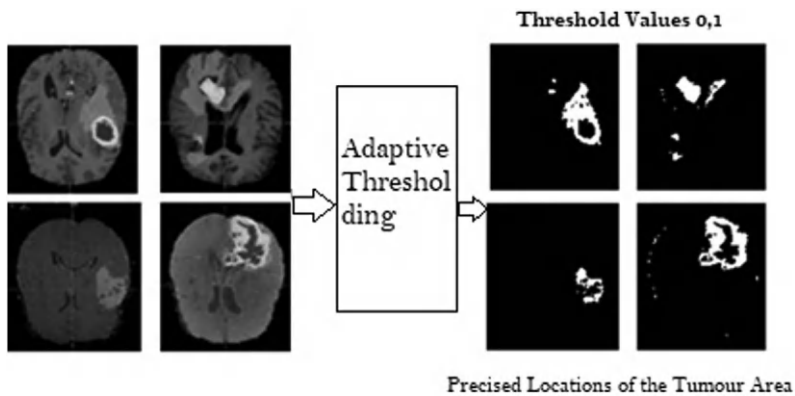

FIGURE 12.3 The precise location of tumor cells.

12.3.3 Feature Extraction

Dimensional reduction analysis is used to extract features from the segmented image. Dimensional reduction analysis is a powerful mathematical tool for decorrelating massive datasets, including linked variables. It is an x-dimensional linear transformation applied to an array (x) of picture rows and columns. The feature extraction is obtained by regulating the image with the number of rows and columns. Note A_x from Equation (12.4):

$$A_x = [R_1, R_2, \ldots..R_m] \tag{12.4}$$

The rows of the pixel matrix are represented as R, and the column representation is denoted as m. The covariance of the pixel matrix S_n is obtained from Equation (12.5):

$$S_n = \frac{1}{L}\sum_{N=1}^{L} A_x \tag{12.5}$$

L represents the number of rows and columns, N represents the features in the image, x represents the covariance of the pixel matrix. The features from the segmented image are obtained from the covariance of the pixel matrix. S_n. The next stage of the process is classifying tumor and nontumor cells.

12.3.4 Classification by Adaptive Convolution Neural Network

ACNN includes mathematical operation and three main components in a neural network: input layer, hidden layer, and output layer. The hidden layer performs traditional techniques like pattern recognition. A neural network is parallel computing and performs computational tasks, including pattern recognition, classification, optimization, approximation, and data clustering. Any deep neural network model needs a lot of data to train and test the model and a lot of computing resources. When comparing regular neural networks, ACNN is the best for understanding the classification of an image. ACNN extracts the features and identifies patterns of the image dataset. The process inside the ACNN model is executed by the input image ($32 \times 32 \times 3$) with the conv2D with the number of filters and rectified Linear Unit Relu(). To generate a down-sampled (pooled) features chart, the max pooling procedure determines the highest result for feature-mapped areas. Dropout is used to avoid overfitting the pixel. The complete stages are shown in Figure 12.4.

ACNNs use max pooling as an operation. The initial volume's geometrical dimensions (width and height) are reduced using a down-sampling method. This lowers the processing effort and the amount of factors, which helps minimize overfitting. The max pooling method splits the input into rectangle subregions that do not intersect and then returns the most significant amount for each subregion.

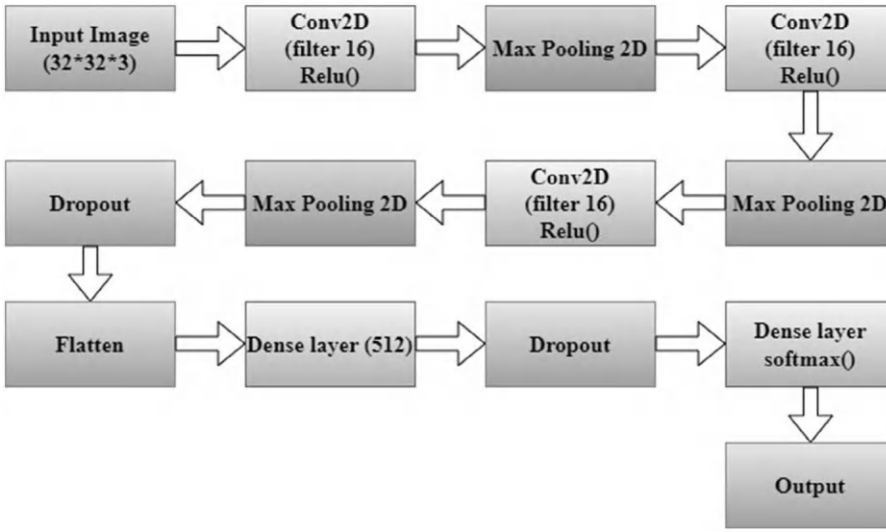

FIGURE 12.4 Stages of adaptive convolution neural network.

The duration and filter capacity are the primary variables of max pooling. The stride controls the amount the filter travels along the input, while the filter size defines the measurements of the zone from which the highest number is extracted. The maximum pooling operation (2 × 2) is shown in Figure 12.5.

To enhance the attention mechanism, max pooling can streamline: that is, it simplifies the system's concentration on key characteristics by simplifying inputs for the attention levels. The attention system can improve the extraction of attributes by giving larger weights to significant elements via max pooling. The function of ACNN is shown in Figure 12.6. ACNN achieves the classification of tumor and nontumor cells.

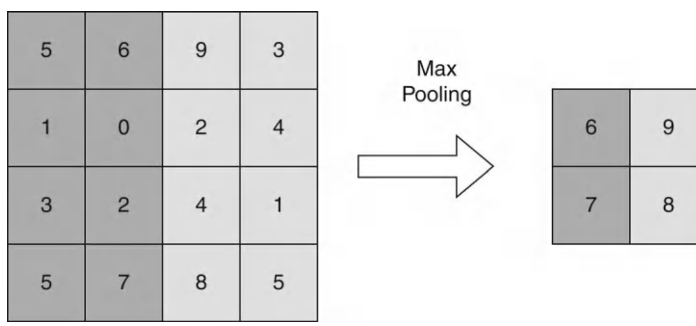

FIGURE 12.5 The maximum pooling operation (2 × 2).

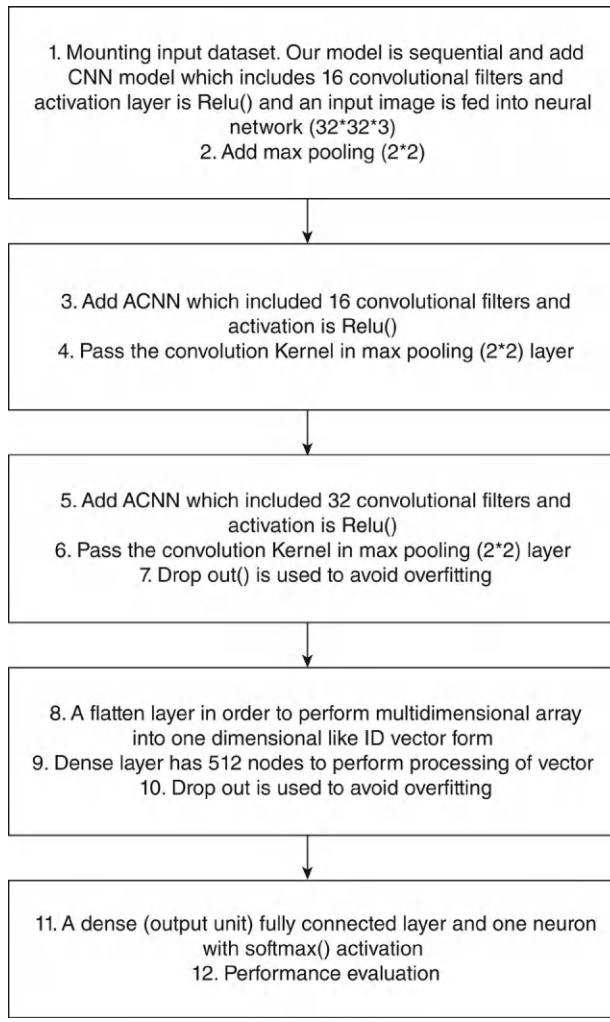

FIGURE 12.6 Function flow of our proposed CNN model.

12.4 RESULT AND DISCUSSION

The experimental evaluation was done using Google Colab and Python. The dataset collection is from, including benchtop magnetic resonance imaging (BT MRI) and non−BT MRI images, and the dataset is mounted onto Google Drive. Our BT MRI image dataset contains two folders, YES and NO, containing 253 MRI images of the brain. The YES folder contains 155 tumorous MRI images. The NO folder contains 98 nontumorous MRI images. The data augmentation technique operates on rotation, scaling, translation, and cropping and is applied to the MRI image (Brain) to increase the high quality of (MRI) brain images. The normalization technique is used for image standardization, and the pixel scaling factor is 0-1.

TABLE 12.1
The Accuracy between Sigmoid and Softmax Function

Optimization	Activation Function	Splitting Ratio	Accuracy
RMSprop	Sigmoid	9:1	95.59%
RMSprop	Softmax	9:1	99.82%

Data splitting is in the ratio of 9:1, i.e., 90% for the training set and 10% for the testing set. The model is trained for ten epochs. Table 12.1 shows the accuracy between the sigmoid () and Softmax () activation functions using the root mean square (RMS) prop optimizer. The plots shown in Figure 12.7–12.10 show the loss and accuracy of the training and validation (testing) model. In our ACNN model, automatic brain tumor (BT) detection is performed very efficiently, achieving an accuracy of 99.82%. Table 12.1 shows the accuracy between the sigmoid () and Softmax() activation functions used in the fully connected layer, and model optimization was done using RMSprop. The complete process for detecting and classifying tumor and nontumor cells is achieved by utilizing accuracy and activation functions. The activation function with the convolutional filters and kernel helps achieve the highest classification accuracy with the splitting ratio.

Training is about running the dataset through the process for a predetermined number of epochs. The accuracy metrics are monitored to evaluate the model's generalizability to new data. The Training Accuracy metric shows how accurately the algorithm matches the data used for training. When a model achieves a high training accuracy, it has successfully mastered the trends found in the training data. The Validation Accuracy metric shows how well the model can apply its findings to other

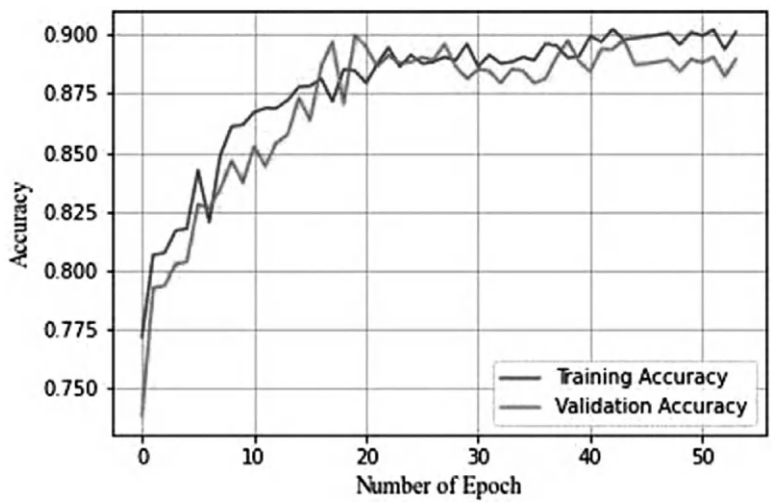

FIGURE 12.7 Accuracy by using the sigmoid activation function.

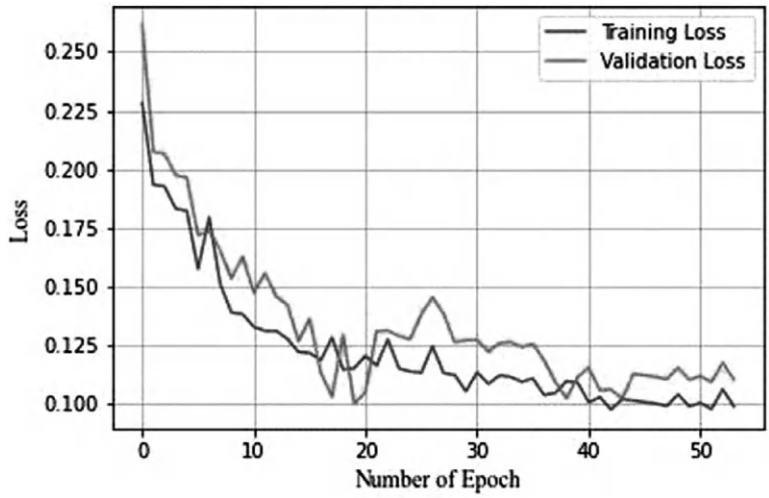

FIGURE 12.8 The loss by using the sigmoid activation function.

datasets. Overfitting can occur if this parameter is not closely monitored. Figure 12.7 shows the accuracy using the sigmoid activation function.

One way to evaluate a system's efficacy on training data is by looking at its training loss. The sigmoid activation mechanism produces a probabilistic result; this result can then be evaluated to the actual values utilizing a loss function, like binary cross-entropy. Figure 12.8 shows the loss using the sigmoid activation function.

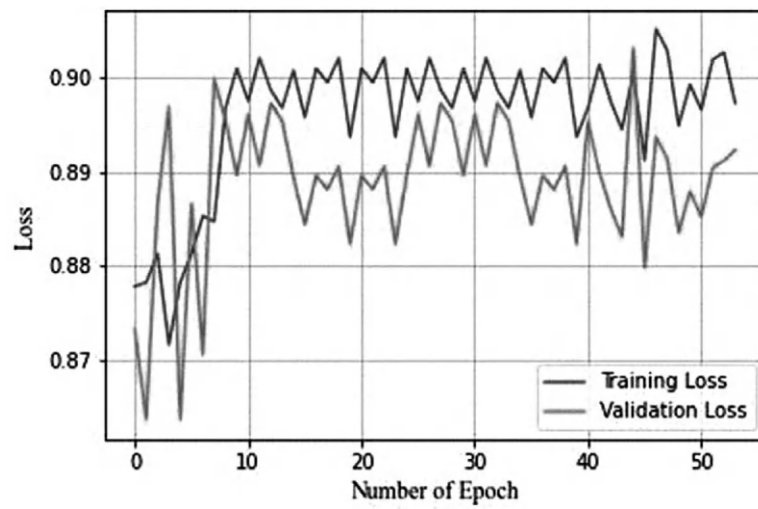

FIGURE 12.9 Accuracy by using the softmax activation function.

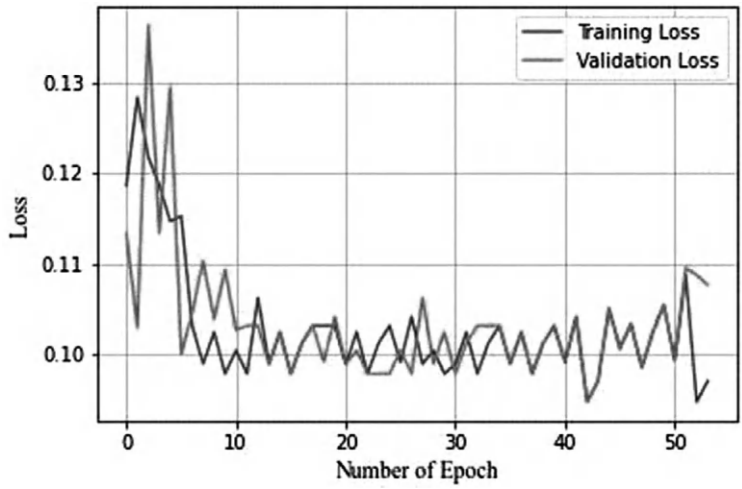

FIGURE 12.10 Training loss by using the softmax activation function.

The softmax activation function finds extensive application in the network's output layer by training neural networks for multiclass sorting. Transferring a class name according to the highest likelihood is easier by converting the raw prediction values into changes that add up to one. Figure 12.9 shows accuracy by using the softmax activation function.

For jobs involving several classes to be classified, using the softmax activation function in neural networks is crucial. This function gives a probability distribution over the classifications. In conjunction with softmax activation, the categorical cross-entropy loss function allows the network to learn by reducing the discrepancy between the actual and expected label patterns. Figure.12.10. shows the loss by the softmax activation function.

Table 12.2 shows the accuracy performance comparison with the existing method: CNN [21], RViT [23], ExpDHO-based ShCNN [24], and CNN-based EfficientNetB4 [25].

TABLE 12.2
Comparison of Accuracy of Existing Methods

Existing Method	Accuracy
RViT	96.6%
ExpDHO-based ShCNN	91%
CNN-based EfficientNetB4	97%
CNN	97.52%
Grad-CAM	98.72%
Proposed ACNN-BTD	99.82%

12.5 CONCLUSION

Identifying brain tumors is the most challenging task for healthcare professionals and doctors. Hospital medical professionals require images of the tumors' appearance and location to diagnose and treat brain tumors. Automatic brain tumor segmentation is a popular method for extracting this data from MRI scans. To resolve MRI scans of the brain and identify tumor cells, this research presents an architecture called ACNN-BTD. Using a bilateral filter to reduce noise and shrink the image is the first step in the preprocessing stage. When applied to the training dataset, data segmentation involves normalizing the obtained data and performing operations such as translation, rotation, and scaling. ACNN is used to identify the visual features. All input photos are fed through a network of fully connected ACNNs, with the training and testing images sourced from the Kaggle dataset. According to the results of the experiments, ACNN-BTD outperforms all other approaches in accuracy.

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13 STN-DRN: Integrating Spatial Transformer Network with Deep Residual Network for Multiclass Classification of Alzheimer's Disease

Prabu Selvam, S. Sudharson, and P. N. Senthil Prakash

13.1 INTRODUCTION

The hallmark of Alzheimer's disease (AD) is the progressive loss of healthy brain cells, which results in a persistent deterioration of memory, cognitive abilities, and intellectual aptitude. It is the primary cause of dementia, a condition that profoundly impairs a person's social and mental skills, disrupts everyday life, and gets worse with time [1]. The loss of nerve cells, the accumulation of neurofibrillary tangles and amyloid plaques and general brain tissue atrophy are the causes of this decrease, which worsens as the illness progresses [1, 2]. In 2021, the World Health Organization estimated that 55 million people worldwide had dementia. According to projections, this number will increase to 78 million by 2030 and a startling 139 million by 2050, meaning more than a twofold increase from 2021 [3]. The likelihood of dementia is much increased in people over 65. Conversely, early-onset dementia, which can result from several underlying illnesses, affects only around 3% of younger individuals [4]. With sophisticated imaging techniques, amyloid beta deposits – a protein closely associated with AD – can now be detected even without overt symptoms [5]. Discovering these early deposits might benefit clinical research and future uses, mainly if AD treatments are created. Imaging tools for AD detection are standard since they offer a noninvasive way of viewing the body's internal organs. Many depend on these medical imaging technologies for diagnosing and treating AD [6]. To identify anomalies in the brain associated with the condition, a variety of neuroimaging methods are necessary, such as magnetic resonance imaging (MRI), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and computed tomography (CT) – a cutting-edge machine learning (ML) method for AD detection that blends quantum and classical methods [7].

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A hybrid classical-quantum transfer learning method was employed to utilize a dataset of 6,400 labeled MRI scans categorized into two classes. This methodology enables effective preprocessing of intricate and high-dimensional data. In [8], initially a custom convolutional neural network (CNN) conducts binary classification of the subject's scan. Then, various deep learning (DL) models, in conjunction with custom CNN, are employed to perform multiclass classification of a subject's scan, assigning it to one of six stages of AD.

Understanding and classifying AD has become increasingly vital in recent years as more accurate diagnostic tools and targeted therapeutic interventions are urgently needed. One major component of this endeavor is classifying AD subtypes, which has thus far proven difficult due to the multifactorial ethology of the disease, as well as the heterogeneous nature of its clinical presentations.

13.2 RELATED WORKS

Numerous DL algorithms are available for the early diagnosis classifications of brain images and to identify the evolution of AD. Suganthe et al. [9] developed a hybrid deep convolutional neural network by combining Inception and ResNet V2 architectures and achieved an accuracy of 79.12% on the Kaggle Alzheimer's dataset. Ban et al. [10] proposed a hypergraph-Laplacian regularized multitask feature learning algorithm for AD detection and classification using multimodal neuroimaging data. This method was divided into four submodules: data preprocessing, multimodal feature selection, hypergraph construction, and classification. The major drawback of this method is that it uses only imaging data. In contrast, demographic, neuropsychological, and genetic data are not used from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, and this study only examines binary classification. In contrast, multivariate classification may be more clinically relevant.

Janghel et al. [11] employed a CNN architecture, specifically the VGG-16 model, for predictive diagnosis of AD. Initially, it performs a preprocessing operation on the input images by converting 3D to 2D, then conducts a segmentation task. The performance of the VGG-16 is compared with classifiers like support vector machine (SVM), K-nearest neighbors, and linear discriminant. Shanmugam et al. [7] used transfer learning with pretrained DL algorithms to classify disparate levels of AD based on MRI images. The deeper network structure of ResNet-18 contributed to improved precision in detecting the early stages of AD and cognitive impairment. Among the three pretrained networks (GoogLeNet, ResNet-18, and AlexNet), AlexNet relatively performed the best using transfer learning.

Tanveer et al. [12] proposed a computationally efficient DL ensemble model called Deep Transfer Ensemble (DTE) that achieves high accuracy on AD classification tasks on both large and small datasets. The key methodological aspects of the study are that DTE is an ensemble model; leveraged diversity is introduced by randomizing hyperparameters to reach different local optima; there are combined advantages of a random search for hyperparameter tuning and snapshot ensembles; transfer learning is used to reduce the computational complexity of training the ensemble model; and the ensemble combines predictions from multiple local optima as well as complementary feature views such as cerebrospinal fluid, white matter, and gray

matter. The main disadvantages of this method are the lack of an ideal method for choosing the DL mechanisms to include in the ensemble and the lack of a process to assign adequate weights to each standalone algorithm.

Sorour et al. [13] implemented a CNN-long short-term memory (LSTM)-with-augmentation algorithm for early AD detection using MRI images. This study included data preprocessing (resizing, labeling, normalization, and color modification of MRI images) and the development of five distinct DL algorithms for AD detection, partitioned into two divisions: DL models without data augmentation and DL models with data augmentation. The goal was to find the DL algorithm that best balances testing time and detection accuracy. Liu et al. [14] proposed a multimodel DL framework that outperforms single-model methods for both disease classification and hippocampal segmentation. A 3D DenseNet network that identifies characteristic representations from 3D patches derived from the hippocampal segmentation outcomes for disease diagnosis. The identified characteristic representations from these two models are combined to make the final disease classification. Limitations in medical interpretation and characterization of the learned features fail to offer sufficient clinical information on brain abnormalities.

Hussain et al. [15] proposed a 12-layer CNN model for AD detection, outperforming several pretrained CNN models. This CNN model achieved better precision, recall, F1-score, and receiver operating characteristic (ROC) scores than the pretrained models such as VGG-19, Inceptionv3, Xception, and MobileNetv2. You et al. [16] proposed a two-step cascade neural network utilizing electroencephalogram (EEG) and gait data to classify better AD, mild cognitive impairment, and healthy controls faster and more accurately. The study used a two-step cascade neural network approach: use of the attention-based spatial temporal graph convolutional networks (AST-GCNs) on gait data (skeleton sequences from Kinect) to distinguish healthy controls from patients (mild cognitive impairment [MCI] and AD) and employed spatial-temporal convolutional neural networks (ST-CNNs) on EEG data to further classify patients into MCI or AD. The key points were selected from the gait data to construct the input scaffolding sequences for the AST-GCN. The ST-CNN was used to extract temporal and spatial features directly from the input data without converting it to the frequency domain.

Ebrahimi et al. [17] introduced a temporal convolutional network (TCN) to improve AD detection from MRI scans. This study used a ResNet-18 as the base model. It compared deep sequence-based algorithms, including TCNs and recurrent neural networks (RNNs) types like GRU, BiLSTM, and LSTM. It considered four main input data management methods: ROI-based, voxel-based, patch-based, and slice-based. This study used 2D CNNs for slice-based approaches and 3D CNNs for voxel-based approaches. It combined 2D CNNs with sequence-based models (RNNs and TCNs) to identify AD from MRI scans. The limitations of this study include loss of data and brain region features when using 2D CNNs on 3D MRI scans, overfitting risk due to the complex structure and many training parameters of 3D CNNs, and inability of 2D CNN + RNN/TCN approaches to perform feature extraction and classification simultaneously.

Nanthini et al. [18] designed a multitask learning framework founded on deep belief neural networks (DBNNs) to diagnose AD at different stages, using techniques

like dropout and zero-masking to improve the model's stability and generalization and incorporating clinical assessment scales to enhance classification accuracy. It employs a two-stage feature selection process involving differentially expressed genes/positions and an ensemble of feature selection methods to address the high-dimensional and low-sample-size problem. The DBNN model outperforms well-trained base classifiers regarding accuracy, sensitivity, and area under the curve (AUC) for mild cognitive impairment and AD classification. Zhang et al. [19] introduced an improved model called ADNet, which builds on the VGG16 algorithm and is designed for AD classification from MRI data, with numerous significant enhancements, including two auxiliary tasks, the SE module, the exponential linear unit (ELU) activation function, and depthwise separable convolution.

Hazarika et al. [20] developed a novel deep neural network (DNN)-based feature extraction method by employing VGG-19 as a backbone network, incorporating dense-blocks to minimize gradient and information loss. The DNN model based on VGG-19, with modifications like dense-block, inception-block, and min-max pooling, is used to extract maximum features. The principal component analysis mechanism was used as a feature selector to extract the more relevant features. The random forest algorithm was used at the end to identify early-stage AD and other dementia stages. The limitations of this study include the use of min-max concatenated pooling layers, which adds complexity to the model. Different convolution kernels may help generate more proficient parameters. El-Assy et al. [21] proposed a new CNN-based method for early diagnosis and classification of AD using MRI images, which achieves excellent accuracy rates for three-way, four-way, and five-way classification tasks and has augmented capability for early AD diagnosis and improved patient outcomes. This model does not assimilate clinical data and only assists physicians in decision-making without supplanting their judgment.

From the literature review, the research problems identified are that existing methods use only imaging data and baseline data, missing out on valuable demographic, neuropsychological, genetic, and longitudinal data. Limited exploration of model architectures, hyperparameters, and single-instance cross-validation reduces robustness and causes overfitting. Due to data variability, existing methods often use a single data modality, impacting classification performance. Multiview methods and complex CNN structures introduce risks of data loss, ambiguity, and overfitting.

13.3 PROPOSED SYSTEM

13.3.1 Deep Residual Neural Network

Figure 13.1 depicts the overall architecture of the proposed system. The residual neural network (ResNet) is a DL model introduced by He et al. [22] in 2015. The concept of residual blocks, as shown in Figure 13.2, is developed to tackle the challenge of vanishing or exploding gradients. This network employs a technique called skip connections. These skip connections bypass specific layers to directly connect layer activations to subsequent layers, forming residual blocks. These residual blocks are then stacked to build ResNets. This model's underlying scheme enables the model to learn the residual mapping rather than having each layer independently.

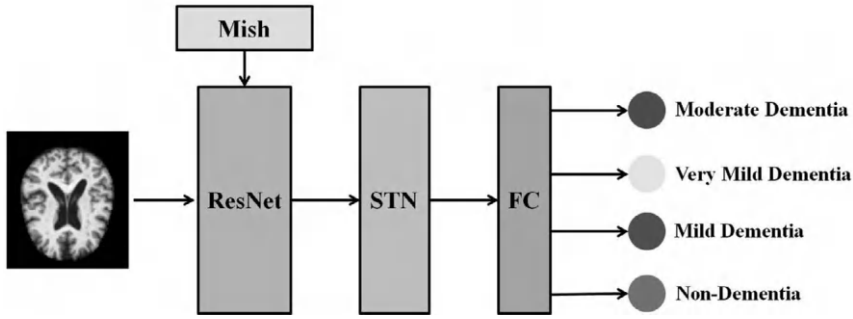

FIGURE 13.1 Pipeline architecture of the proposed STN-DRN model.

In Figure 13.2, the input x is first weighted by the initial layer, followed by applying a nonlinear transformation via the ReLU function and the subsequent weighting by the second layer, resulting in $h(x) = f(x) + x$. This linear combination forms a residual learning module, and a network built from these modules is known as a ResNet. Unlike conventional networks, ResNet introduces "skip connections" that facilitate the unobstructed flow of information from one residual block to the next. This design effectively mitigates issues such as vanishing gradients and network degradation associated with overly deep architectures.

The ReLU activation function frequently results in the permanent inactivation of neurons, causing these neurons to remain occupied. This issue hampers the effective utilization of computational resources, limiting the model's capacity to extract image features efficiently. To address the shortcomings of ReLU, the Mish activation function was chosen as a replacement within the model. The formula for the Mish activation function is shown in Equation (13.1).

$$f(x) = x \tanh\left(\ln\left(1 + e^{x}\right)\right) \tag{13.1}$$

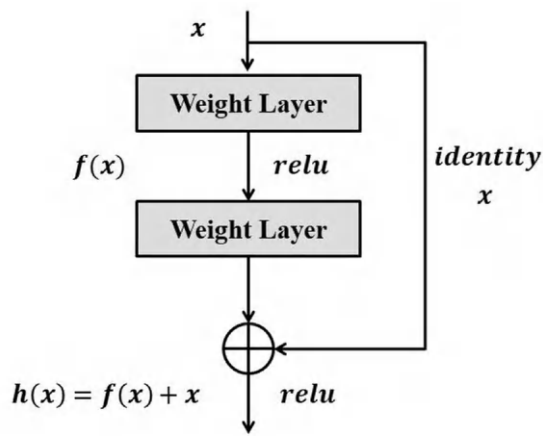

FIGURE 13.2 Workflow of skip connection.

TABLE 13.1
The ResNet-101 Configuration

Network Layer	Configuration	Output Feature Map Dimension
conv1	*Kernal: 7 × 7, channel: 64, stride 2* *Kernal: 3 × 3 max pool, stride 2*	*112 × 112*
Conv. Layer 2_x	$\begin{bmatrix} channel: 64 & kernel: 1\times1 \\ channel: 64 & kernel: 3\times3 \\ channel: 256 & kernel: 1\times1 \end{bmatrix} \times 3$	*56 × 56*
Conv. Layer 3_x	$\begin{bmatrix} channel: 128 & kernel: 1\times1 \\ channel: 128 & kernel: 3\times3 \\ channel: 512 & kernel: 1\times1 \end{bmatrix} \times 4$	*28 × 28*
Conv. Layer 4_x	$\begin{bmatrix} channel: 256 & kernel: 1\times1 \\ channel: 256 & kernel: 3\times3 \\ channel: 1024 & kernel: 1\times1 \end{bmatrix} \times 23$	*14 × 14*
Conv. Layer 5_x	$\begin{bmatrix} channel: 512 & kernel: 1\times1 \\ channel: 512 & kernel: 3\times3 \\ channel: 2048 & kernel: 1\times1 \end{bmatrix} \times 3$	*7 × 7*

The Mish activation function possesses a noteworthy attribute wherein its positive value can ascend without encountering saturation from capping limitations. The smoothness inherent in the Mish activation curve facilitates enhanced information assimilation within the neural network, consequently leading to improved accuracy and generalization [23–25]. Moreover, as the network's depth escalates, Mish demonstrates superior capability in preserving accuracy.

The network configuration of ResNet-101 is depicted in Table 13.1. Figure 13.3 illustrates the bottleneck residual modules at various layers within the ResNet-101 network with the Mish activation function. In the deep ResNet-101 architecture, the bottleneck residual module comprises two 1×1 convolution and a 3×3 convolution layer. The first and last 1×1 convolutions reduce and restore the dimensionality, respectively. This structure of the bottleneck residual module significantly enhances computational efficiency and allows for a greater depth in the residual block. Adding Mish activation functions between the layers further enhances ResNet's representational capacity.

13.3.2 Spatial Transformer Networks (STNs)

The STN can dynamically execute spatial transformations. When significant spatial variations are present in the input data, incorporating this network into an existing convolutional network can enhance classification accuracy. The STN algorithm comprises three components: a localization network, grid generator, and sampler, as

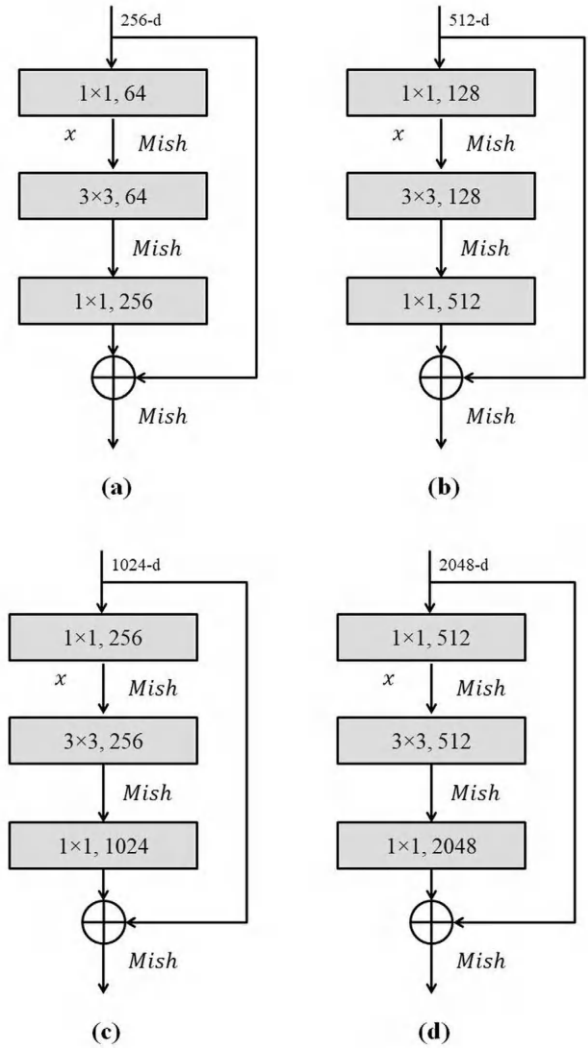

FIGURE 13.3 Pipeline of bottleneck residual blocks of various layers for the ResNet-101 network: (a) Conv. Layer 2_x; (b) Conv. Layer 3_x; (c) Conv. Layer 4_x; and (d) Conv. Layer 5_x.

illustrated in Figure 13.4. Initially, the localization network processes the extracted features. Then, it produces the parameters for the spatial transformation operation using multiple hidden layers that will be operated on the feature space, thereby creating a normalization dependent on the input. Next, the computed conversion variables are utilized to generate a sampling pattern of points where the grid generator subsampled the feature map to generate the transformed outcome [26–28]. Finally, the feature map and the sampling grid are fed into the sampler, which produces the resultant map by sampling the lattice points.

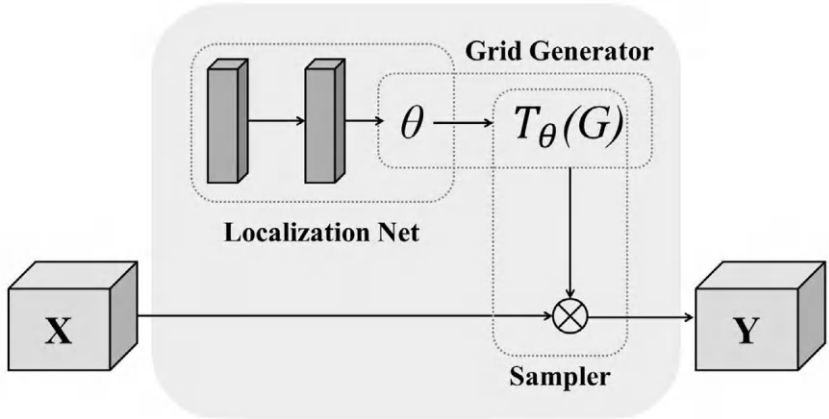

FIGURE 13.4 Working mechanism of the spatial transformer network.

The localization module processes the input feature map $X \in \mathbb{R}^{W \times H \times C}$, where (W) represents the width, (H) represents the height, and (C) denotes the number of channels. This network outputs (θ), and the attributes for the transformation $\left(T_\theta\right)$ are utilized in conjunction with the feature map: $\theta = fun_{LN}(X)$. The function $fun_{LN}()$ within the localization network can be a convolutional network or a fully connected network. However, it must incorporate a regression layer at the end to generate the conversion variables.

In the grid generator module, the individual resultant pixel is calculated by employing a sampling filter centered at a specific position within the input feature map to achieve warping of the input feature map, as given in Equation (13.2).

$$\begin{pmatrix} x_j^s \\ y_j^s \end{pmatrix} = T_\theta\left(G_j\right) = M_\theta \begin{pmatrix} x_j^t \\ y_j^t \\ 1 \end{pmatrix} = \begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} \\ \theta_{21} & \theta_{22} & \theta_{23} \end{bmatrix} \begin{pmatrix} x_j^t \\ y_j^t \\ 1 \end{pmatrix} \tag{13.2}$$

where $\left(x_j^s, y_j^s\right)$ denotes the initial coordinates within the input representation that specify the sample points, while $\left(x_j^t, y_j^t\right)$ represent the target coordinates. Additionally, M_θ refers to the affine transformation matrix (see Equation 13.3).

$$M_\theta = \begin{bmatrix} s & 0 & t_x \\ 0 & s & t_y \end{bmatrix} \tag{13.3}$$

The class of transformations can be more restrictive, similar to the transformations utilized in attention [29]. These allow for translation, cropping, and uniform scaling by adjusting the parameters t_x, t_y, and s.

A sampler module uses input feature map X with a set of sampling points $T_\theta\left(G_j\right)$ to generate the sampled output feature map Y and to carry out a positional

normalization on the input. This sampling algorithm can be executed highly effectively on a graphics processing unit (GPU) by focusing solely on the kernel support region for each output pixel rather than summing over all input locations.

13.4 EXPERIMENT

13.4.1 Dataset Details

The competence of the proposed model is validated using the Open Access Series of Imaging Studies (OASIS) dataset (https://www.oasis-brains.org/#data). The dataset used for this experiment consisted of 382 images sourced from the OASIS database, and these images were categorized into four classes: Non-Dementia, Very Mild Dementia, Mild Dementia, and Moderate Dementia. Figures 13.5 and 13.6 show the OASIS benchmark dataset statistics and sample images, respectively.

The OASIS dataset consists of 382 images in total. Among these, 167 images are categorized under the "No Dementia" class, indicating individuals without any signs of dementia. The "Very Mild Dementia" class includes 87 images representing individuals in the early stages of dementia. The "Mild Dementia" class contains 105 images, signifying individuals at a slightly more advanced stage of dementia. Lastly, the "Moderate AD" class comprises 23 images depicting individuals with moderate AD. Various data augmentation techniques were employed to enhance the dataset size, such as rotation, mosaic, flipping, cropping, and the introduction of noise. Figure 13.7 illustrates the number of samples after performing augmentation techniques. These augmentation methods were crucial in mitigating the scarcity of training data during the development of the AD detection model.

13.4.2 Implementation Details

The proposed STN-DRN model was developed utilizing the PyTorch framework. Experiments were conducted on an HP Windows 10 system with an i3 processor and

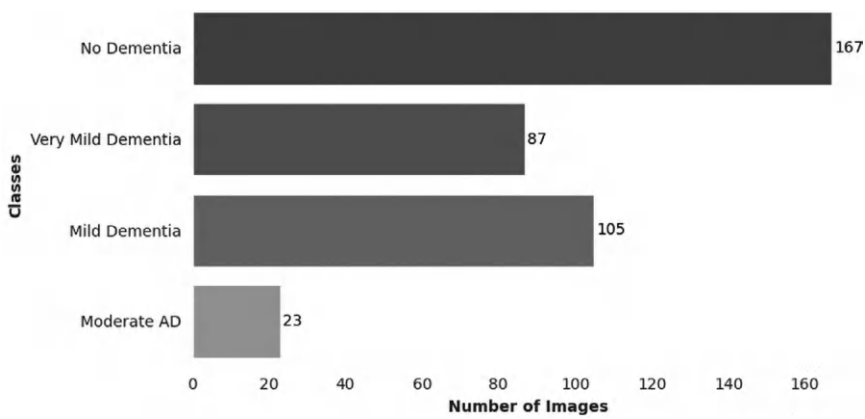

FIGURE 13.5 OASIS dataset details.

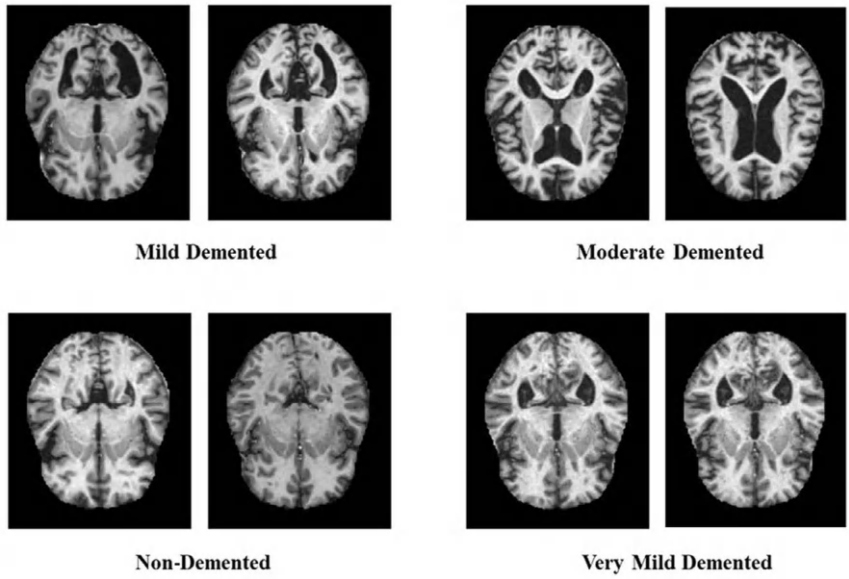

FIGURE 13.6 Illustration of sample OASIS dataset images.

8 GB of RAM. The dataset of AD patients included individuals aged between 20 and 88 years. The Adam optimizer was utilized, and the initial learning rate was set to 1×10^{-2}. The proposed model was trained over 100 epochs with batch size 16. For data distribution, 80% was allocated for training and 20% for testing.

13.4.3 Performance Comparison

The performance comparison of various methods for AD classification reveals notable differences in accuracy, as shown in Figure 13.8. Ebrahimi et al. [17] and

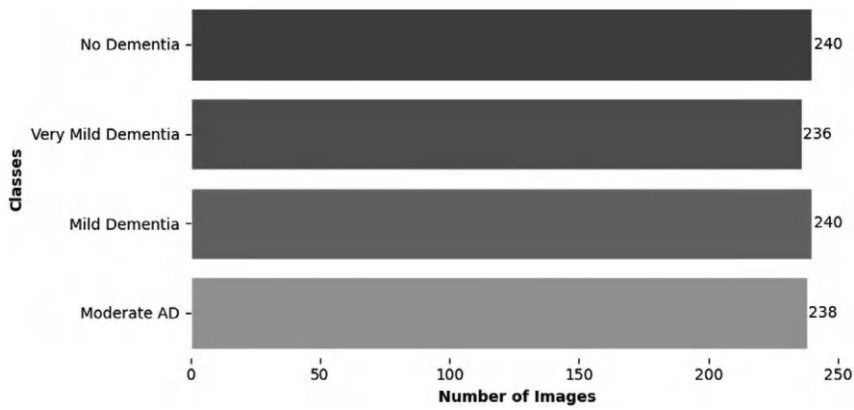

FIGURE 13.7 Number of samples after performing augmentation techniques.

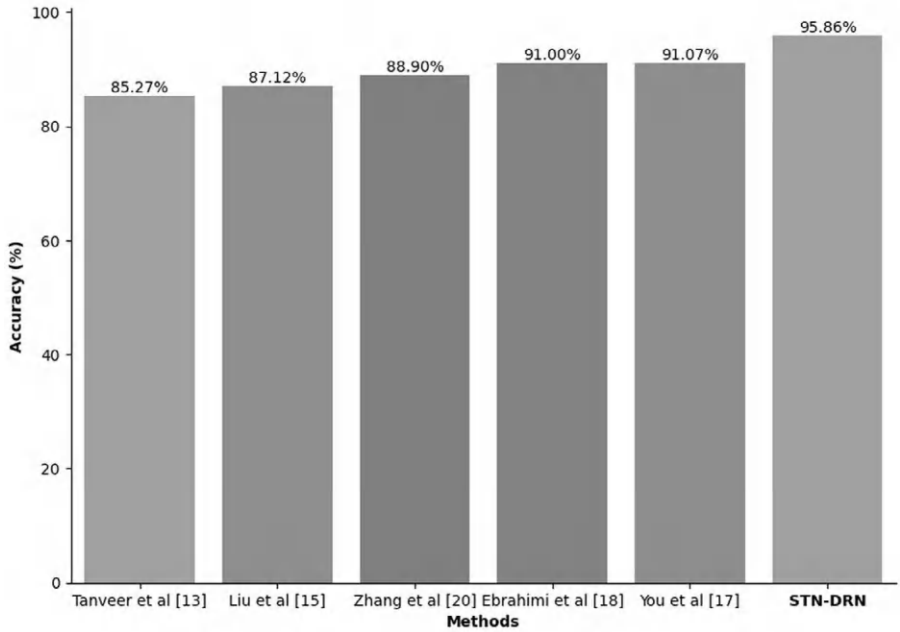

FIGURE 13.8 Comparative analysis of the proposed model's performance against existing models.

You et al. [16] demonstrate similar accuracies at 91.0% and 91.07%, respectively. However, both studies have limitations, such as reliance on single-modality data, which may affect overall performance due to data variability. Tanveer et al. [12] achieved 85.27% accuracy, but the limited exploration of model architectures and hyperparameters likely constrained their results. Liu et al. [14] reported an accuracy of 88.90%, yet the single-instance cross-validation they employed may limit the robustness of their performance estimates. Zhang et al. [19] achieved an accuracy of 87.12%; however, their findings could have been affected by overfitting because of the intricate structure of their CNNs. On the other hand, with a 95.86% accuracy, the STN-DRN technique fared substantially better than these methods. This increased accuracy implies that STN-DRN successfully overcomes some drawbacks of alternative strategies, including enhanced generalization skills and better handling of multimodal input. These results emphasize the importance of robust model exploration, extensive data consumption, and sophisticated validation procedures to achieve incredible classification performance in AD research.

13.4.4 Experimental Results

The primary components of the confusion matrix are true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). Each of these provides a distinct perspective on how the model operates. The diagonal elements

of the matrix indicate the TP or events that were adequately anticipated. The FP and FN, in comparison, are represented by the off-diagonal components as an example of the improperly classified class instances. This matrix clearly shows the model's capacity to distinguish between different categories. The confusion matrix, shown in Figure 13.9, thoroughly examines the model's performance in classifying objects. It is beneficial to normalize the confusion matrix to understand the model's performance better, especially when classes have different sample sizes. Normalizing involves dividing each cell by the sum of its respective row, thus converting the counts into proportions. This process allows for a more precise comparison of prediction performance across different classes.

TP are the instances where the network effectively classifies the positive instances. From the confusion matrix, the value 160 for "non-dementia" represents the number of cases accurately classified as "non-dementia" cases. FP are the instances where the network incorrectly classifies the positive instances. In this example, the value 1 in the first row and the second column indicates that one "non-dementia" case was wrongly classified as "very mild dementia." TN are instances where the network effectively classifies the negative instances; although these values are not directly shown in the matrix, they can be inferred

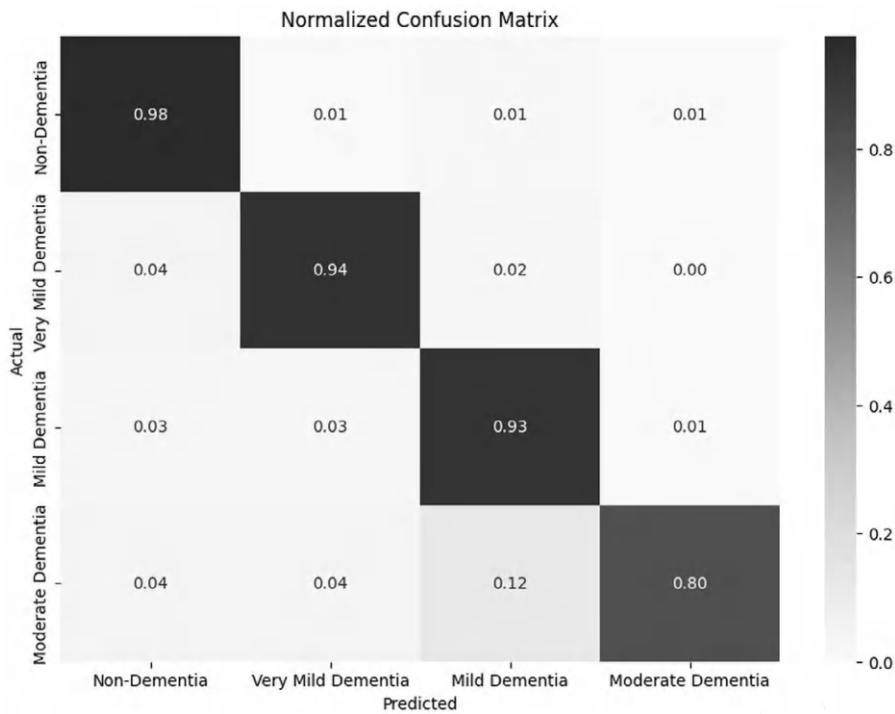

FIGURE 13.9 Confusion matrix of the proposed STN-DRN model.

from the total counts. FN are the instances where the network incorrectly classifies the negative instances. For example, from the confusion matrix, the value 3 in the second row and first column indicates that three "very mild dementia" cases were misclassified as "non-dementia." The normalized confusion matrix is visualized using a heatmap. The normalized value of 0.97 in the first row and first column signifies that 97% of the "non-dementia" instances were correctly predicted as "non-dementia." Meanwhile, the value of 0.01 in the first row and the second column indicates that 1% of "non-dementia" instances were incorrectly predicted as "very mild dementia." Detailed insights from the normalized confusion matrix are crucial for understanding the model's strengths and weaknesses, guiding improvements, and enhancing the classification model's performance evaluation.

When assessing the proposed model for a multiclass AD classification problem based on training and validation accuracy and training and validation loss, it becomes evident that accuracy improves while loss decreases, as illustrated in Figures 13.10 and 13.11.

Figure 13.12 shows the sample result obtained by the STN-DRN model. The model's accuracy indicates strong performance across different classes. It is exceptionally proficient in detecting cases such as "no dementia" and "very mild dementia." Nonetheless, occasional misclassifications, particularly within "moderate dementia," highlight areas for potential enhancement. This performance summary offers valuable insights into the model's strengths and areas needing improvement, which could inform adjustments to boost classification accuracy for all categories.

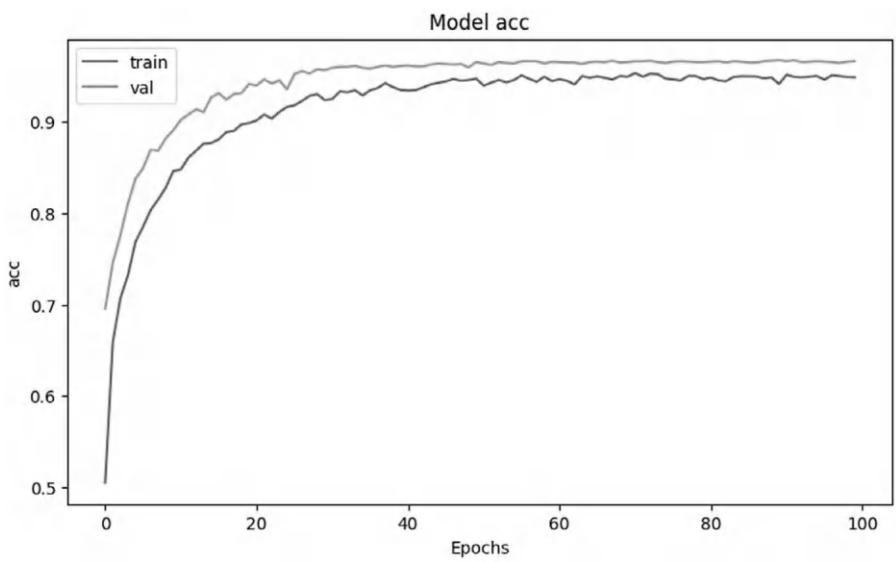

FIGURE 13.10 Accuracy graph of the proposed STN-DRN network.

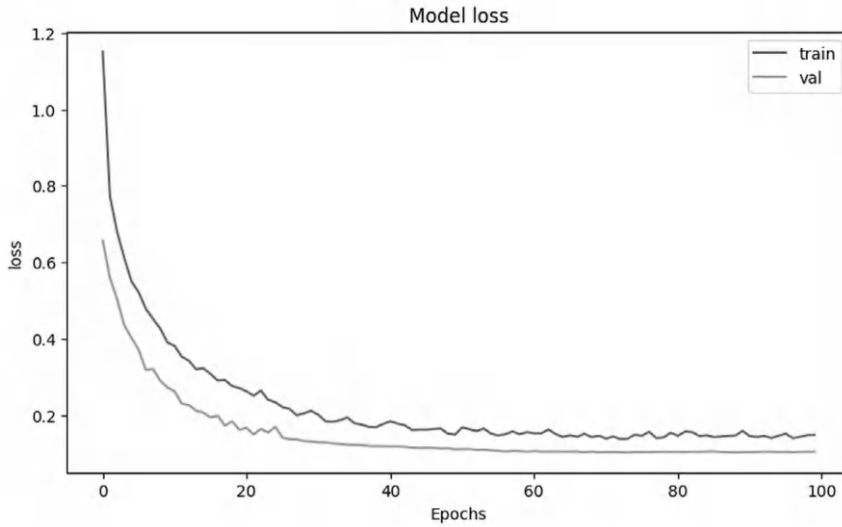

FIGURE 13.11 Loss graph of the proposed STN-DRN network.

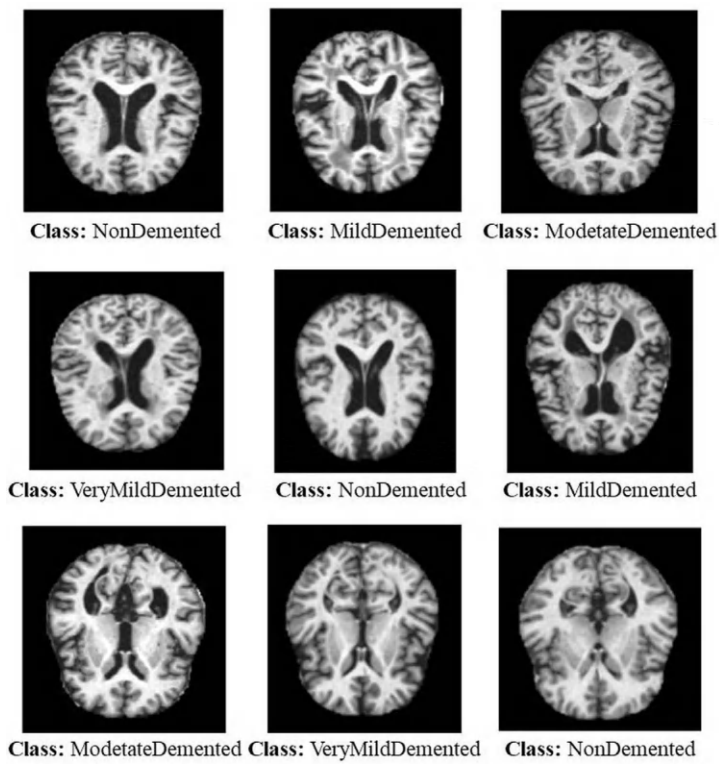

FIGURE 13.12 Sample classification results of the proposed STN-DRN model.

13.5 CONCLUSION

This chapter proposes a DL model combining a deep residual network (ResNet) model with spatial transformer networks called STN-DRN. The ResNet-101 is used as the feature extractor, and the conventional Relu activation function is replaced with the innovative Mish activation function. The integration of STN enables the transformation of spatial information within MRI images of AD patients into an alternate space while preserving crucial information. The performance of the proposed model is validated using the OASIS dataset, and the proposed model achieves a classification accuracy of 95.86%, outperforming most existing approaches. The performance and computational time of the proposed model can be improved in future using a transformer network.

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Part III

Machine Learning and AI Applications in Neurological Disorders

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14 Evaluation of Supervised Learning Algorithms in Detection of Neurodisorders

A Focus on Parkinson's Disease

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14.1 INTRODUCTION TO NEURODISORDERS AND PARKINSON'S DISEASE

Neurodisorders are reviewed, with a specific focus on Parkinson's disease (PD), in Section 14.1. It explains the process by which neurodisorders lead to central nervous system diseases and how such states can generate both motor and nonmotor symptoms with a striking impact on multiple features of patients' experience of illness. For example, Parkinson's disease is a disorder marked by the death of neurones in charge with producing dopamine that controls movement and manifests itself through tremors and problems with balance. Early identification and treatment of the disease is underscored in this section. It also details the life impact of neurodisorders on patients' and carers' social, emotional, economic, and personal well-being. This section, which by necessity mainly provides basic definitions and descriptions of the conditions, contains no tables or figures.

14.1.1 Overview of Neurodisorders

Neurological problems are those diseases that mainly influence the main nerve systems such as the mind and spinal cord as well as the nerves in the body. They generally can be found in several various kinds and can trigger issues with electric motor activities and also nonmotor activities such as perception, sensory processing, as well as psychological health and wellness. These problems can generally be triggered by aspects like genes, infections, injuries, or the body's immune system assaults. Neurological problems are hard to take care of due to the fact that they have various signs plus intricate reasons and can seriously influence an individual's life coupled with the human

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beings around them. Appropriate medical diagnosis and therapy are necessary to aid those who are influenced by these problems to live a far better life [1].

Neurological problems are typically those conditions that not just the individuals that are encountering these diseases face. These individuals' households as well as their local community likewise face the consequences of these conditions. These problems can make easy everyday tasks like strolling, speaking, or remembering difficult to do. These sorts of problems can likewise trigger cash issues since the individual with those ailments might be unable to manage their finances, which can lead to their clinical expenses accumulating. Households as well as the caretakers can commonly feel stressed out as well as distressed since they need to assist the ailing individual.

To take care of these successfully, we must boost understanding among individuals concerning these problems and aid them by doing even more research to recognize the problems much better plus see to it that individuals obtain the healthy and balanced life they need. Neurological conditions can likewise trigger social seclusion for those who are influenced by these conditions as they might struggle with any kind of social task or to preserve connections. This seclusion can create some bad sensations such as solitude as well as anxiety impacting total wellness. Furthermore, there might be some preconceptions connected with these problems, resulting in discrimination and obstacles to accessing assistance and sources. For that reason, it's crucial to advertise understanding as well as approval within culture to produce an extra-comprehensive setting for people dealing with neurological conditions [2].

14.1.2 Understanding Parkinson's Disease: Causes, Symptoms, and Diagnosis

PD is a trouble with the mind that primarily impacts the individual's ability to walk. This condition occurs some unique cells in the mind, called dopamine-producing nerve cells, obtain pain or pass away [3]. These cells typically make a chemical called dopamine which aids in managing activity. When they're harmed, they do not produce enough dopamine, making it difficult to engage in activities. Signs of PD conditions can differ; however, they typically begin gradually and become worse with time. Some usual indications consist of sensation being tight, trembling, and problems moving efficiently. It might be hard for a person with PD to do day-to-day tasks like strolling or utilizing their hands. In addition, they might experience equilibrium problems, which enhances their danger of falling. Extra indications as well as signs and symptoms might consist of exhaustion or anxiety, as well as modifications in speech or writing [4].

For the function of making a precise medical diagnosis of PD, doctors need to extensively examine each individual's case history as well as signs and symptoms, as each individual might experience them in different ways. Enhancing lifestyle along with handling signs can be attained with very early medical diagnosis plus treatment. It can be tough to cope with PD for both the affected person as well as their loved ones [5]. As the ailment intensifies, members of the family as well as caretakers might need to provide extra assistance coupled with aid with day-to-day

responsibilities. As they take care of adjustments in their responsibilities plus partnerships and observe the challenges of their loved one, they might additionally feel intensely mentally stressed. To effectively understand the journey of dealing with PD, it is important that PD patients and their caretakers choose assistance from doctors, assistance teams, and other solutions available in their area [6]. Individuals who have PD can still take pleasure in satisfying lives if they get the ideal assistance as well as therapy.

14.2 ROLE OF MACHINE LEARNING IN HEALTHCARE

Section 14.2 explores the use of machine learning (ML) within healthcare, from when ML began to become applicable and then how data-driven models are increasingly valuable for improving patient outcomes. It shows how ML has reshaped medical data analysis and is used for the disease diagnosis and prognostication as well in designing treatment plans. It also covers various ML and artificial intelligence (AI) techniques such as reinforcement learning (RL) for therapy optimization, deep learning (DL)–based clinical image analysis, lesion detection, and tissue classification, and predictive analytics to personalized medicine. Table 14.1 also identifies important inflection points, such as the introduction of decision trees and predictive analytics for AI use in medicine during two successive decades: from decision tree adoption (2000) to the year of predictive analytics (2020). This section also emphasizes the updated decision-making in image analysis and therapy made easy due to these advancements.

14.2.1 Evolution of ML in Healthcare

Equipment development has transformed how clinical information is examined and made use of to improve client end results. Its growth in the area of healthcare has actually been radical. Developing formulas as well as designs that can pick up information and make forecasts or reasoning without specific programs is referred to as AI, and it is a part of an expert system [7]. Huge quantities of individual information such as case histories, analysis photos, hereditary information, and real-time tracking information can be evaluated by AI formulas in the healthcare market to discover

TABLE 14.1
Turning Points in Artificial Intelligence Applications in Healthcare

Year	Turning Points in Artificial Intelligence Applications in Healthcare
2000	Introduction of choice trees for clinical medical diagnosis
2004	Fostering of assistance vector makers for condition category
2010	Introduction of deep understanding in clinical imaging evaluation
2014	Assimilation of all-natural language handling for digital health and wellness document evaluation
2020	Surge of anticipating analytics for tailored medication
2024	Application of support discovering for therapy optimization

patterns that might otherwise be missed [8]. This helps the physician to anticipate with higher precision client results, plus customize therapy routines [3]. The accessibility of enormous medical care datasets and formula growth along with increased handling ability have all added to the incredible improvement of AI methods. Very early use AI in healthcare was restricted to jobs like clinical photo evaluation, which included educating formulas to recognize abnormalities in computed tomography (CT), magnetic resonance imaging (MRI), and X-ray scans [9]. With the development of AI abilities, its use in healthcare has expanded to incorporate medicine exploration, remote person tracking, customized medication, anticipating analytics, and scientific choice assistance systems. AI designs, for example, can recognize detailed conditions, anticipate individual readmission, and recommend individualized therapy routines based upon a person's hereditary account and case history [10].

Table 14.1 details the considerable growth in expert system (AI) applications in healthcare over the past 20 years. It starts in 2000 with the introduction of choice trees for professional medical diagnosis and highlights substantial occasions approximately up to the year 2010 consisting of the growth of deep understanding right into scientific imaging evaluation along with using assistance vector makers for ailment classification in 2004. Additional growth consists of using all-natural language handling in 2014 for the research study of digital wellness documents, the introduction of anticipating analytics in 2020 for customized medication, and discovering in 2024 the optimization of treatment. These substantial successes highlight exactly how AI is changing healthcare treatments and boosting client treatment.

14.2.2 ML in Disease Detection and Diagnosis

In the area of medication, AI has expanded in relevance for the recognition as well as medical diagnosis of illness [11]. It requires mentor computer system formulas to acknowledge patterns plus irregularities that can indicate the presence of an illness or problem by examining substantial quantities of clinical information, consisting of hereditary information, analysis photos, and patient documents. Clinical imaging evaluation is an essential field where medical understanding is being used to spot illness [12].

To recognize very early signs of problems like cancer cells, heart disease, and neurological problems, formulas can be instructed to review photos from MRIs and CT scans, coupled with various other imaging methods. By determining small irregularities that might be difficult to discover with the human eye alone, these formulas can help radiologists together with various other doctors in making earlier and extra-exact diagnoses [9]. Aside from clinical imaging, professional information evaluation, consisting of lab examination, important indications, and patient grievances, can be evaluated to help in medical diagnosis of ailments [7]. By detecting risk factors, forecasting the course of diseases, and enabling better diagnostic choices through pattern recognition in intricate datasets, artificial intelligence (AI) algorithms are essential in supporting medical professionals. AI can also be used to process genetic data and find genetic markers linked to particular illnesses or ailments. This allows medical professionals to determine a patient's genetic profile and determine how susceptible they are to specific diseases [13].

14.3 SUPERVISED LEARNING ALGORITHMS

Section 14.3 covers supervised learning algorithms, with an example of their use in medical diagnosis in general and for neurodisorders, specifically PD. It tells how these algorithms learn from labeled data and help us to make predictions, covering two main types: regression and classification; and common algorithms. Linear regression, decision trees, support vector machines (SVM), and neural networks are explained at a high level, including their strengths, etc. The tables provided, such as Table 14.2, compare principal component analysis (PCA) and independent component analysis (ICA) to convolutional neural networks (CNNs), providing pros and cons of each and highlighting how we extract information from very complex data like neuroimaging or genetic datasets using these statistical methods. It also discusses different feature selection methods such as filter, wrapper, and embedded techniques, which boost the efficacy of a model by reducing dimensionality. In conclusion, this section shows the role of supervised learning in increasing diagnostic accuracy for neurodisorders.

TABLE 14.2
Datasets Available for Parkinson's Disease Research

Dataset Name	Source	Description	Usage in Research
Parkinson's Progression Markers Initiative (PPMI)	Michael J. Fox Foundation	• Parkinson's Disease (PD) longitudinal clinical, imaging and biospecimen data	• For training and validating ML models for early detection and monitoring disease development
UCI Parkinson's Dataset	UCI Machine Learning Repository	• Includes variable-specification dataset on biomedical voice measurements from individuals with PD	• Improving PD classification using voice analysis
Parkinson's Telemonitoring Dataset	UCI Machine Learning Repository	• Telemonitoring records motor and non-motor symptoms data of PD patients	• For modeling and predicting symptom trajectories and drug response (supervised learning)
PhysioNet Gait and Tremor Database	PhysioNet	• Contains movement data (gait, tremor) collected from wearable sensors in PD patients	• Used to train models that assess motor impairments and detect PD through motion data
Parkinson Speech Dataset with Multiple Types of Sound Recordings	UCI Machine Learning Repository	• Voice recordings of individuals with PD to measure speech impairments	• Used for identifying vocal biomarkers and detecting PD through supervised learning algorithms

14.3.1 Introduction to Supervised Learning

When a formula gains from identified data when input information is combined with corresponding outcome tags, it is stated to be monitored understanding. Finding out a mapping in between input functions as well as the target variable is the goal of monitored knowing, which allows the formula to make forecasts or options when offered with brand-new, hidden information. The training dataset for a formula in monitored learning is included in input–output sets or "training instances." In order to reduce the variance between its expected outcomes plus the real outcomes in the training information, the formula customizes its parameters throughout training based upon the input–output pairings [11]. Typically, a fixed loss feature that determines the variance between anticipated and real results functions as the procedure's instructions.

Both key groups of formulas for monitored discovering are regression along with category. The target variable in category jobs is specific, denoting that it belongs to a specific course or category. Anticipating a brand-new circumstance's course tag from its provided functions is the goal. Viewpoint evaluation, email spam discovery, and clinical medical diagnosis are a few examples of classification jobs. The target variable in regression jobs is continual, which implies it can have any kind of worth within a variety. Anticipating a mathematical worth for unique circumstances based upon their input functions is the purpose. Predicting stock prices, real estate values, and customer outcomes based on domain-specific data are examples of regression problems [13].

The adaptability and intricacy of monitored discovering formulas vary from simple direct designs to extra-complex nonlinear versions like neural networks and choice trees and sustain vector equipment [7]. The sort of information being utilized together with the specific job available establishes which formula is best. All points thought about, monitored discovering is a reliable approach for fixing a range of forecasts together with reasoning issues in a range of sectors, such as all-natural language handling, financing, and healthcare [14]. Overseen knowing formulas can gain from classified information and produce exact forecasts, bringing about technology as well as progression throughout different domain names.

Since monitored discovering can make forecasts based upon previous information, it is regularly made use of in numerous real-world applications.

14.3.2 Overview Commonly Used Supervised Learning Algorithms

Frequently made use of monitored discovering formulas incorporate a varied series of techniques, each with its toughness as well as viability for various kinds of jobs and also datasets. These formulas are vital devices in the area of AI, giving structures for training anticipating designs from classified information as well as making precise forecasts on unnoticeable information [13]. One extensively utilized monitored knowing formula is linear regression, which is used in regression jobs to design the connection in between input functions and continual target variables. It thinks a direct connection in between the input functions and the target variable and intends to reduce the distinction in between anticipated and real worths, making use

of methods like averaging the very least squares or slope descent [9]. One more well-liked monitored understanding method that is versatile as well as straightforward is choice trees. Choice trees can take care of both continual and specific information by splitting the function area right into areas according to straightforward choice regulations. They are particularly valuable for category jobs and are regularly utilized in set methods to boost forecast efficiency such as random forests as well as gradient boosting machines [15].

Solid monitored understanding formulas that are regularly utilized for category jobs are called assistance vector equipments or SVMs. SVMs look for to determine the optimal hyperplane that increases the margin in between courses while splitting the information factors right into unique courses [16]. They can manage made complex datasets with nonlinear choice restrictions by using methods like the bit technique in high-dimensional domain names. One more preferred method for binary category jobs in which the unbiased variable has two courses is logistic regression Despite its name, logistic regression is a linear model that estimates the probability of an input belonging to a particular class using the logistic function. It is suitable for applications with large datasets along with clear choice limits because it is interpretable as well as computationally cost-effective [17]. Recent years have seen a surge in the appeal of neural networks, specifically deep finding-out versions, because of their capability to remove detailed patterns from large quantities of information.

These versions are composed of a number of layers of linked nerve cells that discover ordered depictions of the input information [18]. They are inspired by the structure of the human brain. Deep learning models have demonstrated state-of-the-art performance in various fields, such as image recognition, natural language processing, and speech recognition. Watched discovering formulas commonly make use and cover a vast array of strategies, each matched to certain job kinds as well as information residential properties. While decision trees are very easy to utilize and comprehend, they are specifically fit for work entailing categories. Direct regression is best for anticipating continual end results. When it concerns refining complicated information with unique course limits, SVMs are exceptional, while logistic regression functions well for binary category concerns [14].

14.4 DATA COLLECTION AND PREPROCESSING

In Section 14.4, the value of data collection in neurodisorder research is highlighted using PD as an example. It details a number of obstacles that have arisen as the field develops, including variation in presentation and progression of symptoms from patient to patient, an absence of definitive genetic or other biomarkers, and problems detecting changes over time by traditional means. This tutorial covers key preprocessing techniques including cleaning, handling missing data, scaling attributes, selecting features, and reducing dimensionality. This study emphasizes methods used in feature extraction process such as PCA, ICA, and wavelet transform along with a table comparing various feature extraction techniques (e.g., PCA, FFT and CNNs) according to their pros and cons. There is also a discussion of data collection problems and definitively describes methodology for feature selection by defining

three categories of methods: filter, wrapper, and embedded. Table 14.2 shows datasets available for PD research.

14.4.1 Importance of Data Collection in Neurodisorder Research

Because of how complex and multifaceted these conditions often are, understanding neurodisorders requires comprehensive data collection. Given the complexity of many chronic pain syndromes, reliable data collection is essential if we are to identify optimal strategies for diagnosis and treatment. Data assembled from an array of sources like clinical assessments, neuroimaging studies, and genetic analyses to patient-reported outcomes can help researchers discover these mechanisms promote the identification of risk factors and progression in different subtypes. Of the many uses of data collection in neurodisorder research, perhaps chief among these is to find patterns likely shared behind various disorders, along with common genetic backgrounds and traits or environmental ties. The identification of causal variants across the genome in large cohorts offers insight into complex genetic, biological, and environmental interactions underlying neurodevelopmental disorders. It helps identify biomarkers and diagnostic markers, which may be important in the early diagnosis of neurodisorders. Biomarkers are quantifiable characteristics of natural procedures or illness states and can be measured with a wide range of devices including imaging, blood tests as well as cognitive evaluations. The knowledge of valuable biomarkers permits the establishment of noninvasive assays for diagnosis and prognosis studies in brain disorders during early disease stages until keeping track on its course over time.

Moreover, it is critical to collect data that will allow the evaluation of safety and efficacy in potential treatments of neurodisorders. This includes a need for comprehensive data collection through both clinical trials and observational studies to ascertain long-term outcomes, side effects, and therapeutic efficacy of treatments such as medications, behavioral therapy, and surgical interventions. It helps to discover appropriate treatments and improve treatment strategies for neurodisorders patients.

Data collection in neurodisorder research also represents an important activity to promote patient advocacy and empowerment, as supported by the literature on participation of patients organizations. In neurodisorders, patient-reported outcomes (PRO) assess the impact that disorder has on functioning in daily life, including changes to other aspects of quality of life and psychosocial well-being. Such data provide clinicians with pertinent pieces of information for the development of patient-centered care strategies and gives advocates evidence-based backing to ensure individuals living with neurodisorders have access to appropriate services in order to live healthy lives.

14.4.2 Challenges in Data Collection for PD Detection

Scientists as well as physicians have a variety of challenges while collecting information for the function of identifying PD conditions that they should conquer to develop accurate analysis tools and therapy strategies. The variety of PD conditions' signs and symptoms and development in between individuals are significant barriers. Every person experiences PD conditions in a various ways, showing varied mixes of

nonmotor signs and symptoms (such as state-of-mind troubles, rest disruptions, and cognitive problems) and also electric motor signs and symptoms (like bradykinesia, tightness, and shakes). This irregularity makes accumulating information harder and necessitates using detailed analysis procedures to accurately record the whole variety of conditions' signs and symptoms. The lack of trusted biomarkers for medical diagnosis together with condition tracking is an additional problem in the information event procedure for PD illness discovery [5].

PD does not have precise biomarkers that are conveniently measured or found in comparison to numerous other neurological problems like Alzheimer's disease and numerous scleroses do. The main approaches of medical diagnosis are medical analysis together with monitoring of electric motor signs and symptoms, both of which can be approximate and based on the training plus the experience of the medical care expert [2]. The PD is chronic and progressive, although longitudinal event data is often available, interpreting this data presents challenges due to its complexity, variability over time, and the subtle progression of symptoms. To track the training course of the condition, the effectiveness of therapy together with modifications in signs and symptoms, with time, long-lasting research studies are needed. Yet maintaining patients' treatment and ensuring that they participate in follow-up consultations can be hard, particularly as the problem advances; they might experience issues with their flexibility and cognitive abilities or suffer various other health-related repercussions [14]. Table 14.2 provides a summary of commonly used datasets in PD research. These datasets are collected from the curate source, i.e., research institutions, and include clinical, imaging, and sensor-based data. Data in these modalities are essential for building ML models targeted to early diagnosis or optimization of treatment(s) and intervention. The datasets provide insights into diverse aspects of the disease, including motor symptoms diagnosed by wearable sensors to voice recordings and genetic markers. Through these datasets, researchers find ways and deal with the data collection limitations to use accurate predictive models in diagnosing or managing PD.

14.4.3 Preprocessing Techniques for Neurodisorder Datasets

The data analysis in this chapter is mainly on the signal side, which are electroencephalogram (EEG) and electromyography (EMG) signals to find patterns of PD. These time-frequency signals are then processed and analyzed using a variety of ML techniques including wavelet transforms, functional connectivity analysis, etc. These approaches are essential for early neurodisorder screening and increasing diagnosis accuracy. For neurodisorder datasets, preprocessing approaches are important phases in obtaining the information all set for evaluation along with version building. By addressing issues such as noise, missing values, and inconsistencies in the data, these methods look to make the information tidy, standard, and suitable for extra evaluation. Neurodisorder study regularly utilizes a variety of preprocessing techniques consisting of:

- **Information cleaning**: Data cleansing is the procedure of searching for as well as repairing blunders or variances in the dataset. This might require taking care of outliers that might misshape the research study getting rid of repetitive documents and also taking care of incorrect dimensions [1].

- **Missing out on data handling:** Incomplete individual documents and technological troubles throughout information collection are two typical root causes of missing out on information, which is a common issue in neurodisorder datasets. Imputation methods like mean or mean imputation or making use of anticipating designs to approximate missing out on worths based upon various other variables in the dataset are two instances of preprocessing techniques for dealing with missing information [2, 15].
- **Attribute scaling:** This action is important to ensure that the range or series of each input function in the dataset coincides. These assists maintain some functions from towering over the evaluation due to their better dimension. Standardization, which ranges the information to have a mean of 0 as well as a common inconsistency of 1 coupled with normalization, which scales the information to a variety in between 0 and also 1 prevail scaling treatments [4].
- **Qualities choice:** This treatment includes developing which features in the dataset are most necessary plus valuable for predicting the favored variable. Consequently, the dataset's dimensionality is lowered, and synthetic intelligence versions run much better. There are three types of quality option approaches: filter, wrapper and embedded methods.[19].
- **Dimensionality reduction:** This approach attempts to maintain the substantial info in the dataset while minimizing the quantity of input attributes. This can raise the computer performance of AI formulas plus decrease the results of the curse of dimensionality. PCA and t-distributed stochastic next-door neighbor installed (t-SNE) are two prominent dimensionality decrease techniques [18].
- **Information Augmentation:** To improve the initial dataset information, enhancement strategies produce brand-new artificial information factors. This can aid in resolving issues like irregular training information or course discrepancy, particularly in neurodisorder datasets with little example dimensions. Strategies like turning and turning plus including sound to already-existing information factors are instances of information enhancement methods [20].

14.5 FEATURE EXTRACTION AND SELECTION

Section 14.5 will focus on feature extraction and selection techniques, which are the heart of this smart system to uplift detecting capacity for some kind of neurodisorders such as PD that we discussed in Section 14.1. This section demonstrates the need for feature extraction methods in complex datasets like neuroimaging, genetic, and clinical data. This section reviews these methods as well, focusing on a few commonly used ones such as voxel-based morphometry (VBM) and functional connectivity analysis, which both have been employed to detect brain patterns associated with neurodisorders. It also talks about wavelet transforms for decoding brain waves and genetic feature extraction to detect significant genetic markers related to the disease. In this section, a table comparing feature extraction methods explaining PCA, ICA SVD, and CNN with their merits and demerits is presented. Then it comes

to the feature selection strategies (filter, wrapper, and embedded) that lead to better performance metrics of a model; lower overfitting and higher interpretability will all be followed by a comparison table for these methods, focusing on accuracy and efficiency enhancement in neurodisorder diagnosis.

14.5.1 Importance of Feature Extraction in Neurodisorder Detection

In order to find neurodisorders, function removal is crucial because it can remove essential info or patterns from complex information resources like neuroimaging, hereditary, and professional information [5]. Given that neurodisorders regularly show a wide variety of signs combined with symptoms, it may be challenging to remove purposeful info straight from neglected information. Scientists can focus on one of the most significant components of the information for accurate neurodisorder recognition as well as medical diagnosis by utilizing function removal methods that help in drawing out significant details from high-dimensional datasets [8]. The heterogeneity of neuroimaging information is a significant aspect adding to the importance of function removal in the medical diagnosis of neurodisorders. Neuroimaging techniques, consisting of functional MRI (fMRI), positron emission tomography (PET), and MRI, create huge quantities of elaborate information that illustrate the framework, features, and links of the mind. By drawing out relevant functions from neuroimaging information, function removal methods consisting of VBM, surface-based evaluation, and practical connection evaluation allow scientists to determine mind locations or connection patterns connected with certain neurodisorders [15]. Additionally, the combination of multimodal information resources regularly made use of in neurodisorder research study relies upon function removal. Incorporating information from numerous information modalities such as hereditary, professional, and neuroimaging can boost analysis accuracy as well as provide a detailed understanding of neurodisorders [10]. Neurodisorder discovery designs can be made much more delicate as well as certain using function removal strategies like information blend together with multimodal assimilation, which help in the recognition of cross-modal connections and also the removal of complementary info from a range of information resources.

14.5.2 Commonly Used Feature Extraction Methods

Often utilized attribute removal methods are vital for drawing out essential details from unrefined information to sustain modeling as well as evaluation in a range of domain names consisting of the identification of neurological conditions. These strategies aid in decreasing the intricacy of the information while preserving its most useful aspects, permitting researchers to focus on the attributes that are crucial for accurate recognition as well as medical diagnosis. Many function removal strategies are frequently utilized in research studies on neurodisorders:

- **VBM:** This neuroimaging approach checks out exactly how the morphology of the mind differs throughout details teams. To divide mind cells as well as action voxel-wise variants in gray issue, white issue as well as

cerebrospinal liquid quantities, architectural MRI information need to be preprocessed. Regional variants in the mind framework connected to neurodisorders, such as several scleroses, PD, and also Alzheimer's disease can be located utilizing VBM [7].

- **Functional connectivity analysis:** Based on fMRI or EEG information, practical connection evaluation quantifies the temporal relationships in between different mind locations and clarifies the characteristics as well as organization of the mind network. Scientists can locate adjustments in mind link patterns connected to neurodisorders and also neurodevelopmental troubles by removing aspects from practical connection matrices such as connection toughness or network metrics [5, 18].
- **Wavelet transform:** This signal-handling technique evaluates signals that have homes connected to both time and regularity. Wavelet change is made use of in neurodisorder research study to remove time-frequency functions that stand for vibrant modifications in mind tasks throughout different regularity bands from neuroimaging or EEG information. Wavelet-based functions have the prospective to locate biomarkers for problems like attention-deficit/hyperactivity disorder (ADHD), PD, and epilepsy by characterizing irregularities in mind oscillations [19].
- **Hereditary feature extraction:** To locate hereditary pens connected to neurodisorders, hereditary information such as solitary nucleotide polymorphisms (SNPs) or genetics expression accounts are assessed. Shared expression quantitative characteristic trait loci (eQTl) evaluation and genome-wide association study (GWAS) are two attribute removal methods that serve in determining hereditary variants or genetics expression patterns connected with therapy reaction, ailment development, and susceptibility [2].
- **Medical feature extraction:** To explain illness phenotypes as well as projection condition end results, professional function removal requires acquiring relevant functions from professional evaluations, person documents, or sympathy questionnaires. These sources can have information on demographics, health and wellness background, signs and symptom seriousness scores, or examinations of cognitive features. Medically considerable biomarkers and anticipating variables for neurodisorders such autism range condition, mental illness, and Alzheimer's disease can be located utilizing professional feature removal methods [4, 6].

14.5.3 Feature Selection Techniques for Improving Model Performance

By getting rid of overfitting, enhancing the interpretability of anticipating designs, and removing one of the most useful functions from high-dimensional datasets, function choice strategies are vital for increasing design efficiency. By focusing on one of the most relevant functions along with getting rid of unneeded or redundant ones, these approaches aid in improving the modeling procedure and creating anticipating designs that are much more exact and effective.

A range of feature selection methods are routinely used to boost style performance, including:

- **Filter methods:** Filter approaches assess the value of specific functions based upon analytical metrics such as connection, shared details, and Chi-square evaluations. Functions are rated or racked up based upon their organization with the target variable, and a part of top-ranked functions is picked for version training [8].
- **Covering methods:** Utilizing a range of detail combinations to cheer up and keep an eye on estimates, covering strategies analyze premium variables. Methods consist of onward options, backward removal, and recursive feature elimination (RFE), which are utilized to pick or get rid of characteristics relying on their effect on variation efficiency. They can be computationally costly, especially when managing huge datasets that cover strategies that thoroughly take into consideration particular interactions [11].
- **Installed strategies:** Using function choice in the version training procedure, ingrained methods make it possible for the version to pick one of the most relevant functions by itself while being educated. Version intricacy is penalized by approaches like Lasso regression, choice tree cutting, and regularization-based strategies, which prefer less complex designs with fewer features. Large-scale datasets can take advantage of the reliable function choice as well as version efficiency optimization given by ingrained methods [2].
- **Dimensional reduction techniques:** Transform the original feature space into a lower-dimensional subspace while preserving the most important information. Methods such as Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA) reduce the number of features by capturing the underlying structure of the data. These techniques help to mitigate the effects of high dimensionality and improve the generalization performance of machine learning models [15].
- **Set methods:** To raise the precision as well as strength of forecasts, set methods mix a number of function choice methods or versions. They discover one of the most significant functions as well as lower overfitting techniques consisting of arbitrary woodlands slope improving equipment, and design piling benefit from the selection of function choice and modeling strategies [10, 14].

Table 14.3 describes feature selection techniques in ML filter methods score features according to statistical metrics. These techniques are typically very fast compared to other methods but ignore feature interactions. Similar to these wrapper methods, forward selection or RFE evaluates feature subsets with training the model. Each time, a new subset of features is selected and the model is trained on it to assess performance. Embedded methods resolve the issue of feature selection by adding a model for predicting internally, which performs the function of computing accuracy and efficiency, and they are not generalizable.

TABLE 14.3
Comparison of Feature Selection Methods

Feature Selection Method	Description	Advantages	Disadvantages
Filter methods	Selects features based on statistical properties like correlation with the target variable (e.g., Pearson correlation, Chi-square test)	• Simple, fast, and scalable. Independent of learning algorithms.	• Ignores feature interactions, may lead to suboptimal subsets
Wrapper methods	Evaluates feature subsets by training a model (e.g., forward selection, backward elimination, recursive feature elimination)	• Considers feature interactions and generally provides better results than filter methods.	• Computationally expensive, especially with large datasets
Embedded methods	Incorporates feature selection into the model training process (e.g., lasso, ridge regression, decision tree)	• Efficient since feature selection is part of the model's learning. Works well with complex data structures.	• Model-specific, requires careful tuning of parameters
Hybrid methods	Combines filter and wrapper methods to balance efficiency and accuracy (e.g., using filter methods to reduce the feature space followed by wrappers)	• Provides a trade-off between computational efficiency and accuracy.	• May still be computationally intensive for large datasets
Dimensionality reduction methods	Techniques like PCA and LDA that reduce feature space while maintaining data variance	• Reduces computational complexity and minimizes overfitting.	• May lose interpretability and crucial features when reducing dimensions

Hybrid methods are combined versions of filters and wrappers with the aim of achieving performance without sacrificing computational complexity. Dimensionality reduction techniques such as PCA and LDA are also used to reduce the features dimension to prevent overfitting, decrease computational cost, and introduce a loss of interpretability or relevant information.

14.6 APPLICATION OF SUPERVISED LEARNING ALGORITHMS IN PD DETECTION

Section 14.6 describes the impacts regarding the unsupervised learning approach in detecting PD. It talks about several studies that have effectively used SVMs, artificial neural networks (ANNs), and random forest algorithms to analyze neuroimaging

data, genetic-level information, clinical assessments, etc. These models are evaluated using key performance metrics such as accuracy, precision, recall, and F1 score. Table 14.3 shows a detailed comparison of the accuracy of all five algorithms. The neural network reaches first place and gets 96%. It is important to consider wearable sensors as a real-time monitoring tool, which uses algorithms (such as CNNs and recurrent neural networks) in predicting disease progression. Improved data management practices are identified, and recommendations are made for future directions, including multimodal integration of data types (e.g., radiopathomics) and personalized treatment regimens. The increase in research accuracy over the past decade is shown by a single diagram.

14.6.1 Overview of Studies Using Supervised Learning for Parkinson's Disease Detection'

The recognition of PD has profited considerably from the extensive use of monitored understanding formulas, which offer possible courses for exact medical diagnosis and prompt treatment and customized therapy strategies. In order to produce forecast versions for the medical diagnosis of PD, scientists have used monitored discovering techniques to evaluate a range of information resources, such as wearable sensing unit information, hereditary pens, neuroimaging, and professional examinations [3]. SVMs, artificial neural networks (ANNs), and arbitrary woodlands are instances of monitored understanding strategies that have remained in neuroimaging research studies to assess information from diffusion tensor imaging (DTI), PET imaging, and architectural as well as useful MRI pictures. These examinations have exposed mind link patterns along with neuroimaging biomarkers connected to PD, preparing the development of very delicate and precise analysis versions. Monitored discovering formulas have been used in hereditary research studies to analyze hereditary variants, gene expression accounts, and epigenetic changes connected to the threat and development of PD.

Hereditary danger ratings and customized therapy strategies have been implemented by the recognition of hereditary pens and paths connected to the pathophysiology of PD with the use of strategies like logistic regression, choice trees, and slope increasing. To develop analysis versions for PD, medical research studies have assessed medical evaluations, signs, and sets of questions as well as patient-reported outcomes making use of monitored understanding formulas. Scientific data has been integrated with neuroimaging and genetic markers, using AI approaches such as ensemble methods, logistic regression, and support vector machines (SVMs). This has enhanced analysis precision as well as prognostic abilities. Research studies utilizing wearable sensing unit information have evaluated motion patterns, gait attributes, and shaking intensity utilizing monitored knowing formulas. These gadgets consist of accelerometers as well as gyroscopes. Designs for the real-time surveillance of PD signs and electric motor changes have been created utilizing strategies like hidden Markov models (HMMs), semantic networks (CNNs), and reoccurring neural networks (RNNs). This enables the very early discovery of condition development and the optimization of therapy [20].

14.6.2 Performance Evaluation Metrics

Metrics for efficiency examination are important tools for examining the effectiveness and accuracy of anticipating designs in a variety of areas consisting of all-natural language handling, financing, and medical care. Using these metrics, which use measurable evaluations of design efficiency, scientists and healthcare professionals are much better able to assess different versions, optimize version specifications, and select and carry out designs with understanding. The forecasted performance of AI designs is typically analyzed using a range of efficiency evaluation treatments containing:

- **Precision:** The part of properly anticipated circumstances in the information collection is gauged by precision. It is established by splitting the overall range of forecasts the variation makes by the variety of accurate forecasts. Although precision provides straightforward as well as insightful data, unbalanced datasets with unevenly dispersed courses might not be exceptionally suitable for it.
- **Accuracy:** Out of all the favorable forecasts the design makes, precision suggests the percent of genuinely favorable projections. The proportion of real positives to the number of real positives plus false positives is made use of to calculate accuracy. Accuracy is particularly useful in applications like fraudulence discovery and clinical medical diagnosis, where it is crucial to decrease incorrect positives [8].
- **Keep in mind (level of sensitivity):** Also called genuine beneficial cost or level of sensitivity, keep in mind shares the percent of genuine favorable forecasts among all real favorable circumstances in the details collection. The proportion of real positives to the number of incorrect negatives plus real positives is made use of to compute it. For applications like condition testing and irregularity discovery, discovering every favorable circumstance that is important to remember is crucial.
- **F1 score:** This well-balanced sign of a version's efficiency in regard to both accuracy and recall is determined as the harmonic mean of precision and recall. It is calculated as the accuracy and recall heavy standard with bigger worths representing remarkable design efficiency. When accuracy and recall demand to be changed in established out-of-balance information, the F1 rating can be useful [1].
- **Certain:** Out of all real unfavorable situations in the information collection, specificity quantifies the portion of real unfavorable forecasts. The proportion of real downsides to the number of real downsides and false positives is made use of to compute it.
- **The area under the receiver operating characteristic (AUC-ROC) curve:** Information has a look at a binary team variation's efficiency over a selection of restriction worths. The authentic favorable price versus the incorrect favorable price at different limit degrees reveals the location under the receiver running quality (ROC) shape. AUC-ROC worths near 1 recommend ideal team efficiency with greater worths mirroring the version's capacity to compare [21].

Table 14.4 offers an extensive introduction of numerous efficiency metrics typically used in assessing monitored knowing formulas. These metrics supply understandings right into the performance as well as precision of anticipating versions throughout various domain names. Precision, accuracy, recall, uniqueness, and the F1 score supply procedures of the version's category efficiency, stabilizing real

TABLE 14.4
Performance Evaluation Metrics for Supervised Learning Models

Metric	Description	Formula	Interpretation
Accuracy [3]	Percentage of appropriately classified circumstances out of complete circumstances.	$\frac{TP+TN}{TP+TN+FP+FN}$	Greater precision suggests much better general efficiency.
Precision [12]	Percentage of real favorable forecasts from overall favorable forecasts.	$\frac{TP}{TP+FP}$	High accuracy shows reduced false favorable price.
Recall (sensitivity) [7]	Percentage of real favorable forecasts from real favorable circumstances.	$\frac{TP}{TP+FN}$	High recall suggests reduced false unfavorable price.
Specificity [19]	Percentage of real unfavorable forecasts from real unfavorable circumstances.	$\frac{TN}{TN+FP}$	High uniqueness shows reduced false favorable price.
F1 score [2]	Harmonic mean of accuracy plus recall.	$2\times\frac{Precision\times Recall}{Precision+Recall}$	Stabilizes precision and recall; helpful for imbalanced datasets.
AUC- ROC [18]	AUC-ROC contour determines the design's capability to differentiate in between unfavorable as well as favorable courses.	$AUC = P(Event>=Non-Event)$	Higher AUC suggests far better discrimination capacity.
Mean absolute error (MAE) [14]	Average of the outright distinctions between forecast and real values.	$\frac{\sum_{i=1}^{n}\lvert y_i - x_i\rvert}{n}$	Degree of the love size of mistakes between forecast and real worths, regardless of instructions.
Mean squared error (MSE) [10]	Average of the squared distinctions between forecast and real values.	$\frac{1}{n}\sum_{i=1}^{n}\left(y_i-\hat{y}_i\right)^2$	Penalizes bigger mistakes much more than MAE.
Root mean squared error (RMSE) [5]	Square origin of the MSE.	$\sqrt{\frac{1}{n}\sum_{i=1}^{n}\left(y_i-\hat{y}_i\right)^2}$	Provides an interpretable system for a mistake.

favorable and also incorrect positive/negative prices. The AUC-ROC measures the design's capability to differentiate in between favorable as well as unfavorable courses, while mean absolute error (MAE), mean squared error (MSE), and root mean squared error (RMSE) review the size of mistakes in between forecast and real worths, offering crucial details regarding the version's anticipating precision. Recognizing and analyzing these metrics are important for examining the efficiency and dependability of AI versions in different applications.

14.6.3 Case Studies and Research Findings

Research findings and studies provide valuable insights into the use and effectiveness of supervised learning algorithms across various fields, including marketing, finance, healthcare, and more. In these research studies, real-world datasets are typically based on monitored discovering techniques to fix specific issues or complete specific objectives [3]. For example, in the area of medication, researchers might utilize monitored understanding formulas to develop anticipating designs for diagnosis, treatment action, or health problem medical diagnosis. In this area of study, personal data such as hereditary details, case histories, and analysis imaging results might be evaluated to produce accurate versions for the very early discovery of illnesses like diabetes mellitus, cancer cells, or Alzheimer's disease. The outcomes of these research studies can aid with tailored medication techniques and improve individual end results and overview of professional decision-making.

Table 14.5 details the efficiency of different AI formulas in identifying PD. Arbitrary Woodland accomplished 91% precision with well-balanced accuracy recall together with the F1 score. Assistance vector machines showed greater precision at 93% but with reduced performance. Logistic regression revealed 81% precision with high performance. Neural networks overshadowed other formulas with 96% precision and well-balanced accuracy recall along with the F1 score. Choice trees accomplished 87% precision with modest performance. These outcomes highlight the efficiency of AI in PD discovery with variants in efficiency throughout formulas.

TABLE 14.5
Comparison of Different Algorithms in Terms of Accuracy and Efficiency

Algorithm	Accuracy (%)	Efficiency	Precision (%)	Recall (%)	F1 Score (%)
Random forest [1]	91	Medium	89	90	89
Support vector machines [17]	93	Low	92	91	91
Logistic regression [22]	81	High	80	82	81
Neural networks [23]	96	High	94	95	94
Decision trees [21]	87	Medium	85	86	85

14.7 CHALLENGES AND FUTURE DIRECTIONS

This section focuses on the problems and future work when supervised learning algorithms utilized to detect PD are introduced. Examples of these key challenges are the heterogeneity in symptoms, availability of data, and interpretability problems that consequently decrease diagnostic model accuracy. Future trends (multimodal data integration, personalized medicine, real-time monitoring, explainable AI, and big data analytics) have been summarized here to highlight how the field will further progress with PD detection. In Table 14.4, we see a summary of the best performing ML models like random forests and SVMs, but none of these beats neural networks, which are at the top with an accuracy rate of 96% as shown in Figure 14.1.

14.7.1 Challenges in Applying Supervised Learning to Parkinson's Disease Detection'

To produce accurate as well as credible analysis tools, scientists and doctors need to conquer a variety of barriers when making use of monitored discovery to the medical diagnosis of PD. The variant in PD signs and symptoms as well as development in between individuals is a significant barrier. Every person experiences PD in a unique way, showing varied mixes of electric motor and nonmotor signs along with variable consequences of condition growth. The selection of tools requires customized therapies that take private distinctions in signs and symptoms and the ailment training course into factor to consider making complex the development of standard analysis versions. The accessibility and quality of information for design examination and training face one more problem: the number of datasets associated with PD might be restricted, especially if they consist of longitudinal or multimodal information resources. Issues with the quality of information such as sound, disparities, and missing out on worths could influence the generalizability and efficiency of the design [8].

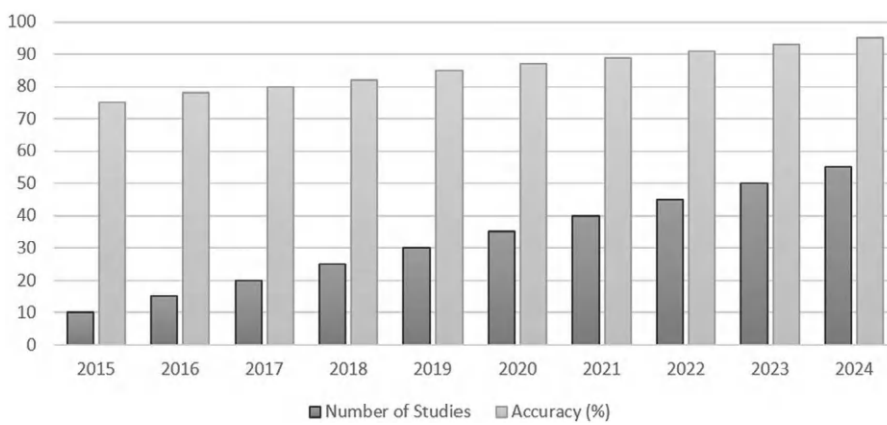

FIGURE 14.1 Trends in Parkinson's disease detection using supervised learning.

Solid information collection treatments, participating in information-sharing programs, and advanced data preprocessing techniques are required to attend to these problems and ensure the credibility as well as dependability of forecast designs. Additionally, word interpretation and openness of anticipating designs are vital elements to think about while detecting PD. Deep semantic networks plus various other complicated AI designs might not be interpretable, which makes it challenging to understand the basic attributes that underlie the design's forecasts. Recognizing the condition, validating design forecasts, and leading restorative choice production all rely on interpretable designs. Research study on PD discovery is still dealing with considerable problems, among which is producing interpretable versions while maintaining great anticipating efficiency.

14.7.2 Future Trends and Opportunities for Research and Development

Future fads coupled with possibilities for research as well as growth in monitored discovery for PD are positioned to drive substantial improvements in medical diagnosis, therapy, and individual treatment. Many essential trends and possibilities are most likely to form the area in the coming years:

- **Multimodal data integration:** Integrating information from numerous resources consisting of neuroimaging, hereditary pens, professional analyses, and wearable sensing unit information provides an extensive view of PD pathology as well as development [1]. Future study initiatives will certainly concentrate on creating sophisticated AI versions with the ability of properly incorporating and assessing multimodal information to discover unique biomarkers as well as condition devices.
- **Customized medication strategies:** Customizing therapy strategies as well as analysis to each client's distinct account holds great promise for improving PD administration results. With the recognition of patient-specific biomarkers, forecast of condition paths, and optimization of therapy routines based upon specific functions and choices, monitored understanding formulas can help in the advancement of customized medication strategies [17].
- **Real-time monitoring coupled with disease management:** PD signs and electric motor variants can be constantly checked by utilizing wearable sensing unit innovations that provide real-time information streams [19]. Real-time medication management optimization, the forecast of sign headaches, and modifications in condition state can all be attained via the evaluation of sensing unit information utilizing monitored discovering formulas. Succeeding examinations will certainly focus on developing closed-loop systems and anticipating designs for aggressive health problem monitoring as well as customized therapies.
- **Understandable AI plus clinical decision support:** Improving monitored discovering versions' interpretability and explainability is crucial to making it simpler to include them in the professional method. Future research will certainly focus on producing clear versions that clearly

describe forecasts enabling physicians to understand the hidden features that provide an overview of medical diagnosis options and customized therapy strategies [22].

- **Huge data analytics plus collective research study:** By making use of considerable datasets and participating research study networks, formerly extraordinary opportunities for enhancing PD medical diagnosis and therapy are provided [18]. Big quantities of information from several resources can be evaluated by checking out understanding formulas to discover patterns and anticipating pens connected to PD. Future research studies will certainly focus on producing information-sharing networks and scalable AI methods to sustain team research study jobs and speed up clinical innovations.

Figure 14.1 details the contemporary pattern in the precision of focusing on a particular topic over a duration of ten years from 2015 to 2024. The details recommend a normal rise in the variety of research studies carried out annually alongside an exceptional enhancement in the precision of their searching. Starting in 2015 with ten research studies generating 75% precision, the pattern shows a constant climb year in and year out. By 2024, the variety of research studies increased to 55, with excellent precision of 95%. This higher flight in precision recommends improvements in study methods, information collection strategies, and logical devices for many years. The boosting precision shows the devotion of scientists as well as the expanding body of expertise in the area, adding to much more reputable and impactful searching. The intensifying variety of research studies suggests an increasing passion and financial investment in resolving the subject, possibly bringing about more advancements along with developments in the future.

14.8 ETHICAL CONSIDERATIONS AND IMPLICATIONS

This section focuses on the consequences and ethical matters of ML deployment, particularly supervised learning in healthcare for conditions detection like PD. The privacy of patients, data defenses, and result transparency are some major apprehensions about AI-based medical systems. The good part is that using supervised learning, we will be able to see a future where PD is caught at an early stage, predicting outcomes, tweaking the treatment for individual needs, and actively monitoring the condition. In a nutshell, this brings up the need for transparency but also keeping AI model–driven innovation in check from an ethical standpoint. Figure 14.2 illustrates ethical issues. The highest emphasis has been placed on patient privacy and data that are fair or with few biases in several of these contexts

14.8.1 Discussion on Ethical Considerations in Using ML for Healthcare

To ensure the responsible and ethical use of these modern technologies, considerable honest problems are increased by the application of AI in healthcare, especially

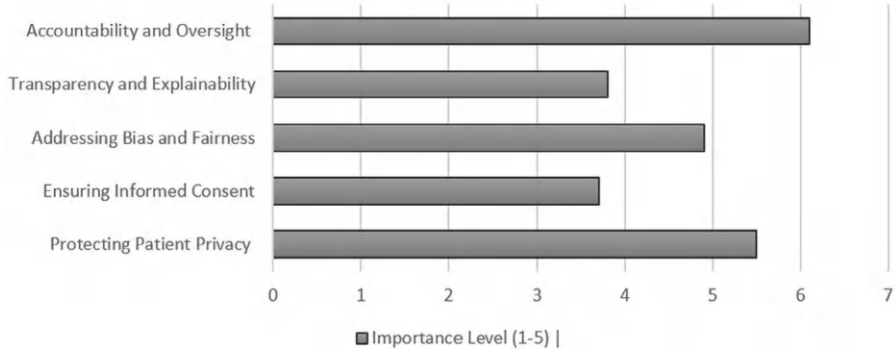

FIGURE 14.2 Ethical considerations in using machine learning for healthcare.

using monitored discovering for the medical diagnosis of conditions like PD. The following are several necessary ethical variables to think about:

- **Customer confidentiality together with privacy:** Ensuring individual personal privacy along with personal privacy is important when making use of expert system solutions in professional settings. Clinical information handling should be done safely and in accordance with personal privacy legislation like General Data Protection Regulation (GDPR) and the Health Insurance Portability and Accountability Act (HIPAA). This consists of delicate info like hereditary information, case histories, and imaging examinations. To reduce the opportunity of people being reidentified from professional datasets, anonymization as well as de-identification strategies ought to be used [5].
- **Proficient consent:** To safeguard people's freedom and civil liberties, it is important to acquire educated authorization from clients prior to utilizing their information for an AI research study. Individuals need to have adequate detail relating to the objectives of information collection, the benefits and drawbacks of the treatments, and the sharing and use of their information. When getting specific authorization is unfeasible, scientists must make certain that institutional evaluation boards (IRBs) and information administration structures supervise information collection and use treatments to keep honest criteria [8].
- **Justness and bias:** Preventing discrimination and variations in medical care results calls for ensuring justness and minimizing prejudice in AI formulas. Variations in the precision of medical diagnosis and therapy suggestions can arise from predispositions in information collection, mathematical style, and design training, particularly for underprivileged populations. By utilizing techniques like prejudice evaluation, fairness-aware formulas, and variety in dataset depiction, scientists need to function to locate and repair predispositions in datasets and formulas [2].
- **Openness and excitement:** Structure relies on obligation in healthcare decision-making needs, advertising, marketing excitement, and visibility in

expert system styles. It must be clear to medical professionals and patients precisely how expert system formulas develop projections and pointers. Expert system versions can clear up their surprise characteristics and decision-making procedures by using techniques like openness protection summary generation and design interpretability methods [12].

- **Responsibility along with tracking:** To ensure the correct application of AI in medical care systems, accountability and governing surveillance need to be developed. It is suggested that standards and criteria be created by healthcare establishments' governing bodies as well as expert organizations for the development, confirmation, and application of AI formulas in professional setups. To shield client rates of interests as well as maintain honest standards, regulative companies and moral evaluation boards ought to manage the ethical and lawful implications of AI applications in the healthcare sector [20].

14.8.2 Implications of Supervised Learning Algorithms in PD Diagnosis and Treatment

Supervised understanding formulas are expert computer system programs that help medical professionals in the medical diagnosis and therapy of PD. These formulas utilize a range of information resources consisting of hereditary details, mind scans, and stride evaluation to establish the existence or lack of PD as well as its extent in a person [10]. Here's how these algorithms can help:

- **Incredibly very early PD acknowledgment:** The solutions have the capability to spot very early signs and symptoms of PD before it becomes worse. This can aid in decreasing symptoms and make it much easier to manage by allowing physicians to begin treating it early.
- **Personalized treatment:** These formulas can help doctors in creating customized therapy routines for every person. Given that everyone's PD is a bit different, having a personalized therapy strategy can dramatically affect exactly how well the therapy succeeds [8].
- **Observing signs:** Specific gadgets have the capacity to continually keep an eye on a person's tasks. These devices' details can be utilized by computer systems to forecast when a person's signs and symptoms can get worse. This aids in medical professionals' prep work and prompt monitoring for the correct therapy [2].
- **Advancing medical professionals:** These formulas offer additional assistance to medical professionals in their restorative decision-making. After assessing a plethora of information, they make suggestions concerning what may be most reliable for every person. This assists in doctors' decision-making pertaining to the very best strategy [24].
- **Determining new clues:** These formulas can recognize brand-new info by assessing all the information that might help doctors get a much better understanding of PD [7]. They can recognize fresh indicators of health issues and make sensible restorative suggestions [19].

Figure 14.2 outlines ethical concerns related to the use of healthcare data and AI applications. "Responsibility and Oversight" received the highest score of 6.1, emphasizing the critical importance of establishing clear accountability and governance in AI-driven healthcare systems. Close behind, "Protecting Patient Privacy" scored 5.5, reflecting strong concerns about individual confidentiality and data protection. "Addressing Bias and Fairness" received a rating of 4.9, underscoring the need to ensure equity and minimize algorithmic bias in AI-based decision-making. Meanwhile, "Ensuring Informed Consent" scored 3.7, pointing to room for improvement in ensuring that individuals fully understand how their data are being used in AI applications. Lastly, "Transparency and Explainability" was rated 3.8, indicating a demand for greater clarity in how AI algorithms function and the rationale behind their outputs. Typically, the assessments expose that healthcare companies understand the moral problems that emerge when making use of customer info to notify AI-driven solutions. They furthermore determine the prompt demand for strong structures that can both relieve these problems as well as take full advantage of the benefits of AI in medical care.

14.9 CONCLUSION

The research findings demonstrate that there is a great deal of capacity for improving individual end results and increasing our expertise of PD via the use of monitored discovering formulas in medical diagnosis and therapy of the disease. Very early discovery, personalized treatment, responsive condition monitoring, professional choice assistance, and biomarker recognition are simply a few of the benefits that these formulas give. Monitored discovering formulas aid medical professionals in detecting individuals a lot more precisely, personalizing therapy routines to satisfy each individual's demands, and properly anticipating exactly how conditions will proceed by analyzing a selection of information resources and recognizing patterns and partnerships.

Future growths in monitored understanding formulas are expected to thrust a lot more progression in the recognition and therapy of PD. To enhance medical diagnosis accuracy and therapy effectiveness, future developments could utilize brand-new information resources consisting of hereditary sequencing, electronic biomarkers, and patient-reported end results. Additionally, the production of choice assistance devices and interpretable AI designs will certainly progress visibility and self-confidence in professional decision-making treatments.

Furthermore, to attend to concerns like information personal privacy predisposition along with moral factors to consider and to ensure responsible and moral use of AI innovation in medical care, teamwork among scientists, doctors, clients, and market stakeholders is vital. With each other, we can completely utilize supervised knowing formulas to transform the methods by which PD is dealt and improve the lifestyles of those who suffer from the disease.

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15 Comparative Analysis of Supervised and Unsupervised Learning Algorithms in the Detection of Alzheimer's Disease

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15.1 INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and a range of other neurological symptoms that interfere with daily life. It is the most common cause of dementia among the elderly, accounting for about 60–80% of dementia cases globally [1, 2]. The prevalence of AD is increasing rapidly due to the aging population, with an estimated 50 million people affected worldwide, a number projected to triple by 2050. In the United States alone, approximately 5.8 million people are affected with AD, with a new diagnosis every 65 seconds. The disease poses a significant public health challenge, not only due to its high prevalence but also because of the substantial emotional and financial burden it places on patients, families, and healthcare systems [3].

The diagnosis of AD currently relies on a combination of clinical evaluation, neuropsychological testing, and imaging techniques [4–6]. The primary diagnostic criteria include a thorough assessment of the patient's medical history, mental status, and physical examination. Neuropsychological tests are essential for evaluating cognitive functions, such as memory, attention, language, and problem-solving abilities. Invasive diagnostic methods include cerebrospinal fluid (CSF) analysis, which involves measuring the levels of amyloid-beta and tau proteins, biomarkers strongly associated with AD pathology [7]. Noninvasive methods encompass neuroimaging methods such as magnetic resonance imaging (MRI) and positron emission tomography (PET), which provide critical information about brain structure and function [8]. MRI can detect brain atrophy, while PET scans can identify amyloid plaques and glucose metabolism patterns. However,

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these traditional methods have limitations, including invasiveness, high costs, and limited availability, prompting the need for more accessible and efficient diagnostic approaches.

In recent years, machine learning (ML) has become an invaluable tool for improving the diagnosis of a wide range of human diseases, including respiratory, neuro, heart, infectious diseases, noninfectious diseases, and deficiency diseases [9–16]. ML methods are also used for the detection of AD by analyzing complex datasets, including neuroimaging, genetic information, and clinical data. Supervised learning techniques, which are trained on labeled datasets, have shown great potential in classifying different stages of AD and distinguishing it from other forms of dementia. For instance, convolutional neural networks (CNNs) have been widely used in analyzing MRI and PET images, achieving high accuracy in identifying brain regions affected by AD. A study by Wen et al. showed that a CNN model could classify AD with an accuracy of 89% using MRI data, outperforming traditional methods [17]. Other supervised techniques, such as support vector machines (SVMs) and random forests, have also been employed to analyze biomarkers and genetic data, contributing to the early detection and progression monitoring of AD [18–21].

Unsupervised learning algorithms, which do not require labeled datasets, have also been applied in AD research to uncover hidden patterns and structures in the data [22]. Various techniques like clustering and dimensionality reduction have been used to identify subgroups of patients with similar disease characteristics and progression patterns. For example, the use of principal component analysis (PCA) has allowed researchers to reduce the dimensions of complex datasets, facilitating the identification of significant features related to AD [23, 24]. Additionally, clustering methods such as k-means and hierarchical clustering have been found effective for grouping patients based on similar cognitive and biological profiles, aiding in the personalized treatment of the disease. The recent approach by Zhang et al. demonstrated the utility of unsupervised learning in discovering novel biomarkers for AD by analyzing multimodal data, including genetic, neuroimaging, and clinical information [25].

This chapter provides a comprehensive comparison and analysis of supervised and unsupervised learning algorithms in the detection of AD. The objective is to assess the pros and cons of each approach, highlight the most effective algorithms, and discuss their potential for clinical implementation. This chapter is relevant as it synthesizes the latest research findings, providing a valuable resource for researchers and clinicians aiming to improve diagnostic accuracy and patient outcomes. The chapter is organized as follows: the first section reviews the fundamental aspects of AD and its traditional diagnostic methods. The subsequent sections discuss supervised and unsupervised learning approaches, respectively, providing detailed analyses of recent studies and methodologies. Finally, the chapter concludes with a discussion on the future directions and potential of ML in AD, along with practical recommendations for integrating these technologies into clinical practices.

The objectives of the work include

- Comparing supervised and unsupervised learning algorithms for detecting AD
- Evaluating the effectiveness of various ML models in AD diagnosis

- Identifying the advantages and limitations of different ML approaches
- Discussing the potential for clinical implementation of ML techniques
- Outlining future directions and opportunities in AD research using ML

15.2 ML METHODS

The application of ML in detecting AD has become increasingly prominent, as it offers the ability to analyze large datasets and identify patterns that might not be apparent through conventional statistical methods. The techniques used in this domain are primarily divided into supervised and unsupervised learning algorithms, each offering unique advantages for the analysis and prediction of AD progression.

15.3 SUPERVISED LEARNING METHODS

Supervised learning is a foundational concept in ML where the primary objective is to learn a mapping from input data to output labels based on a labeled dataset. This learning process involves a training stage where the algorithm is fed a dataset consisting of input–output pairs. The inputs, also known as features, are variables that describe the data, while the outputs, or labels, represent the target variable that the model intends to predict [26, 27]. This type of learning is classified into two main tasks: classification and regression. While classification involves predicting discrete labels, such as whether an email is genuine or spam, regression involves predicting continuous values, such as the price of a house, given its features. The working of supervised ML methods is shown in Figure 15.1.

A variety of algorithms fall under supervised learning, each having specific strengths and applications. SVMs are robust classifiers that work well in high-dimensional spaces and are particularly effective when the number of dimensions exceeds the number of samples [28]. Decision trees and their ensemble methods like random forests are another popular choice, especially valued for their interpretability and ability to handle both categorical and continuous data [29]. Random forests improve on this by constructing multiple decision trees and merging their results to

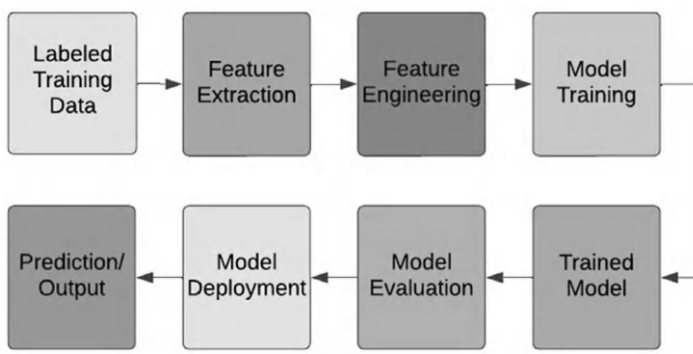

FIGURE 15.1 Working of a supervised machine learning method.

enhance accuracy and control overfitting. K-nearest neighbors (KNN) is a nonparametric method utilized for tasks such as classification and regression [30]. Logistic regression, despite its name, is a powerful classifier and models the probability of a discrete outcome, which is particularly useful for binary classification problems [31]. Naive Bayes, a probabilistic classifier based on Bayes' theorem, assumes independence between the features, which often works surprisingly well even when the independence assumption is violated [32].

Supervised learning's power lies in its ability to build predictive models that are highly accurate and interpretable [33]. The availability of labeled data allows these algorithms to learn complex relationships and make precise predictions. In the medical field, supervised learning algorithms are extensively used for diagnostic purposes, like predicting the likelihood of a disease based on patient data [34–38].

15.4 UNSUPERVISED LEARNING METHODS

In contrast to supervised learning, unsupervised learning deals with unlabeled data. Unsupervised learning intends to uncover the underlying structure or patterns within the data without the guidance of a known outcome variable [39]. Since the data lack labels, the algorithms must infer the natural groupings or relationships directly from the input features. This type of learning is primarily exploratory, aiming to provide insights into the data's intrinsic properties. Two primary tasks in unsupervised learning are clustering and dimensionality reduction. Clustering deals with grouping similar data points together, whereas dimensionality reduction involves reducing the feature size while retaining as much information as possible [40–42]. Working of unsupervised learning is depicted in Figure 15.2.

Clustering algorithms are a fundamental aspect of unsupervised learning. K-means clustering is among the simplest and most widely used clustering methods. It splits the data into "k" clusters. Here, every data point would belong to the cluster with the nearest mean, serving as a prototype of the cluster [43]. Hierarchical clustering is another popular method, which builds a hierarchy of clusters either by progressively merging smaller clusters (agglomerative)

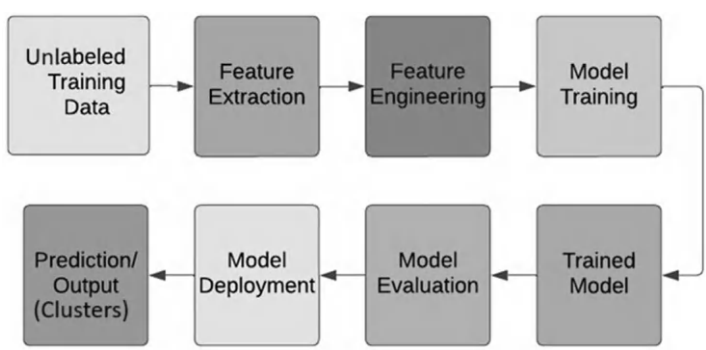

FIGURE 15.2 Working of an unsupervised machine learning method.

or by recursively splitting larger clusters (divisive) [44]. Density-Based Spatial Clustering of Applications with Noise (DBSCAN) is a more advanced clustering technique that groups data points that are closely packed together and marks points that lie alone in low-density regions as outliers [45]. Dimensionality reduction is another crucial aspect of unsupervised learning, especially useful in high-dimensional datasets where visualization and computation can become challenging. PCA is a commonly used method that transforms the data into a new coordinate system, where the largest variance by any projection of the data lies on the first coordinate (the first principal component), the second largest variance on the second coordinate, and so on [46, 47]. t-Distributed Stochastic Neighbor Embedding (t-SNE) is another dimensionality reduction method that excels at preserving the local structure of the data, making it especially effective for visualizing complex datasets in a reduced-dimensional space. In healthcare, unsupervised learning can help identify patient subgroups with similar characteristics, leading to more personalized treatment plans [48–50].

15.5 SUPERVISED LEARNING ALGORITHMS FOR DETECTING AD

Supervised learning algorithms have been instrumental in the early detection of AD by leveraging labeled datasets to identify patterns and biomarkers related to the condition. The general structure of supervised learning algorithms in AD detection is shown in Figure 15.3. These models can classify patients based on imaging data, genetic information, and cognitive test scores, providing valuable support for early diagnosis and treatment planning. Table 15.1 shows different approaches from literature that utilized supervised learning techniques for AD detection.

15.5.1 SVMs

In connection with AD detection, SVMs are particularly useful for handling high-dimensional data, such as neuroimaging data. SVM works by identifying the hyperplane that most effectively separates the data into distinct classes – in this case, identifying patients with AD, mild cognitive impairment (MCI), or normal cognitive function [57]. The algorithm tries to maximize the margin between the classes, which aids in the reduction of the error of misclassification. SVM is statistical supervised

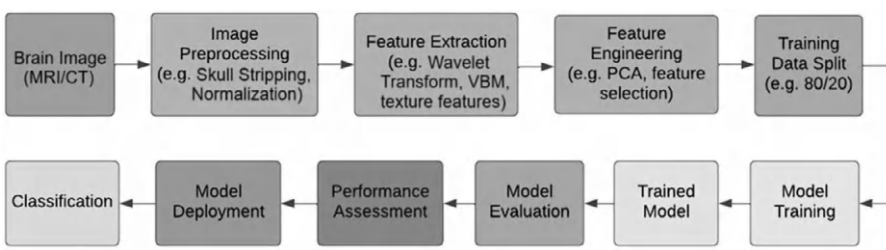

FIGURE 15.3 Supervised learning algorithms in AD detection based on brain images.

TABLE 15.1
Studies with Supervised Learning Algorithms for Alzheimer's Disease Detection

Author Year	Dataset	Method	Accuracy (%)	Sensitivity (%)	Specificity (%)	Reference
Liu et al. (2014)	77 HC, 65 AD	Stacked autoencoder + softmax	87.76	88.57	87.22	[34]
Li et al. (2015)	52 HC, 51 AD	RBM + drop out, SVM	91.4	–	–	[18]
Ortiz et al. (2016)	68 HC, AD 70	Ensemble of deep belief networks	90	86	94	[51]
Jha and Kwon (2016)	44 HC, 51 AD	PCA-KNN	89.47	94.12	84.09	[52]
Rabeh et al. (2016)	50 HC, 8 AD	Decision tree	90.66	–	–	[20]
Aderghal et al. (2017)	228 HC, 188 AD	CNN	83.7	79.16	87.2	[53]
Khedher et al (2017)	229 HC, 188 AD	ICA–SVM	89.5	92.4	86.6	[19]
Korolev et al. (2017)	61 HC, 50 AD	3D-CNN	80	–	–	[54]
Valliani and Soni (2017)	233 HC, 188 AD	ResNet	81.3	–	–	[55]
Bi et al. (2018)	35 HC, 25 AD	Random SVM cluster	94.44	–	–	[21]
Lin et al. (2018)	229 HC, 188 AD	ROI-based CNN	88	–	–	[56]
Zeng et al. (2018)	92 HC, 92 AD	SDPSO-SVM	81.25	–	–	[57]
Raza et al. (2019)	232 HC, 200 AD	DNN, SVM	98.74	98.5	98.21	[58]
Kruthika and Maheshappa (2019)	137 HC, 178 AD	Gaussian naive Bayes classifier + SVM + KNN	96.31	91.27	89.9	[36]
Richhariya et al. (2020)	228 HC, 187 AD	USVM -RFE	89.2	84.87	93.13	[59]
Liang and Gu (2020)	68 HC, 81 AD	ADGNET with attention	98.71	98	99.24	[60]
Wen et al. (2020)	330 HC, 336 AD	PCA, extreme learning machine, CNN	88.79	–	–	[17]
Li et al. (2022)	226 HC, 186 AD	FSNet	84.4	83.6	85.9	[61]
Kim et al. (2022)	61 HC, 37 AD	DBAD CNN model	87.1	93.3	85.5	[62]
Zeng et al. (2023)	92 HC, 92 AD	DBN-based multitask learning	98.62	–	–	[63]

Notes: HC = healthy control; AD = Alzheimer's disease; CNN = convolutional neural network.

learning algorithms designed to solve linear classification tasks, effectively distinguishing between two distinct groups of data, as outlined in Equation (15.1).

$$f: R^m \rightarrow R \tag{15.1}$$

Given a set $S = \{(x_1, y_1), \ldots, (x_n, y_n)\}$, where $x_i \in R^m$ and $y_i \in \{+1, -1\}$, using a linear function:

$$f(x) = w^T x + b = \sum_{i=1}^{n} w_i x_i + b \tag{15.2}$$

A hyperplane is identified within the variable space that divides the two classes, ensuring the maximum possible separation margin M

$$M = \frac{2}{\|w\|}$$

The primary goal of the SVM is to maximize the margin M by minimizing the objective function:

$$\begin{aligned} &\min \frac{1}{2}\|w\|^2 + C\sum_{i=1}^{m}\zeta_i \\ &s.a.\ y_i\left(w^T x_i + b\right) \geq 1 - \zeta_i, \zeta_i \geq 0 \end{aligned} \tag{15.3}$$

where ζ_i denotes the distance from hyperplane to misclassified points, $\zeta_i \geq 0$, w is the support vector, y is the category, and C is a regularization parameter to regulate the overfitting [38]. Li et al. demonstrated an approach to detect AD using a dataset comprising 52 healthy control (HC) individuals and 51 patients diagnosed with AD [18]. They employed a hybrid approach combining restricted Boltzmann machines (RBMs) with a dropout technique, followed by an SVM classifier. RBM, an unsupervised learning algorithm, was utilized to extract high-level, relevant features from the data by learning a probabilistic model. After feature extraction, these distilled features were then fed into an SVM, which was used to classify the individuals as either HC or AD. This combination of deep feature learning through RBM and robust classification with SVM resulted in a notable accuracy of 91.4%, demonstrating the efficacy of their method in distinguishing between healthy controls and AD patients.

15.5.2 Decision Trees

Decision trees are a straightforward and interpretable method for supervised classification tasks. They function by recursively splitting the dataset based on feature values, creating a tree-like structure where each node represents a feature, each branch

corresponds to a decision rule, and each leaf indicates an outcome [29]. The entropy and information gain calculation formulas follow:

$$Entropy = -\sum_{i=1}^{c} P_i log_2 P_i \tag{15.4}$$

where P_i is the probability of class i, and c is the total number of classes.

$$Information\ Gain = Entropy - [(weighted\_average \times entropy(each\_attribute)] \tag{15.5}$$

In AD detection, decision trees can help identify key biomarkers or clinical features that differentiate between AD, MCI, and healthy controls. The simplicity of decision trees makes them easy to interpret, which is crucial in a clinical setting where understanding the decision-making process is important. However, decision trees are prone to overfitting, especially with noisy data, which can be mitigated by techniques such as pruning or using ensemble methods like random forests. Rabeh et al. conducted a study using a decision tree algorithm to distinguish between HC individuals and those with AD [20]. They utilized a relatively small dataset consisting of 50 HC participants and eight AD patients. Despite the limited sample size, the decision tree method proved to be effective, achieving an accuracy rate of 90.66%.

15.5.3 KNN

KNN is a nonparametric, instance-based learning algorithm employed for tasks such as classification and regression. The KNN algorithm classifies a sample based on the majority class of its k-nearest neighbors in the feature space [29]. For a designated positive integer K, the KNN algorithm identifies the K nearest observations to a test point and computes the conditional likelihood of x belonging to a certain class, labeled as j using the equation

$$P\left(Y = j \mid X = x\right) = \frac{1}{K} \sum_{i \in A} I\left(Y^{(i)} = j\right) \tag{15.6}$$

where x is the test point, X is the feature matrix, and Y the class labels.

In AD research, KNN can be applied to different types of data, including neuroimaging and genetic data, to classify patients into various diagnostic categories. The choice of k, the number of neighbors, is crucial as it affects the algorithm's bias-variance trade-off. KNN is simple and effective in instances where the relationship between the input data and the output class is complex.

In their study, Jha et al. applied PCA along with a KNN algorithm to classify individuals into two categories: normal controls (NC) and AD patients [52]. The dataset comprised 44 NC subjects and 51 AD patients. The use of PCA helped in reducing

the dimensionality of the data, allowing the model to focus on the most significant features that differentiate the two groups. The subsequent application of the KNN algorithm yielded promising results. The model achieved an accuracy of 89.47%, which indicates that it correctly classified the majority of the cases. Moreover, it demonstrated a high sensitivity of 94.12%, meaning it was very effective in correctly identifying the AD cases. The specificity was 84.09%, showing a reasonable ability to correctly identify the NC cases.

15.5.4 Ensemble of Deep Belief Networks

The ensemble of deep belief networks (DBNs) is a powerful approach in the field of M:, especially in the realm of deep learning, where multiple DBNs are trained and then combined to improve the accuracy and robustness of predictions [51, 64, 65]. A DBN is a variant of a deep neural network comprising multiple layers of RBMs or autoencoders, where each layer learns to represent the data in increasingly abstract ways. The ensemble method involves training several DBNs independently and then aggregating their predictions, typically through averaging or majority voting, to reach a final decision. The advantage of using an ensemble of DBNs lies in the "wisdom of the crowd" effect, where the combination of multiple models can often outperform a single model by reducing the risk of overfitting and increasing generalization. Each DBN in the ensemble may capture different aspects of the data, and their combined output can smooth out the variability that might affect a single network.

In their study, Ortiz et al. utilized an ensemble of DBNs to differentiate between 68 NCs and 70 patients with AD [51]. The research aimed to leverage the strengths of ensemble learning in enhancing the accuracy as well as reliability of detecting AD, a task that requires discerning subtle and complex patterns in neuroimaging or other diagnostic data.

15.5.5 CNNs

CNNs are a variant of the supervised learning method popularly employed in the detection of AD due to their ability to automatically extract and learn hierarchical features from medical imaging data [54, 56, 66, 67]. The structure of CNN includes convolutional layers, pooling layers, and fully connected layers, which makes them particularly well suited for analyzing visual data such as MRI scans, PET scans, and even functional MRI (fMRI) [68]. For AD detection, CNNs are trained on labeled datasets containing brain scans from both AD patients and healthy controls. During the training phase, CNNs learn to identify complex patterns and biomarkers associated with AD, such as atrophy in specific brain regions or abnormalities in brain activity [69–71]. CNNs are particularly effective in this domain because they can handle the high-dimensional nature of imaging data and automatically extract relevant features, eliminating the need for manual feature engineering. Recent studies have depicted the efficacy of CNNs in accurately diagnosing AD. For instance, by leveraging large, well-annotated datasets

such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), researchers have achieved impressive results, with some models reaching accuracies exceeding 90%. Furthermore, CNNs can also be fine-tuned or adapted for various stages of ADs, potentially aiding in early diagnosis, monitoring disease progression, and even identifying individuals at risk of developing AD. Aderghal et al. utilized a dataset comprising 228 healthy controls and 188 AD patients to evaluate the effectiveness of CNNs for AD detection. The CNN model achieved an accuracy of 83.7%, demonstrating its capability to distinguish between AD and non-AD cases [53]. Furthermore, the model attained a sensitivity of 79.16% and a specificity of 87.2%, indicating a relatively high ability to correctly identify true positives and true negatives, respectively.

15.6 UNSUPERVISED LEARNING ALGORITHMS FOR DETECTING AD

Unsupervised learning algorithms are used to find hidden patterns or intrinsic structures in unlabeled data. In the context of AD, these methods can be used to discover subgroups of patients, detect outliers, or reduce the dimensionality of the data for further analysis. Table 15.2 shows different studies that utilized unsupervised learning algorithms in the detection of AD. Unsupervised learning methods, particularly clustering, are invaluable in AD research for discovering new disease phenotypes and understanding the heterogeneity of the disease [35, 37]. By uncovering distinct patient groups, researchers can tailor treatment approaches and improve diagnostic accuracy.

15.7 K-MEANS CLUSTERING

This technique partitions the data into k clusters such that each data point belongs to the cluster with the nearest mean. It is commonly used for segmenting patients into different diagnostic categories based on similarities in clinical and imaging data [42, 43]. However, k-means requires the specification of the number of clusters in advance and is sensitive to initial cluster center placement.

Al-Nuaimi et al. conducted a study utilizing k-means clustering to differentiate between healthy controls and AD patients [40]. The dataset comprised eight healthy controls and three AD patients. Through this unsupervised learning technique, they achieved an accuracy of 84.6%. Notably, the model demonstrated perfect sensitivity (100%), meaning it successfully identified all AD cases. However, the specificity was relatively low at 50%, indicating a higher rate of false positives, where healthy individuals were incorrectly classified as having AD. This highlights the model's ability to detect AD with high sensitivity but suggests a need for further refinement to reduce false positives and improve overall specificity. Liu et al. utilized a combination of PCANet and k-means clustering to analyze a dataset consisting of 231 healthy controls and 198 AD patients [24]. The approach obtained an accuracy of 84.17%, indicating a reasonably good performance in distinguishing between HC and AD.

TABLE 15.2
Studies with Unsupervised Learning Algorithms for Detecting Alzheimer's Disease

Author Year	Dataset	Method	Accuracy (%)	Sensitivity (%)	Specificity (%)	Reference
Tong et al. (2014)	234 HC, 198 AD	Multiple instance learning	89	84.9	92.6	[35]
Al-nuaimi et al. (2015)	8 HC, 3 AD	K-means clustering	84.6	100	50	[40]
Kumar et al. (2018)	145 HC, 68 AD	K-means	85.5	–	–	[72]
Ju et al. (2017)	79 HC, 91 MCI	Autoencoder based on unsupervised learning	86.47	92	81	[37]
Lazli et al. (2019)	50 HC, 45 AD	Possibilistic FCM clustering	93.65	90.08	92.75	[73]
Razavi et al. (2019)	52 HC, 51 AD	Sparse filtering and soft max regression	98.3	–	–	[74]
Bi et al. (2020)	307 HC, 243 AD	Two-sample t-test, PCANet, k-means++	89.15	–	–	[23]
Mallik and Zhao (2020)	–	DBSCAN and hierarchical clustering	92.9	–	–	[41]
Shin et al. (2020)	–	GAN with discriminator-adaptive loss fine-tuning	94.1	94	–	[75]
Baydargil et al. (2021)	148 HC, 25 AD	Unsupervised adversial deep learning	96.03	–	–	[50]
Jin et al. (2021)	530 HC, 202 AD	Variational autoencoder, generative adversarial network, and multilayer perceptron	94	99	94	[49]
Zhang et al. (2021)	287 HC, 159 AD	CMC: consensus multiview clustering	57.26	–	–	[25]
Cabreza et al. (2022)	755 HC, 622 AD	Generative adversarial network	74.44	73.86	–	[76]
Shi et al. (2022)	83 HC, 57 AD	Generative adversarial network with multiple losses	92.9	–	–	[48]
Liu et al. (2023)	231 HC, 198 AD	PCANet, k-means	84.17	79.65	88.05	[24]
Zhang et al. (2024)	–	Generative adversarial network with pyramid attention blocks	89.9	82.5	85.9	[77]

15.8 POSSIBILISTIC FCM CLUSTERING

Possibilistic Fuzzy C-Means (PFCM) clustering is an advanced variant of the traditional Fuzzy C-Means (FCM) algorithm, designed to handle data uncertainty and ambiguity, which is particularly useful in medical image analysis, like the detection of AD [78–80]. Unlike traditional clustering methods, PFCM assigns membership probabilities and possibility values to data points, allowing for a more flexible and robust classification, especially in cases where data may not clearly belong to one cluster. In the context of AD detection, PFCM can be used to analyze neuroimaging data, such as MRI or PET scans, by clustering different brain regions or patterns of atrophy and providing a nuanced classification that accounts for the inherent uncertainty in clinical diagnoses [81]. This approach can improve the distinction between healthy controls, MCI, and AD patients, leading to better diagnostic accuracy and more personalized treatment planning. In the study by Lazli et al., the PFCM clustering method was applied to classify a dataset of 50 HC and 45 AD cases [73]. The results demonstrated high performance, with an accuracy of 93.65%, meaning the method correctly classified 93.65% of all cases.

15.9 HIERARCHICAL CLUSTERING

Hierarchical clustering is a popularly used method for organizing data into a hierarchical structure based on similarities or distances between data points. In AD detection, hierarchical clustering can be instrumental in analyzing and classifying patient data to reveal patterns indicative of the disease [82–84]. This method typically employs two approaches: agglomerative and divisive. The agglomerative approach begins with each data point as its own cluster and progressively merges the closest clusters using a distance metric, such as Euclidean distance, until all points are combined into a single cluster or a predefined number of clusters is reached [85]. In contrast, the divisive approach starts with all data points in a single cluster and iteratively divides this cluster into smaller clusters until each point is isolated or the desired number of clusters is achieved [86]. In the context of AD detection, hierarchical clustering has been utilized to identify distinct patterns and groupings within patient data, such as neuroimaging, genetic profiles, or cognitive assessments. For example, studies have shown that hierarchical clustering can differentiate between AD and healthy controls by analyzing features from structural MRI scans [87–89].

15.10 DBSCAN

DBSCAN is a clustering algorithm that groups data points based on their density, making it particularly useful for identifying clusters of varying shapes and sizes in complex datasets [41]. In the context of AD detection, DBSCAN can be an effective tool for analyzing patient data to uncover patterns and classify cases [90, 91]. Unlike hierarchical clustering, which relies on a hierarchical structure of clusters, DBSCAN focuses on the density of data points to form clusters. The

algorithm operates by identifying clusters as regions of high density separated by regions of low density. It uses two key parameters: the radius (ε) within which to search for neighboring points, and the minimum number of points required to form a dense region (MinPts). Points within dense regions are grouped into clusters, while points in sparse regions are labeled as noise or outliers [92]. In AD research, DBSCAN has been applied to different types of data, including neuroimaging, genetic, and clinical data, to identify distinct patterns related to the disease. For instance, DBSCAN has been used to analyze structural MRI scans to detect abnormal brain regions associated with AD [41].

15.11 GENERATIVE ADVERSARIAL NETWORKS

Generative adversarial networks (GANs) are a type of ML framework created to generate new data samples that mimic a given dataset [93, 94]. They consist of two neural networks – a generator and a discriminator – engaged in a competitive process. The generator creates synthetic data samples, while the discriminator evaluates them against real data samples, providing feedback to the generator. This adversarial process continues until the generator produces samples indistinguishable from real data [95].

In the context of AD detection, GANs can be leveraged to enhance diagnostic processes and research. One application is in generating synthetic neuroimaging data, such as MRI scans, to augment existing datasets. This is especially useful in cases where data are scarce or imbalanced, as GANs can create high-quality, realistic images that can be used to train more robust diagnostic models [96].

15.12 DISCUSSION

The comparative analysis of supervised and unsupervised learning techniques in AD detection reveals their respective strengths and limitations in addressing the complexities of this neurodegenerative disorder. Supervised learning algorithms, such as SVMs and neural networks, rely on labeled datasets to train models, achieving high accuracy when substantial annotated data are available. For example, while SVMs are effective in high-dimensional spaces, often benefiting from feature selection techniques, neural networks, particularly CNNs, excel in analyzing complex neuroimaging data like MRI and PET scans [53, 67]. These models offer robust performance in classification tasks but are heavily dependent on the quality and quantity of labeled data, which can be challenging to acquire in the context of AD due to its variability and the effort required for data annotation.

In contrast, unsupervised learning algorithms, such as clustering methods and dimensionality reduction techniques, offer valuable insights into the intrinsic structure of AD-related data without relying on predefined labels [72–75]. Hierarchical clustering and DBSCAN, for instance, reveal underlying patterns and groupings within neuroimaging and genetic data, which can uncover novel disease subtypes or biomarkers not readily apparent through supervised learning. Dimensionality reduction methods like PCA and t-SNE aid the visualization and interpretation of high-dimensional data, highlighting key features associated with AD progression.

Despite their advantages, unsupervised methods face challenges such as difficulty in interpreting clusters, the potential for overfitting to noise, and the lack of ground truth for performance evaluation.

Combining supervised and unsupervised approaches can leverage the strengths of both methods, offering a more comprehensive understanding of AD [24]. Integrative methods that combine multimodal data, such as neuroimaging and genetic information, can further improve diagnostic accuracy and predictive power. Moreover, techniques like transfer learning and domain adaptation can help bridge the gap between different datasets, enhancing the generalizability of models and their applicability across diverse populations [55]. Addressing ethical considerations related to data privacy, consent, and algorithmic bias is also crucial for the responsible use of ML in healthcare. By addressing these challenges and leveraging the complementary strengths of supervised and unsupervised learning, researchers and clinicians can advance the field of AD detection and improve diagnostic and therapeutic strategies for this debilitating condition.

15.13 CONCLUSION

The comparative analysis of supervised and unsupervised learning methods shows the potential and limitations of each approach in the detection and understanding of AD. Supervised learning methods, such as SVMs and neural networks, offer high accuracy and reliability when trained on extensive, labeled datasets, making them effective for precise classification tasks. However, their dependence on large volumes of annotated data and susceptibility to overfitting highlight the need for enhanced data collection and regularization techniques. On the other hand, unsupervised learning algorithms, including clustering methods and dimensionality reduction techniques, provide valuable insights into the underlying structure of AD-related data and reveal novel patterns and biomarkers without requiring labeled examples. These methods facilitate the exploration of complex, high-dimensional datasets but face challenges in cluster interpretation and performance validation. Integrating supervised and unsupervised approaches can leverage the strengths of both, offering a more comprehensive understanding of AD and improving diagnostic and therapeutic strategies. Future research should focus on combining multimodal data, enhancing model interpretability, and addressing ethical considerations to advance the field.

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16 Deep Learning Techniques in Neurological Disorder Detection

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16.1 INTRODUCTION

Neurological problems affect people of all ages. The prevalence of these disorders has significantly risen over the past four to five years. In numerous instances, there are no detectable tools for diagnosing neurological disorders. A primary cause of these disorders is electrical abnormalities in the brain. Today, various neurological disorders can be diagnosed using advanced technologies such as electroencephalogram (EEG), magnetic resonance imaging (MRI), computed tomography (CT) scans, and positron emission tomography (PET) scans. In previous years, machine learning (ML) algorithms were primarily used to analyze neuroimaging data when datasets were small. However, with larger datasets, deep learning (DL) has become necessary.

Parkinson's disease (PD), schizophrenia (SZ), and Alzheimer's disease (AD) are three prevalent neurological conditions [1]. AD is observed by increasing mental decline; it usually affects elderly persons as a result of specific brain regions deteriorating. Extensive research has been undertaken to accurately identify the causes of this degeneration and develop automated methods for detecting degeneration patterns in neuroimages. It ranks as the fourth leading contributor to mortality worldwide, following heart disease, cancer, and brain hemorrhage. AD has three states: very mildly demented, mildly demented, and moderately demented [2] (see Figures 16.1–16.3).

In the very mildly demented stage, patients begin to forget where they have kept their belongings and may have difficulty remembering recently learned names. In the mildly demented stage, patients have difficulty remembering words, often get lost even on familiar routes, and show a decrease in focus and work abilities. In the moderately demented stage, they begin to forget recent activities and significant past events, struggle with budgeting, find it difficult to go outside alone, and experience a loss of empathy [3].

Tremors, bradykinesia, stiffness, and unstable posture are among the motor signs of PD disease, a neurodegenerative condition brought on by the loss of

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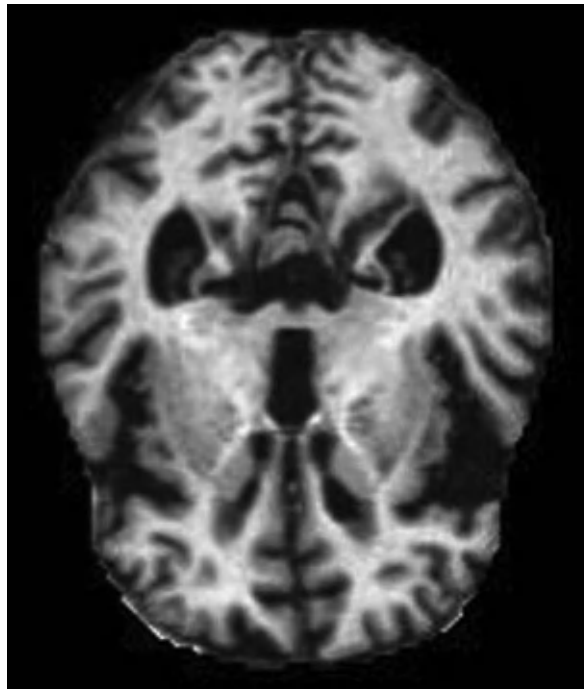

FIGURE 16.1 MRI of a mildly demented patient.

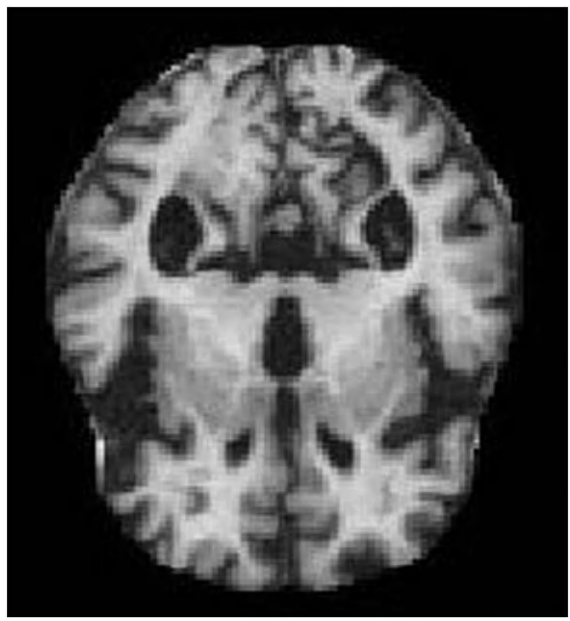

FIGURE 16.2 Moderately demented.

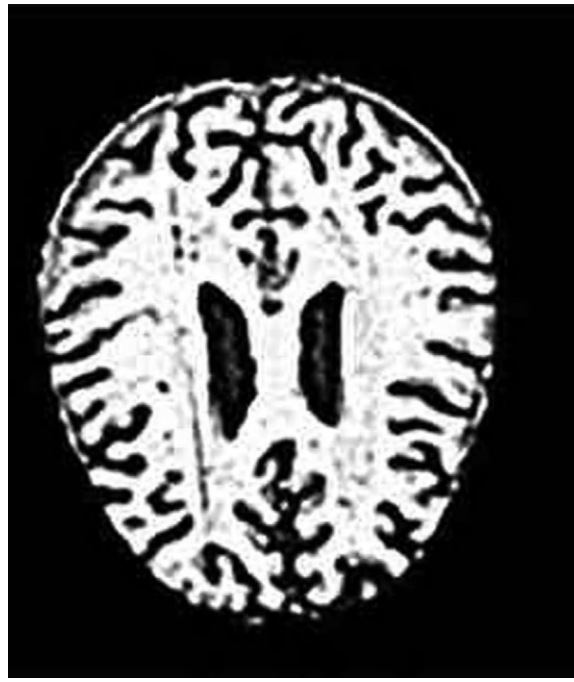

FIGURE 16.3 Very mildly demented.

dopaminergic activity. PD is the second foremost neurological disease affecting older persons [4]. The exact cause of the disease remains unknown. PD has high rates of mortality and requires early diagnosis and proper treatment to alleviate personal, social, and national burdens. Two imaging techniques commonly utilized to detection are PET and single photon emission computed tomography (SPECT). Table 16.1 presents an overview of the procedures followed in recent research that employed statistical and ML methods to forecast the presence of PD from MRI data.

Schizophrenia is a chronic mental condition that impacts around 1% of the population globally. According to a World Health Organization (WHO) report, around 24 million individuals around the world, or roughly one in every 300, are affected by schizophrenia (0.32%). The incidence is higher among adults, at one in 222 (0.45%). Schizophrenia is not very common compared to several other mental diseases. It typically begins in adulthood or in the 20s, usually men suffering it sooner than women. Some schizophrenia symptoms may be explained by difficulties with the neurological system's corollary discharge process, which may make it difficult for patients to distinguish between internally and externally produced feelings. The exact cause of schizophrenia remains unknown, but factors such as stressful life events, drug use, and their combinations have been proposed to have contributed to its growth. Neuroimaging is crucial for revealing both functional and structural changes in the human brain. Individuals with

TABLE 16.1
An Overview of the Procedures Followed in Recent Research that Employed Statistical and ML Methods to Forecast the Presence of PD from MRI Data

Reference	Input Data	Active Method	Accuracy (%)
[5]	PD (57)	Voxel-based morphometry (VBM), diffusion tensor imaging (DTI)	100
[6]	PSP (21)	Support vector machine (SVM)	
[7]	PD (27)	Functional connectome	80
	HC (38)	SVM	
	HC (26)		
[8]	PPMI cohort	Connectivity measures	93
	PD (374)	SVM	
	HC (169)		
[9]	PD (30)	Region of interest based	86.67
	HC (30)	SVM	

schizophrenia often face human rights breaches in both treatment facilities and the community. People with this illness experience social exclusion, and relationships with family and friends suffer as a result of the solid and pervasive stigma against them. Due to discrimination brought on by this stigma, they may have fewer options for housing, work, education, and general healthcare. Structural MRI of brain anatomy offers a reliable method for diagnosing schizophrenia. In the domain of medical imaging, convolutional neural networks (CNNs) have shown to be beneficial instruments for the automated diagnosis of a variety of neurological disorders, including schizophrenia. Millions of people worldwide suffer from schizophrenia, which has a major negative impact on both individuals and society. Early and correct diagnosis is critical to effective treatment and management. However, clinical evaluations and manual brain scan interpretation are significant components of traditional diagnostic techniques, which can be inconsistent and error-prone. The development of CNNs, which use DL to recognize complex patterns in MRI images that may be suggestive of schizophrenia, has made a potent substitute available.

The motivation of this chapter is to address the limitations of traditional MRI analysis in diagnosing neurological disorders and to explore how DL can revolutionize this field. Conventional approaches often struggle with accuracy, scalability, and efficiency, leading to unreliable diagnostic results.

The objective of this chapter is achieved through the following subtasks:

i. Compare DL methods with traditional MRI analysis for diagnosing schizophrenia, PD, and AD.
ii. Outline each disorder's data preprocessing steps and algorithm choices.
iii. Explore performance analysis of DL in neurological diagnosis and identify challenges in extending these methods to new conditions.

16.2 RELATED RESEARCH

Zhang et al. [10] demonstrated a DL-based strategy for identifying the difference between healthy brains and those with AD. Because AD affects many people, there has been much interest in detecting the condition using MRI and DL. CNNs have been utilized in several works to categorize various AD phases and distinguish them from mild cognitive impairment (MCI) and fit persons. The use of MRI and DL for AD detection has become a primary research focus due to the disease's prevalence and impact. Suk et al. [11] utilized a DL model combining sparse autoencoders and a deep belief network to extract features from MRI images, achieving significant accuracy improvements in AD classification. Payan and Montana [12] developed a 3D CNN to process volumetric MRI data, demonstrating superior performance in detecting early AD stages compared to traditional ML methods. Liu et al. [13] used a multimodal approach integrating MRI with PET data, using a DL framework to enhance the diagnostic accuracy of AD.

In [14], the authors applied a CNN to structural MRI scans, focusing on the substantia nigra region, which is critical in PD pathology. Their model obtained significant accuracy as well as specificity in identifying PD patients from fit persons. Pereira et al. [15] used resting-state functional MRI (fMRI) data, CNNs could distinguish PD patients and healthy controls, yielding encouraging findings. MRI-based DL has showed promise in detecting and diagnosing schizophrenia, a complicated psychiatric condition with various symptoms. Vieira et al. [16] created a deep neural network (DNN) to examine brain connection patterns in fMRI data. Their approach distinguished between patients with and without schizophrenia.

16.3 SUMMARY OF DL TECHNIQUES

Recent developments in neuroimaging modalities, including PET, magnetoencephalography (MEG), and MRI, have improved our knowledge of how the brain functions. Numerous machine and DL approaches, along with high-performance computer tools, have made diagnosing and classifying neurological diseases possible. PD has been identified in MRI scans using various ML approaches, such as SVM, artificial neural networks (ANN), decision tree (DT) models, and Bayes algorithms. The symptoms of PD frequently begin on one side of the body and may be related to asymmetries in the brain's cortical or subcortical systems [17]. Table 16.2 summarizes recent research employing MRI techniques to predict PD using ML methodologies. Supervised learning approaches are practical for ML applications such as regression, classification, pattern recognition, and feature extraction. Neurological problems involve the entire body, including the brain, spinal cord, and nerves, according to scientific classifications. Three prevalent neurological ailments include PD, AD, and mental disorders, such as schizophrenia. In this context, computational intelligence algorithms, particularly DL techniques, have emerged as powerful tools for automating the analysis of medical images and improving the accuracy of neurodisorder diagnosis. Currently, various DL approaches are being used to study and cure neurodiseases. These include neural networks such as ANN, DNN, Autoencoder (AE), CNN, probabilistic neural networks (PNN), K-nearest neighbors (K-NN), recurrent neural networks (RNN), and long short-term memory (LSTM).

TABLE 16.2
Different DL Techniques for Detecting Neurodisorders

Model	Description	Application
ANN (Artificial Neural Networks)	ANN technique simulates the brain and nervous system's electrical activity.	Network Architecture, language translation, sentiment analysis, and speech recognition.
Convolutional Neural Networks	CNN has shown impressive outcomes in image segmentation, detection, and classification tasks.	Image classification, image segmentation, medical image analysis, etc.
LSTM and Recurrent Neural Networks (RNNs)	RNNs, including LSTM variants, are instrumental in analyzing sequential data, such as time-series electroencephalogram (EEG) recordings or longitudinal patient data.	Language modeling, speech recognition, sentiment analysis, machine translation, text generation, etc.
Generative adversarial network (GAN)	GANs are used to produce synthetic data that approximately resemble real patient image. This capability is valuable for data augmentation, enhancing the robustness of DL models in neuroimaging tasks.	Data generation, style transfer, super-resolution, text-to-image synthesis, etc.
Graph neural network (GNN)	GNNs are tailored for analyzing complex networks, such as brain connectivity networks derived from MRI or diffusion tensor imaging (DTI) data.	Social network analysis, drug discovery, traffic prediction, knowledge graph reasoning, etc.
Pretrained models and transfer learning	Transfer learning techniques, utilizing pretrained models on large-scale datasets, enable the transfer of knowledge from related tasks to neurodisorder classification and prediction.	Image classification, object detection, speech recognition, medical image analysis, bidirectional encoder representations from transformers (BERT) (for natural language processing [NLP], residual neural network (ResNet) (for image classification), etc.
K-Nearest Neighbors (K-NN)	The K-NN approach is mostly utilized for regression and classification applications.	Image recognition, medical diagnosis, pattern recognition

16.4 CONVOLUTIONAL NEURAL NETWORK (CNN)

Convolutional, pooling, and fully connected are the three components of a CNN, which is a mathematical process. Features are removed from the input data and placed in the convolutional layer. The pooling layer automatically reduces the dimensionality of the data by applying filters. The fully linked layer maps the retrieved characteristics to the final output.

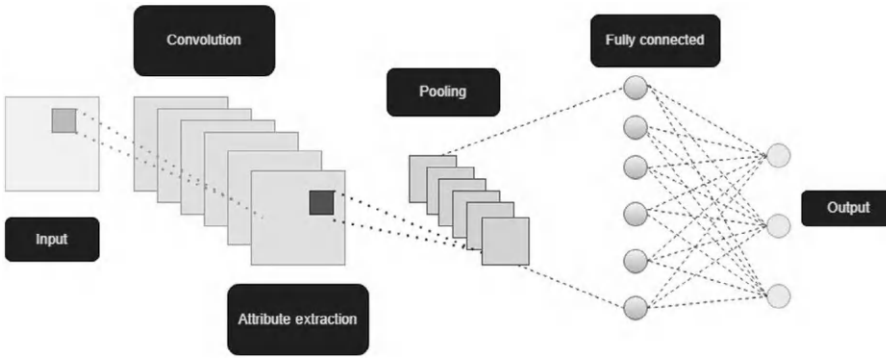

FIGURE 16.4 CNN architecture diagram.

CNNs are very helpful since they automatically recognize features, saving human labor. The term "convolution" in CNNs describes a mathematical procedure in which two functions are multiplied to produce a third function that shows how the shape of one function is changed by the other. The CNN model used for feature extraction aims to reduce a dataset's feature count. It is mostly applied to unstructured datasets (such as pictures and videos) and creates new features that contain the data from the initial features. The CNN architecture diagram in Figure 16.4 depicts the numerous layers involved in this process.

Fully connected, activation, pooling, and convolutional layers are all part of a CNN's structure. Convolutional layers create feature maps by applying a series of learned filters to their inputs. Each feature map's neurons are connected to a particular group of neurons in the receptive field – a small portion of the previous layer – to guarantee that the entire image is captured. A nonlinear activation layer usually comes after convolutional layers. Next, by reducing the spatial dimensions of their inputs, pooling layers help to prevent overfitting by lowering the number of parameters and computations. Models for MRI can be created using a range of CNN architectures, including LeNet, AlexNet, VGGNet, GoogLeNet, ResNet, and ZFNet.

16.5 RECURRENT NEURAL NETWORK (RNN)

Because of their highly nonlinear dynamic mapping, RNNs (Figure 16.5) are helpful for several tasks, such as forecasting, control, optimization, and spatiotemporal pattern classification. RNNs are networks of various instances of an identical architecture, each passing information to the subsequent instance sequentially.

RNNs' hidden state, which keeps particular details about a sequence, is their primary and most important characteristic. Because the network needs to implement similar operations on every input behind the hidden layers to produce the output, every input utilizes the same parameters. Because RNNs have a memory that maintains records of their current state, they are suitable for time-series signal prediction, such as RNN. EEGs do not require knowledge of the artifacts of an EEG signal in

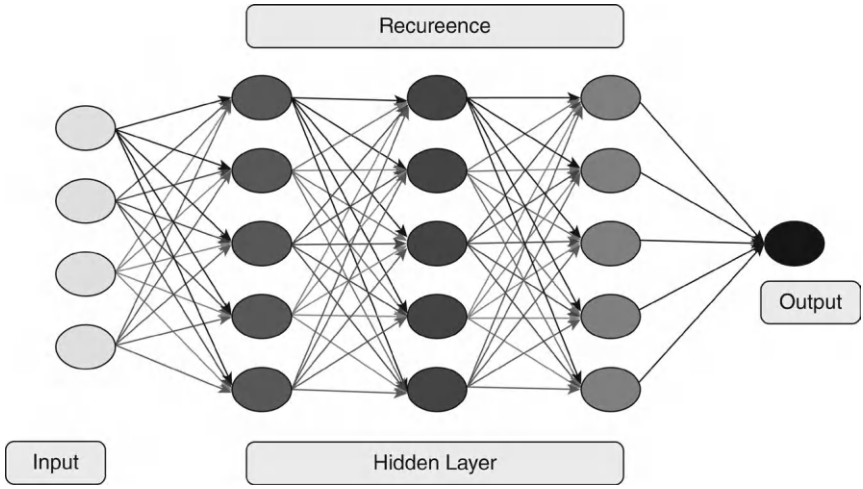

FIGURE 16.5 RNN.

order to filter any signal. The primary objective is to assess the temporal order of data points using calculations from earlier sequences.

16.6 DNN

A neural network with a specific degree of complexity is called a DNN, or Deep Net (see Figure 16.6). Deep Neural Network (DNN) learning approaches have been applied to complex problems across various fields, including image recognition, such as detecting cracks in pavements [18]. An improved method for improving the data flow rate of an event-related potential-based brain–computer interface combines two stimuli with a CNN. A DNN includes more layers than an ANN.

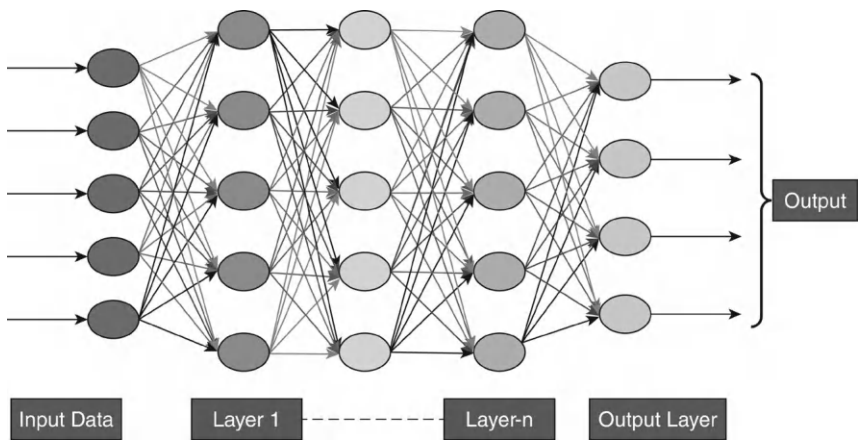

FIGURE 16.6 DNN.

A DNN is a neural network that has many nodes in each of its many hidden layers. A neural network's layers use a series of nonlinear transformations to process the input data, permitting the network to learn complex data representations. DL entails creating algorithms that can predict and learn from complex data.

16.7 DEEP BELIEF NETWORK (DBN)

DBNs are made to recognize and pick up patterns in massive databases automatically (see Figure 16.7). Imagine them as multilayered networks, where each layer builds upon the knowledge from the previous one to create a more thorough understanding of the data. Each DBN layer aims to separate distinct features from the incoming data. DL using probabilities that are unsupervised is known as DBN. There are two main stages in which DBNs function: pretraining and fine-tuning. Layer by layer, the network learns to represent the input data during the pretraining stage. The network learns the inputs' probability distribution during the pretraining phase, which helps it understand the underlying data structure. Backpropagation is frequently used in this procedure, where the network's effectiveness is evaluated on the job, and any failures are used to change the network's parameters. DBNs employ a mix of mathematical techniques.

The DBNs principles, merging probability theory with neural network architectures. Restricted Boltzmann machines (RBMs) are based on probabilistic graphical models. In a DBN, RBMs are stacked on top of each other, where one RBM's hidden layer serves as the subsequent RBM's visible layer. Every RBM within the DBN operates as an energy-based model, retaining an energy value to characterize

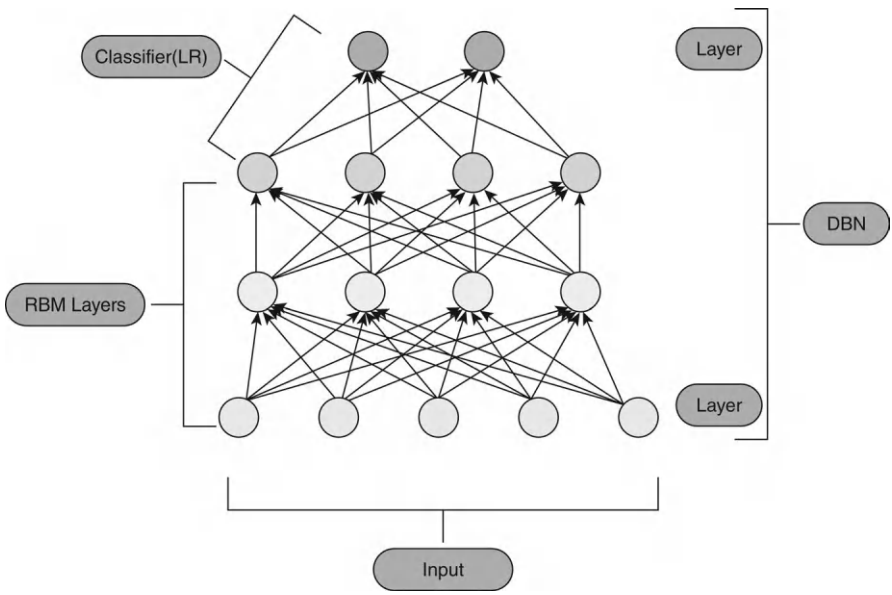

FIGURE 16.7 DBNs.

the relationship between its hidden and visible units. Lower energy corresponds to a higher probability of association between the units. The RBM constructs a credible representation of the original image by minimizing the energy value across the entire network.

16.8 AUTOENCODER

Autoencoders (AEs) are unique algorithms that can autonomously learn compact representations of input data without requiring labels (see Figure 16.8). An AE is a neural network developed to learn how to reconstruct images, text, and other data from their compressed representations. It is composed of two components: an encoder and a decoder. The encoder transforms the input data into a lower-dimensional representation (referred to as "encoding"), and the decoder layer restores the original dimensions of the encoded data. AEs are especially helpful in noise reduction, feature extraction, compression, and similar tasks. Denoising AEs, sparse AEs, and contractive AEs are the three main categories of AE.

AEs serve as a data augmentation method, where the restored images are used as augmented data, thereby creating additional training samples. The sparse AE type of autoencoder usually has more hidden units than input units, but only a few are permitted to be active at any given time. This characteristic is known as network sparsity. In the sparse AE design, there are more hidden units than input units, but only a certain number of hidden units can be active at any given time. An explicit regularization is incorporated into the objective function of a contractive AE, which forces the model to learn a function resilient to small changes in input values.

16.9 PROBABILISTIC NEURAL NETWORK (PNN)

PNNs address classification difficulties (see Figure 16.9). Using a Parzen window and a nonparametric function, the PNN approach predicts each class' parent probability distribution function (PDF). Next, the PDF function determines the likelihood of a fresh input data point.

Furthermore, the new input data are allocated to the class having the greatest posterior likelihood via Bayes' rule. This method is widely applied in supervised and

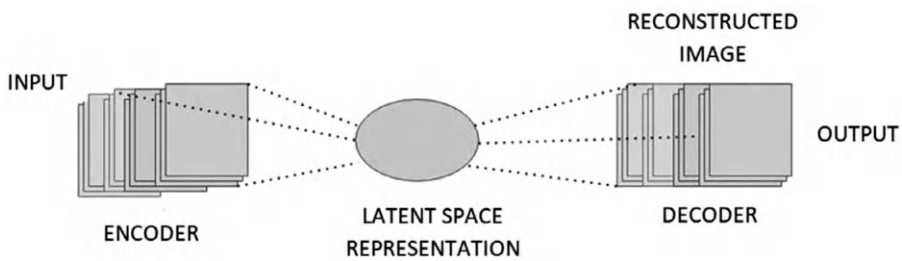

FIGURE 16.8 Autoencoder.

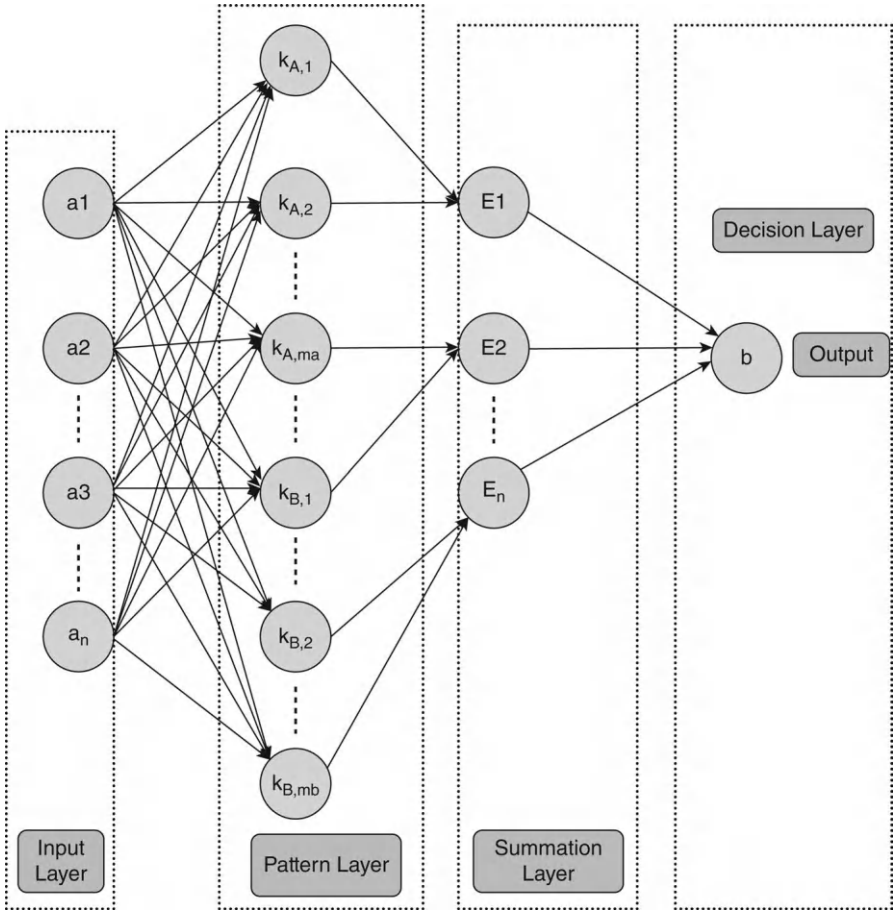

FIGURE 16.9 Probabilistic neural networks.

ML applications to estimate class-conditional densities. The widespread adoption of PNNs stemmed from the use of kernel functions for discriminant analysis and pattern recognition. The four layers of the PNN architecture are comprised of input, output, and summation layers. The input layer contains the characteristics of data points (or observations). The pattern layer computes the class-conditional PDF. The summation layer handles interclass patterns.

16.10 ANN AND MULTILAYER PERCEPTRON (MLP)

ANNs have driven many recent breakthroughs in AI, such as voice recognition, image recognition, and robotics (see Figure 16.10). For instance, ANNs can recognize hand-drawn digits in image recognition tasks. An ANN comprises three or more interconnected layers. The initial layer contains input neurons that forward data to the subsequent layers. These deeper layers then process the data and send the

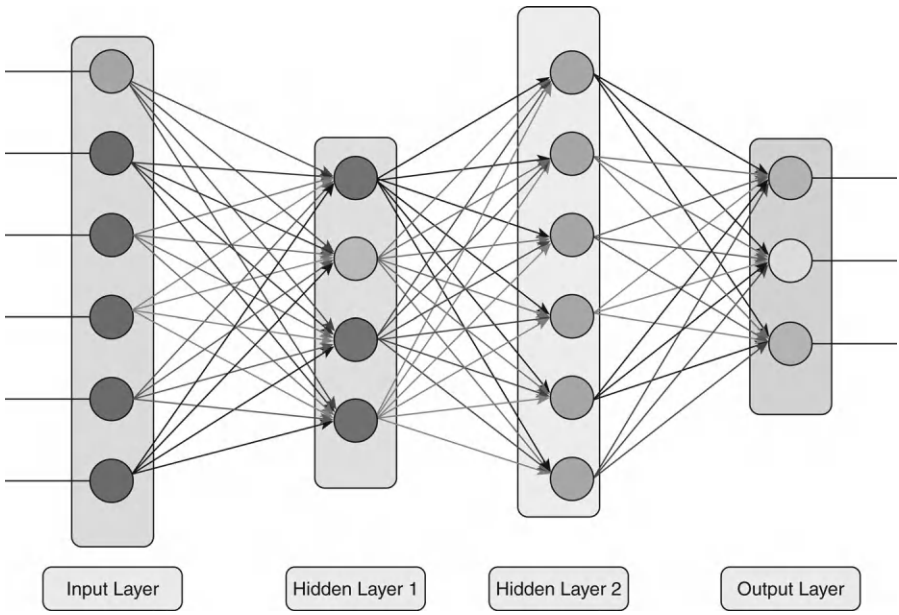

FIGURE 16.10 Artificial neural network.

final output to the last output layer. A simplest feedforward neural network is a type of ANN and can have multiple or no hidden layers. However, a multilayer perceptron (MLP) specifically includes at least one hidden layer.

16.11 KNN

The KNN approach (see Figure 16.11) is utilized for both classification and data regression tasks, however it is more commonly used for classification. Its premise is based on the assumption that similar data points are frequently found close together in the feature space.

The KNN algorithm establishes the class or value of a given data point through a majority vote or an average of the numerical values of its K-nearest neighbors. Thanks to this flexible approach, the algorithm can adjust to different patterns in the data and can also predict things according to the regional configuration of the dataset.

16.12 PREPROCESSING METHOD FOR PREPARING DATA

The preprocessing stage is crucial for preparing experimental data for additional statistical analysis and improving its quality. Many MRI scan modalities from different sources can introduce various noises, such as motion artifacts, signal intensity variations, and spatial distortions, which need to be eliminated to guarantee reliable analysis.

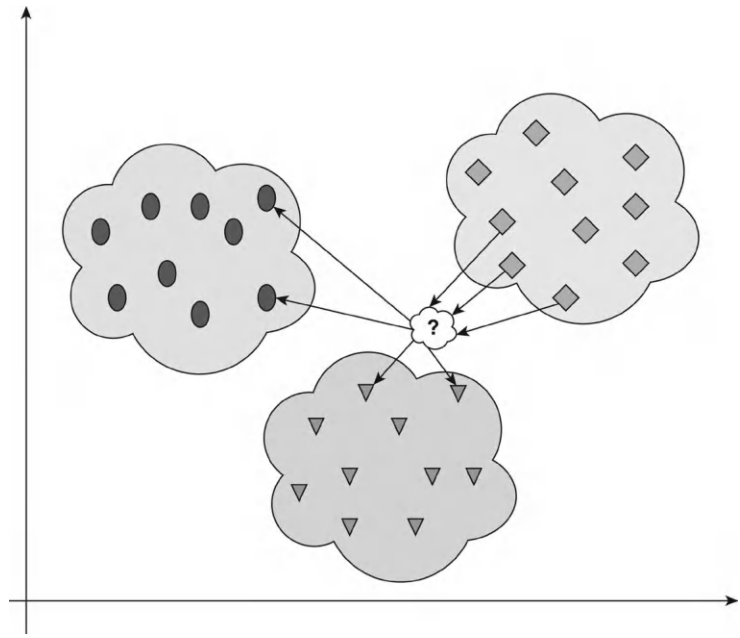

FIGURE 16.11 The K-NN classifier.

16.12.1 Noise Reduction

Noise reduction techniques improve the quality of images by removing unnecessary noise while retaining important diagnostic information. Numerous DL approaches have been developed to reduce noise in medical photos. CNN-based denoising algorithms eliminate noise from new input images by analyzing noise distributions in pairs of noisy and clean images. Prominent CNN structures for denoising are ResNet, U-Net, and DenseNet. GANs are another approach to denoising.

16.12.2 Image Registration

Image registration involves aligning and matching multiple medical images of the same or different individuals to compare, evaluate, and integrate data. Image registration is a process of geometric transformation that aligns various images into a standard coordinate system. Linear registration and nonlinear registration are two types of registration algorithms. DL-based registration methods often involve training a neural network to predict deformation fields or transformation parameters for picture alignment purposes

16.12.3 Image Segmentation

CNN-based segmentation approaches leverage the neural network's ability to withdraw hierarchical features from input data, resulting in the generation of

segmentation maps on a pixel-by-pixel basis. In traditional CNNs, the fully connected layers are substituted with convolutional layers to facilitate dense pixel-wise predictions [19].

16.12.4 Correction

Motion correction and slice timing correction are critical preprocessing techniques for addressing slice-dependent delay concerns. Slice timing correction (STC) is a preprocessing method that adjusts for slice-dependent delays. It is performed by changing each slice's time series to bring all slices temporally into alignment with a reference time point. Most fMRI investigations capture slices individually, resulting in timing differences of several seconds between data from various slices. Two basic methodologies for STC have been developed: data shifting and model shifting. Data shifting is the most widely used technique, in which recorded points are corrected to reflect their proper offset from the stimulation time. Model shifting is a postprocessing technique. The hemodynamic response function's (HRF) expected location differs when the model is shifted. The FEAT tool of the FMRIB Software Library (FSL) can also be used to correct slice timing. Head motion is the primary source of error in fMRI studies, and various strategies have been developed to address this issue. Motion correction can also be done using the MCFLIRT module from the FSL [20, 21].

16.12.5 Stripping/Trimming

Skull removal or brain extraction is an essential preprocessing step for removing nonbrain tissues from brain MRI data. Automated skull stripping is a useful tactic for improving data analysis speed and accuracy. One popular tool from the FMRIB Applications Library is the Neurological Extraction Tool.

16.12.6 Normalization (NM)

In image processing, normalization is adjusting the range of pixel intensity values in an image. This is often done to ensure that images are consistent in brightness and contrast, facilitating better comparison and analysis. Through data standardization, normalization can enhance the efficiency of different image processing algorithms. Intensity normalization is crucial for image analysis involving multiple subjects or time points to ensure comparability across images. White Stripe normalization may be more effective and provide better interpretability than whole-brain normalization for subsequent lesion segmentation algorithms and analyses.

Intensity normalization is a commonly used technique to reduce data variance, with methods ranging from uniformity transformation to histogram equalization. Spatial normalization (SN) is a transformation process used to account for these differences by aligning a set of brain features to those derived from a standard brain template.

Spatial normalization is one stage in image processing, precisely an image registration technique. Spatial normalization attempts to distort brain scans so that a particular location in one is representative of the various sizes and shapes of human brains.

One method of data normalization that helps with outliers is called Z-score normalization. Z-score normalization entails modifying each value in a dataset to make the standard deviation equal to one and the overall mean equal to zero. This is accomplished by deducting the mean of the feature from each value and dividing the result by the standard deviation.

Smoothing filters, also known as blurring filters, are a diverse set of image filters frequently used in image processing. They serve the specific functions of noise reduction and elimination of small details. In image processing, filtering is instrumental in tasks such as smoothing, sharpening, and edge enhancement, thereby enhancing the overall quality and contrast of the image. Spatial filtering techniques are applied directly to an image's pixels. A mask is typically defined with a specific size and a central pixel.

16.12.7 Smoothing

Minimizing noise within an image is called smoothing. Image smoothing is a crucial technique in image enhancement, used to eliminate noise from images. In neuroimaging, spatial smoothing is a preprocessing step that lowers noise and artifacts in the data. However, selecting the right smoothing kernel size can be difficult, as it can lead to unintended changes in the finished images and functional connectivity networks. Spatial smoothing aims to address functional anatomical variability that spatial normalization ("warping") has not corrected, thereby improving the signal to noise ratio (SNR). Smoothing filters are utilized to reduce noise and perform blurring operations. A spatially stationary Gaussian filter is used to perform spatial smoothing; the user is required to specify the kernel width in millimeters as the "full width half maximum" (FWHM) [20–22]. The form of this Gaussian kernel resembles a typical distribution curve [23].

16.12.8 Evaluation Metrics

This section presents various evaluation metrics. The true positive (TP) rate was impressive, indicating that the model effectively identified individuals with the disorders. The low false positive (FP) rate further validated the model's specificity, reducing the likelihood of misclassifying healthy individuals as affected. The model's accuracy in identifying nonaffected individuals was validated by the high true negative (TN) rate. Even with these encouraging results, there were some cases where the model could not identify the disorder, according to the low false negative (FN) rate. This underscores the need for further refinement of the neural network architecture by including more diverse training data or adjusting hyperparameters to minimize false negatives and improve the model's overall diagnostic accuracy. The discussion of these results emphasizes the potential and current limitations of using

advanced neural architectures to accurately and reliably detect neurological disorders. Here is some standard performance evaluation metrics used in DL:

Accuracy: The proportion of cases that were accurately predicted to all instances.

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}} \tag{16.1}$$

Suitable for balanced datasets where the number of instances in each class is roughly equal.

Precision: the proportion of all anticipated positives to successfully predicted positive observations.

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \tag{16.2}$$

F-score: The precision and recall weighted average.

$$F - Score = \frac{Recall * Precision}{Recall + Precision} \tag{16.3}$$

Useful for imbalanced datasets where you need to find a balance between precision and recall.

Specificity: Specificity refers to the accuracy with which negative items are detected.

$$Specificity = \frac{TN}{TN + FN} \tag{16.4}$$

Positive entries accurately identified in sensitivity.

16.13 CONCLUSION

Early disease diagnosis remains an active area of research, with many researchers striving to achieve the highest accuracy in detection and diagnosis. DL models have the potential to contribute to the medical field. DL algorithms within different image data have proven effective in diagnosing different diseases. Neurological disorder detection using DL algorithms is discussed in this chapter. Other neurological diseases have been also discussed in this chapter, like schizophrenia, PD, and AD. The chapter examined which DL algorithm can detect neurological disorders more effectively. The chapter is likely to be valuable to researchers working on artificial intelligence (AI) and medical applications in general, as well as ML/DL-based brain illness diagnosis in particular. A detailed discussion of several performance indicators was held to assess the algorithm's efficacy. So, the DL algorithm is a very effective method for diagnosing diseases in the early stages to save human life.

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17 From Data to Diagnosis
Supervised Learning's Impact on Neurodisorder Detection, with a Focus on Autism Spectrum Disorder

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17.1 INTRODUCTION

In the field of machine learning, supervised learning is an essential approach that has a significant impact on the identification and diagnosis of neurological illnesses. This method uses labeled datasets to train algorithms so they can classify or predict new data never seen before. Supervised learning models play a crucial role in the identification of patterns and anomalies linked to neurological illnesses, including multiple sclerosis, Parkinson's disease, and Alzheimer's disease [1] when it comes to neurodisorder detection. In supervised learning, a machine learning model is trained on a dataset in which every instance is associated with a label or result. Through learning from these examples, the model is able to effectively predict or classify fresh data. In neurodisorder detection, this approach is crucial since precise prognoses can have a big impact on patient care and therapy.

Improving the management of neurological illnesses and improving patient outcomes need early identification and detection of neurodisorders [2]. Multiple sclerosis, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis are among the neurodisorders that frequently develop slowly, with early symptoms that may be mild or readily mistaken for other conditions. Early detection is important because it can intervene before the disease progresses to a more advanced level, which can lead to opportunities for more successful treatment, delay the progression of the disease, and improve the overall quality of life for patients. There are more possibilities for controlling a neurodisorder the sooner it is discovered. For example, early diagnosis of Alzheimer's disease permits the use of drugs and nonpharmacological therapies intended to slow cognitive loss and maintain functional abilities. Early intervention might potentially prolong the time that people can remain independent and engage in everyday activities by slowing the progression of symptoms. Similar to this, early detection of Parkinson's disease [3] allows for the development of therapy regimens that can postpone the onset of motor symptoms and improve the efficacy of medications used to manage stiffness, tremors, and other motor deficits.

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Early identification is critical in multiple sclerosis since it can have a substantial impact on the disease's long-term trajectory. Early implementation of disease-modifying medicines has been demonstrated to improve long-term results by lowering the frequency and severity of relapses and delaying the accrual of impairment. Early diagnosis also makes it possible to incorporate lifestyle changes and rehabilitation techniques that can enhance patients' quality of life and help manage symptoms more successfully. Early diagnosis has advantages that go beyond simply treating symptoms right away. By providing knowledge and control over the course of the illness, it enables patients and their families to plan ahead and get proactive support. Early diagnosis allows families to plan ahead and make educated decisions regarding caregiving techniques, treatment alternatives, and other matters. This can provide a clearer approach for controlling the disease and lessen some of the psychological difficulties associated with neurodisorders, such as anxiety and ambiguity. Personalized medicine also appears to benefit from early detection. Genetic studies, biomarkers, and neuroimaging advances are making it possible to diagnose neurodisorders even before substantial clinical symptoms appear. The efficacy of treatment can be greatly increased by creating individualized treatment plans that are specific to the patient and the disorder's features. Genetic screening, for example, can identify those who are more likely to develop specific neurodisorders, enabling early monitoring and the beginning of treatment or preventive actions.

Early diagnosis can also have a big impact on research and public health. Early neurodisorder identification can help to improve our understanding of the disease's processes and course, which is essential for creating novel treatments and interventions. Early-stage data may expedite the search for better treatments and cures by enhancing clinical trial design and assisting in the assessment of novel treatments' efficacy. It can also help with planning and resource allocation for healthcare services so that they better suit the needs of an aging population.

17.2 SUPERVISED LEARNING ALGORITHMS

In order to predict outcomes or categorize input data, supervised learning is a fundamental machine learning technique where the model is trained on labeled data. Creating a prediction model that can make precise judgments or projections based on fresh, unobserved data is the aim of supervised learning [4]. In order to enable the model to understand the relationship between inputs and outputs, this method requires a dataset in which each training sample is matched with an output label.

17.2.1 Support Vector Machines

A supervised learning approach called an SVM is used to determine the optimal border or hyperplane between various classes in a dataset. Regression activities can also be performed with it. To provide the best possible separation, the primary objective of SVM [5] is to design a decision border that optimizes the margin between various classes. A hyperplane is a decision boundary used in support of SVMs that

divides classes. To put it simply, this is a line in two dimensions. It is referred to as a hyperplane in higher dimensions and as a plane in three dimensions. The SVM method looks for the hyperplane that splits the data into two classes as efficiently as possible. The distance between the nearest data points from each class and the hyperplane is known as the margin. This margin should be maximized by SVM. Greater separation between the hyperplane and the data points, indicated by a bigger margin, typically results in improved generalization on fresh data. The data points that are closest to the hyperplane are known as support vectors. These points are essential for determining the hyperplane's orientation and position. They serve as the hyperplane's "support" and have a direct impact on where it is placed.

The SVM steps are as follows

Data preparation: Gather and prepare your information. This entails dividing the dataset into training and testing sets, scaling features, and handling missing values.

Locate the ideal hyperplane: SVMs look for the hyperplane that maximizes the difference between two classes. This is simple with a dataset that is linearly separable. More sophisticated techniques are applied to nonlinear datasets.

Use kernels for nonlinear data: SVMs employ a method known as the "kernel trick" to convert nonlinear data into a higher-dimensional space that has a linear separator. This method is useful when your data cannot be separated into classes using a straight line. When the data can be separated linearly, the linear kernel is utilized.

- *Polynomial kernel*: Uses polynomial functions to map data into higher dimensions.
- *Radial basis function (RBF) kernel*: This useful tool for more intricate boundaries maps data into a higher-dimensional space based on the separation between points.

Train the model: Fit the SVM model to your training set of data to train the model. The best hyperplane will be found by the model, which will then learn to divide the classes.

Make predictions: Based on fresh, untainted data, create predictions using the trained model.

- *Effective in high dimensions*: SVMs are effective for datasets with a large number of features.
- *Versatile*: Through the use of different kernels, SVMs can handle both linear and nonlinear data.
- *Robust to overfitting*: SVMs can be less prone to overfitting, especially in high-dimensional spaces.

17.2.2 K-Nearest Neighbor (KNN)

KNN, a supervised learning technique, is used for classification and regression. KNN [6] estimates the distance between each training point and the test data to

predict the correct class for the test data. The K points closely related to test data should be selected by the following phase. When using the KNN approach, the class with the highest possibility is chosen after calculating the likelihood that the test data will fall into each "K" training data class. If regression is considered, the value is established by the mean of the "K" chosen training points.

The KNN operation may be explained using the following approach:

Step 1: Choose the neighbor with the K-number.
Step 2: The K-number of neighbors' Euclidean distance should be calculated.
Step 3: Based on the estimated Euclidean distance, use the K-nearest neighbors.
Step 4: Count the number of data points in each class among these K-neighbors.
Step 5: Place the new data points in the class with the highest neighbor count.
Step 6: The proposed model is designed.

17.2.3 Decision Tree

A decision-support tool is the decision tree (DT), which utilizes a model of decisions and their probable outputs as a tree. It considers random events' usefulness, resource costs, and outcomes. A DT is a way to show an algorithm solely using conditional control statements. In statistics, DTs are used as a predictive modeling tool. A DT [7] is used to proceed from observations about a feature to judgments about the feature's intended value. Classification trees are tree models with a defined range of possible values for the objective variable. The branches are the classes for the feature combinations that result in those class names, while the leaves represent the class labels. A DT or classification tree frequently labels each interior node (nonleaf) with an input attribute. The title of a class or a probability distribution across the categories attached to each tree leaf indicates that the tree has classed the dataset into either a specific type or a specific probability distribution. This shows that the tree has correctly categorized the dataset.

On both discrete and continuous data, C4.5 is frequently used as a DT. It uses entropy to create the DT from a large training dataset. If $S = (s_1, ..s_i)$ is followed by each sample in the training set of categorized samples, s_i has a p-dimensional vector in it $(x_{1,i}, \ldots x_{p,i})$, which relates to the sample's class and its property values s_i. Subsets of data characteristics that belong to one class or another are separated into subsets. The highest entropy leaves are chosen for the split's conclusion because they have the most information or entropy.

The following regulations are included in C4.5:

- The tree becomes a leaf and is tagged with the class and retrieved if all the cases are present in a single class.
- Compute the critical information from a test performed on every attribute during the calculation of information gain.
- Get the feature to group based on a choice.

17.3 AUTISM SPECTRUM DISORDER (ASD)

ASD is a complex neurodevelopmental condition characterized by a range of symptoms and challenges affecting social interaction, communication, and behavior. This section is an overview of ASD [8] and the diagnostic challenges associated with it. ASD is a developmental disorder that affects how a person thinks, interacts with others, and experiences the world. It encompasses a broad range of symptoms and severity levels, hence the term "spectrum." Common characteristics include difficulties with social communication, repetitive behaviors or interests, and a range of sensory sensitivities. Individuals may also have unique strengths, such as attention to detail or exceptional skills in specific areas.

The diagnostic challenges are as follows

Variability in symptoms: The wide range of symptoms and severity can make it difficult to identify and diagnose ASD consistently. Individuals may present with different combinations of symptoms, making standardization of diagnosis challenging.

Early detection: Early diagnosis is crucial for effective intervention, but detecting ASD in very young children can be challenging. Symptoms may not become fully apparent until later in development, especially in cases where symptoms are less severe.

Diagnostic criteria: The diagnostic criteria for ASD outlined in *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), focus on specific behaviors and symptoms. However, these criteria may not capture the full range of experiences or variations in presentation, leading to potential misdiagnosis or underdiagnosis.

Overlapping conditions: ASD shares symptoms with other developmental disorders, such as attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, and language disorders. This overlap can complicate the diagnostic process and lead to challenges in distinguishing ASD from other conditions.

Cultural and linguistic differences: Cultural and linguistic factors can affect the presentation and perception of ASD symptoms. Differences in communication styles and social norms may influence how symptoms are observed and reported, impacting the diagnosis.

Resource availability: Access to qualified professionals and diagnostic resources can vary significantly. In some areas, there may be limited availability of specialists trained to diagnose ASD, which can delay or impede accurate diagnosis.

Gender differences: ASD is more commonly diagnosed in males than females, which may partly be due to differences in symptom presentation. Females with ASD may exhibit less overt symptoms or present with different characteristics, leading to underdiagnosis or misdiagnosis.

17.4 IMPLEMENTATION OF SUPERVISED LEARNING ALGORITHMS FOR AUTISM SPECTRUM DISORDER

The methodology outlined in this chapter is structured into three distinct phases. The initial phase focuses on addressing missing values [9] within the datasets. The

second phase is dedicated to the process of feature extraction [10], and the final phase involves classification. For this analysis, datasets on ASD are utilized [11], sourced from the University of California, Irvine (UCI) Machine Learning Repository. The datasets encompass different age groups: children, adolescents, and adults. Specifically, the child dataset includes 21 attributes and 292 records in which 141 individuals belong to the positive class, i.e., with ASD, and 151 individuals belong to the negative class, i.e., without ASD; the adolescent dataset contains 21 attributes and 104 records, out of which 63 are positive cases and 41 are negative cases; and the adult dataset comprises 21 attributes and 704 records. Out of 704 records, 189 fall under the positive category and 515 fall under the negative category. Each of these datasets contains missing values, which are handled in the first phase of the methodology. Figure 17.1 depicts the proposed architecture.

The first phase addresses the issue of missing values. In this phase, instances with missing data are excluded, resulting in a dataset with no missing values. The second phase focuses on feature extraction, employing factor analysis as the technique of choice. Factor analysis is a statistical approach used for dimensionality reduction. It aims to explore the underlying structures within a dataset by identifying patterns among observed variables. The primary objective of factor analysis is to reveal latent factors that account for the correlations observed among the variables.

Factor analysis [12] involves several methodical steps to simplify and interpret datasets. The process begins with gathering the dataset and identifying the initial factors along with their loadings on each observed variable. Next, Kaiser's criterion is applied – retaining factors with eigenvalues greater than 1, along with examining the scree plot or considering theoretical implications – to determine which factors to retain. The analysis then employs a rotation method, such as Varimax, to enhance the interpretability of the factors. This rotation aims to achieve a simpler factor structure, with higher loadings concentrated on a fewer number of factors. Following this,

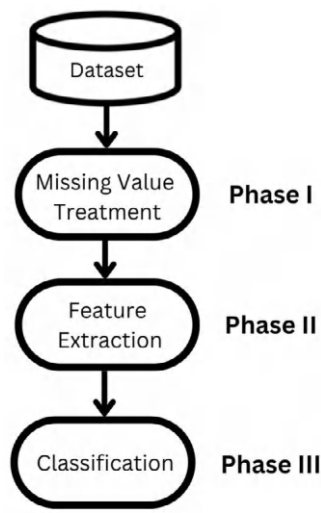

FIGURE 17.1 Proposed architecture for the chapter's methodology.

the factors are interpreted based on the pattern of loadings, with variables showing high loadings on a particular factor, indicating a strong relationship with that factor. Finally, the identified factors are used as a reduced set of dimensions that capture the variance in the original dataset, with factor scores computed to represent individual observations on these dimensions. Through these steps, factor analysis condenses the dataset into a manageable number of features for the classification process.

The third phase of the proposed methodology involves the classification process. In this phase, the features extracted during the second phase are fed into various classification algorithms for prediction. Specifically, DT, SVM, and KNN algorithms are utilized for the analysis. To evaluate the effectiveness of the classification approach [13], performance metrics such as recall, precision, and accuracy are employed. Figure 17.2 depicts the overall framework.

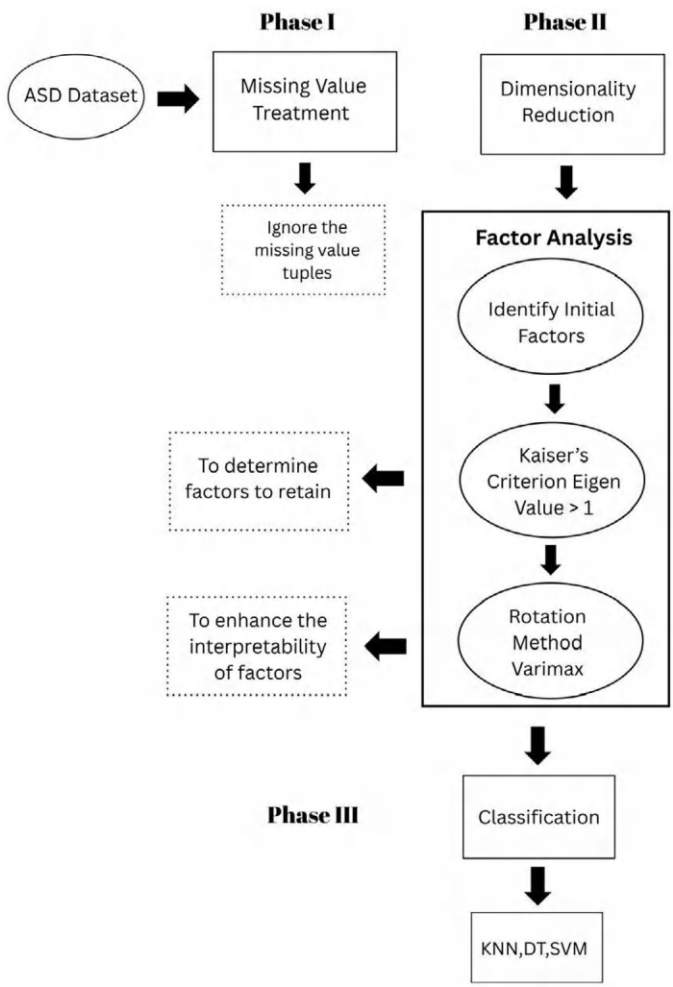

FIGURE 17.2 Overall framework of the classification process.

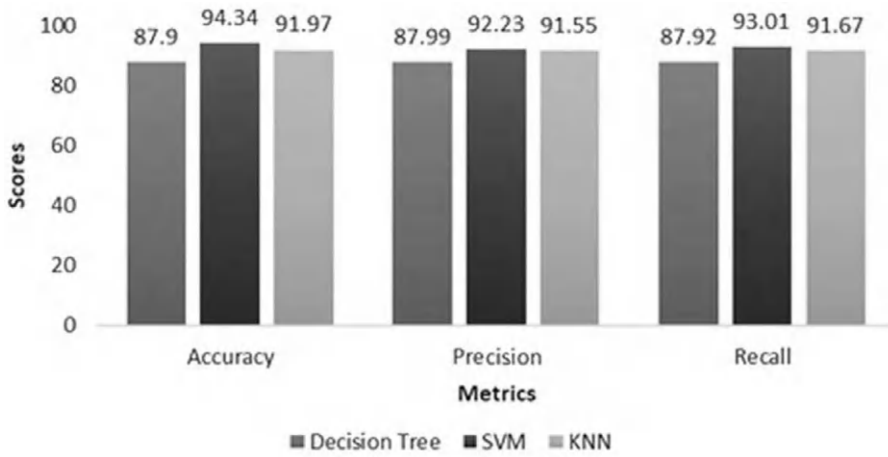

FIGURE 17.3 Performance of the child dataset.

The classifiers are evaluated using bar charts and heat maps. A heat map is a powerful visualization tool for comparing the performance of classifiers across multiple metrics and datasets. It provides a clear and intuitive way to understand how different classifiers perform in various scenarios. A bar chart is a straightforward and effective visualization tool for comparing the performance of classifiers across different metrics and datasets.

For the Child dataset as shown in Figure 17.3, the SVM stands out as the top performer across all metrics. It leads in accuracy (94.34), precision (92.23), and recall (93.01), suggesting it is the most effective classifier for this particular dataset. The KNN algorithm follows closely behind, demonstrating strong performance but falling slightly short of the SVM's scores. The DT, while still effective, consistently ranks lower in all metrics, indicating it might be less suitable compared to SVM and KNN for this dataset.

In the *Adolescent* dataset, SVM again shows superior performance, particularly in precision (92.34) and recall (90.01). The results are shown in Figure 17.4. KNN performs competitively but does not quite reach the levels achieved by SVM, particularly in recall. The DT is less effective across all metrics, with the lowest scores in accuracy, precision, and recall. This suggests that SVM and KNN are better suited for handling the Adolescent dataset.

For the *Adult* dataset, SVM excels in all metrics, achieving the highest values in accuracy (98.34), precision (98.01), and recall (98.67). KNN performs slightly behind SVM, showing high scores in accuracy, precision, and recall. The DT lags behind SVM and KNN. This indicates that SVM is the most effective classifier for the Adult dataset, with KNN also performing exceptionally well, as shown in Figure 17.5.

Overall, SVM generally outperforms both KNN and DT in most scenarios, particularly excelling in precision and recall. KNN shows competitive results, especially in datasets with moderate to high performance, while the DT, despite being a

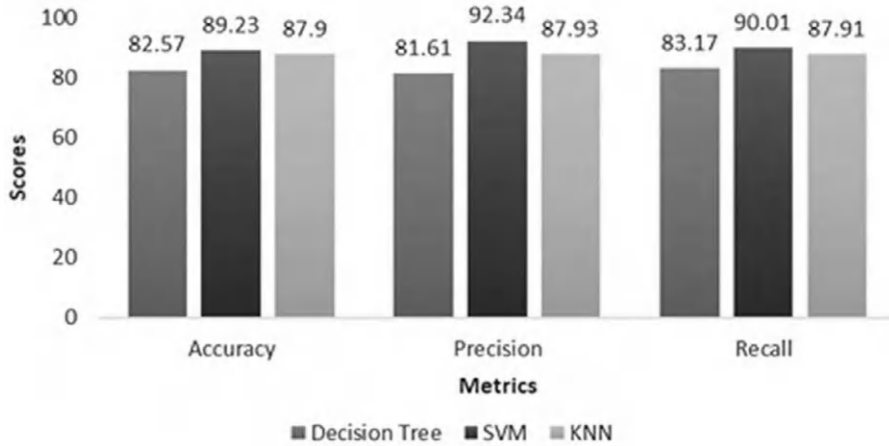

FIGURE 17.4 Performance of the adolescent dataset.

robust and interpretable model, often underperforms relative to the other classifiers in these datasets.

Overall, SVM outperforms DT and KNN in terms of accuracy, precision, and recall across all datasets. It achieves the highest accuracy with scores of 94.34% for the Child dataset, 89.23% for the Adolescent dataset, and 98.34% for the Adult dataset. In precision, SVM again leads with 92.23% for Child, 92.34% for Adolescent, and 98.01% for Adult. Additionally, SVM excels in recall, recording 93.01% for Child, 90.01% for Adolescent, and 98.67% for Adult. While KNN shows strong recall performance, especially in the Adult dataset where it matches SVM, DT falls short, particularly in precision for the Adolescent dataset, as shown in Figure 17.6.

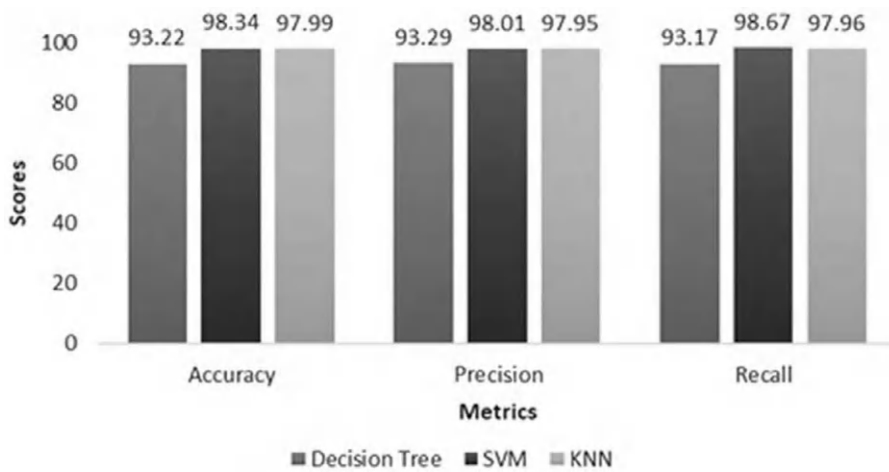

FIGURE 17.5 Performance of the adult dataset.

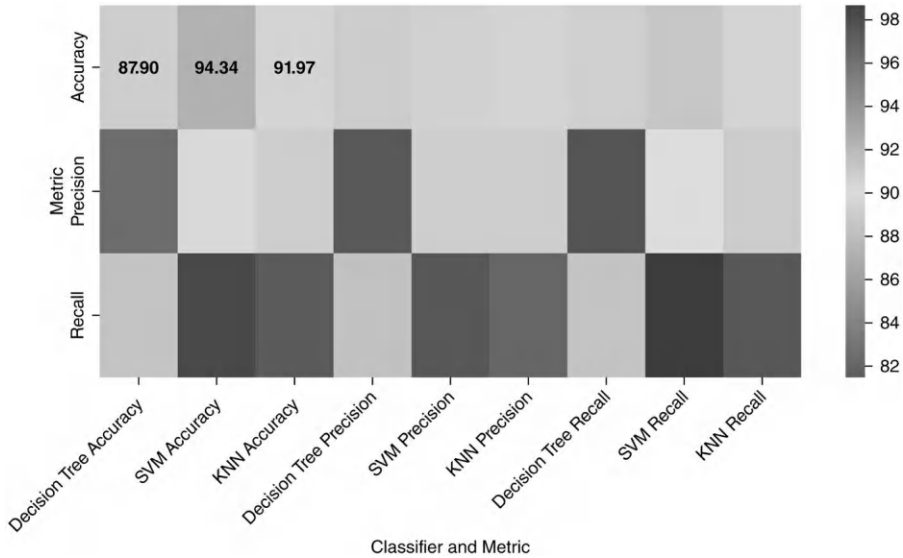

FIGURE 17.6 Performance of classifiers in metrics.

In the Child dataset, SVM leads in accuracy, precision, and recall, surpassing both DT and KNN. For the Adolescent dataset, SVM continues to dominate in all three metrics – accuracy, precision, and recall – though KNN shows a notable gap in precision compared to SVM. In the Adult dataset, SVM delivers the highest scores across all metrics, including accuracy, precision, and recall. Here, DT outperforms KNN, especially in recall, demonstrating a stronger performance relative to KNN.

For the DT classifier, its notable strength lies in achieving better recall compared to KNN in the Adult dataset. However, it generally underperforms relative to SVM across all metrics and datasets, especially in the Adolescent and Child datasets. The SVM classifier, on the other hand, consistently excels in accuracy, precision, and recall across all datasets, showing no weaknesses compared to the other classifiers. KNN demonstrates solid recall performance, particularly in the Adult dataset, but tends to fall short in accuracy and precision when compared to SVM, and occasionally even lags behind DT in the Child and Adolescent datasets.

Overall, the SVM classifier demonstrates superior performance in all metrics across the datasets, making it the preferred model for this particular set of data. The DT model shows more variability but performs well in specific cases, such as the Adult dataset for recall. KNN, while showing decent recall, lags in accuracy and precision compared to SVM and DT.

17.5 CONCLUSION

The importance of early detection and diagnosis in neurodisorders cannot be overstated. It is a critical factor in improving patient outcomes, managing symptoms more effectively, and enhancing the overall quality of life. Early diagnosis not only

provides the opportunity for timely intervention but also empowers patients and families with the information and control necessary for proactive management. It plays a crucial role in the advancement of personalized medicine and public health, contributing to a deeper understanding of neurological diseases and the development of more effective treatments. As research and technology continue to evolve, the ability to detect and diagnose neurodisorders at earlier stages will remain a cornerstone of effective healthcare and patient care. Supervised learning significantly enhances the diagnosis and management of neurodisorders by leveraging labeled datasets to train algorithms for precise pattern recognition and anomaly detection. This approach is crucial for early and accurate identification of conditions such as Alzheimer's, Parkinson's, and multiple sclerosis, where timely intervention can profoundly impact disease progression and patient quality of life. Techniques like SVM, KNN, and DT offer valuable tools for analyzing complex neurological data and improving diagnostic accuracy. Despite challenges, particularly in diagnosing ASD, advancements in machine learning, including personalized medicine and the integration of genetic and neuroimaging data, promise to further refine and enhance early detection and treatment strategies, ultimately leading to better patient outcomes and a deeper understanding of neurodisorders. The analysis reveals that SVM consistently outperforms both KNN and DT across all datasets – children, adolescents, and adults – in terms of accuracy, precision, and recall, demonstrating its superiority as a classifier for ASD detection.

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18 Parkinson's Disease Detection from Drawing Images Using Deep Pretrained Models

Sourabh Shastri, Sachin Kumar, and Vibhakar Mansotra

18.1 INTRODUCTION

Parkinson's disease (PD) is an increasingly common neurological illness that impairs both motor and nonmotor (nonmovement) abilities, hence compromising a person's general quality of life [1–3]. PD is the second-most predominant neurological condition. It is brought on by a breakdown of dopamine-producing neurons in the brain's substantia nigra [4, 5]. Several other reasons, viz. genetic factors, environmental factors, biological factors, pathological factors, and complex interactions, also contribute to the development of Parkinsonian disorder. Although there is no single test to detect PD, there are several techniques that can assist in identifying the illness and enhance sufferers' quality of life. The following techniques are employed: observation, tracking, dopamine transporter imaging (DaTscan), computed tomography (CT) scan, magnetic resonance imaging (MRI), reaction to medicine, physical and neurological tests, and clinical diagnostic criteria. PD patients may have bradykinesia, involuntary shaking, rhythmic movements, problems with balance and stability, and a temporary loss of the ability to begin or continue walking (gait interruption). Conversely, PD's nonmotor symptoms include changes in sensory perception, behavioral abnormalities, and cognitive function deficits. The number of people suffering from PD is increasing gradually and exceeding 10 million worldwide [6–8]. Therefore, the efficacy of novel medications and the quality of medical care for PD patients depend greatly on early diagnosis [9]. To evaluate the fine motor control and coordination in clinical assessments, spiral shape images are drawn by patients on paper to get valuable insights, and this process is also used as a diagnostic tool for assessing PD. These spiral-shaped images differ between healthy individuals and those who suffer from PD. To ensure that the PD patients receive prompt care, it is necessary to have professionals evaluate the drawings of both groups as soon as possible [10–12]. Deep learning (DL) is widely used for diagnosing diseases and achieves high-performance results by utilizing voluminous medical data and complex computational models. By using the DL models, the classification of spiral

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shape images drawn by the individuals having PD symptoms and those who are healthy becomes quite easy and assists healthcare professionals and experts in the early diagnosis of PD disorder among individuals [13–17]. The present study compares the performance measures of the six pretrained DL models – VGG16, VGG19, DenseNet121, DenseNet169, InceptionNetV3, and Xception – in terms of their ability to classify both healthy groups and PD patients.

The present work has made the following principal contributions:

i. The proposed study reduces the likelihood of misdiagnosis and helps in the early identification of Parkinson's illness thanks to DL's processing power.
ii. The work offers a comprehensive performance analysis of these various deep pretrained models on PD data.
iii. The study assists medical practitioners in early PD diagnosis using the best-performed model.

The present work is organized into six sections, beginning from the earlier research in Section 18.2 followed by material and methods in Section 18.3. Additionally, Section 18.4 presents the experiments and findings, and Sections 18.5 and 18.6 explain the current work's discussion and conclusion, respectively.

18.2 LITERATURE REVIEW

This section discusses several studies to detect Parkinsonian disorder using various state-of-the-art methods. Researchers from different parts of the world used different methods for diagnosing PD, including MRI scans, speech and gait signals, electroencephalogram (EEG) and electromyography (EMG) signals, and single-photon emission computerized tomography (SPECT) scans. In addition, researchers have also proposed various methods of diagnosing PD with the help of handwritten images, especially spiral drawings. Several aspects, including kinematic, geometrical, entropic, energetic, temporal, spectral, and nonlinear features, were extracted from the raw datasets using graphical tablets, which were used to analyze handwriting samples. To ascertain the state of PD, several preprocessing, feature selection, and supervised learning strategies have been used in conjunction with machine and DL techniques. [18] worked to diagnose PD early by estimating the changes in handwriting. The dataset about handwritten spirals drawn by the PD patients has been utilized and kinematic features have been extracted from the same. They used XGBoost, AdaBoost, random forest (RF), and support vector machine (SVM) as their four classifiers. With the mutual information gain feature selection approach used, the AdaBoost algorithm fared better than the other algorithms, achieving scores of 96.02%, 91.93%, 100.00%, 100.00%, and 95.79% for sensitivity, accuracy, and precision, respectively. In another study [19], authors used an equal amount of data about spiral and sinusoidal handwritten drawings of PD patients and normal individuals for identifying one of the cardinal signs of PD, i.e., tremor detection.

Analogously, [20] worked on digitized spiral drawings and extracted in-air and on-surface kinematic features using mathematical models. Four machine learning (ML) algorithms, random forest, K-nearest neighbor (KNN), SVM, and logistic

regression, were used to identify PD. Using random forest and logistic regression among others, 91.6% accuracy was obtained. An attempt was made by [21] to diagnose PD at an early stage by differentiating between PD patients and healthy controls using convolutional neural network (CNN) architecture. A total of 87 subjects comprising 58 PD patients and 29 healthy controls of the same age were engaged to draw wire cubes and spiral pentagons, and it was concluded that these two tests have almost the same ability to differentiate PD patients and healthy controls. Two distinct hand-drawn data patterns, spiral, and wave, have been used by [22] for early detection of PD wherein six pretrained models, viz. VGG16, VGG19, ResNet18, ResNet50, ResNet101, and Vit were used. Each of these models was assessed based on three performance criteria: accuracy, precision, and F1 score. Together, the VGG19 model and the recommended model produced the best average accuracy of 96.67% out of all of them. In another study on PD using handwriting-balanced data from 42 subjects, [23] proposed an automatic classification system by applying CNN and CNN–bidirectional long short-term memory (CNN-BLSTM) for PD detection. The CNN-BLSTM model, which was trained utilizing jittering and synthetic data augmentation approaches, had the best results, with an accuracy of 97.62%. It has been proposed to stop the progression of PD by developing an early automated diagnosis technique for the treatment of symptoms using several handwriting datasets and deep transfer learning-based algorithms [24]. When paired with CNN fine-tuned architectures, the usage of data-augmented pictures yields the greatest results, with 99.22% accuracy. A novel method has been proposed by [25] based on the segmentation of online handwritten text into lines. PD early identification has been achieved by using the temporal and spectral characteristics of Arabic online handwriting. Three classifiers that are KNN, SVM, and decision tree (DT) as well as a stratified nested ten-cross-validation were used for the experiments. Of the three classifiers, DT provided the greatest accuracy, at 92.86%. In the same direction, [26] worked on two publicly accessible datasets including PaHaW and NewHandPD of sequence-based dynamic handwriting for the early diagnosis of PD using the combination of one-dimensional (1D) convolutions and bidirectional-gated recurrent unit (Bi-GRU) layers for the classification purpose. The NewHandPD handwriting dataset has been used for the accurate detection of PD by utilizing transfer learning models such as ResNet50, VGG19, and InceptionV3 along with the optimization algorithm, viz. the genetic algorithm, by [27]. The proposed model provided an accuracy of 95.29%, recall of 0.86, precision of 0.98, and area under the curve (AUC) of 0.90.

One of the important symptoms of PD is gait abnormality, i.e., unusual walking patterns, and [28] have worked to build a model for analyzing gait data for the detection of PD. For this, a 1D CNN has been proposed and worked on 166 subjects (93 PD patients and 73 normal). The detection of abnormalities in gait has been obtained with an accuracy of 98.7%, and the prediction of a subject's Unified Parkinson's Disease Rating Scale (UPDRS) severity has been achieved with an accuracy of 85.3%. The voice measurements dataset used is available to the public via UCI. The static and dynamic features of the speech-related dataset of 45 subjects about PD have been studied by [29] and bi-directional LSTM has been used for capturing time-series dynamic features. The results of the study were found have been better than those of previous similar works of ML using static features. As PD progresses

due to the deficiency of dopamine, [30] used MRI images that capture the structural changes in the brain. The images of patients suffering from PD and normal subjects have been trained by using AlexNet DL architecture and tested for evaluating its performance. [31] used MRI images for the classification of healthy individuals and patients suffering from PD using transfer learning techniques and data augmentation. The original data were increased by generative adversarial network (GAN), and pretrained Alex-Net has been utilized for the classification purpose.

18.3 MATERIALS AND METHODS

The study's dataset, the DL pretrained models that were utilized for analysis, and the suggested research methods are all described in this section.

18.3.1 Dataset Description

The dataset that this research used includes 204 spiral and wave drawing pictures that were obtained from [12], which contains a total of 204 spiral and wave drawing images. These images are evenly divided between patients and healthy/normal individuals diagnosed with PD, with each class containing 102 images. The drawings are used to evaluate the motor symptoms associated with PD, as the disorder often affects fine motor skills. For this study, the images from the dataset were resized to 224×224 pixels to meet the input requirements of the DL models. The dataset was split into training and testing sets using an 80:20 ratio (80% of the images used for training and 20% for evaluating model performance). The distribution chart of data is shown in Figure 18.1, and sample images of spiral and wave drawing are shown in Figure 18.2.

18.3.2 Deep Learning Pretrained Models

In this work, drawing images of people with PD and healthy people are distinguished from each other using six pretrained DL models: VGG16, VGG19, DenseNet121, DenseNet169, InceptionNetV3, and Xception. The VGG architecture serves as the foundation for both VGG16 and VGG19, with VGG19 having a deeper network structure. Both are suited for transfer learning since they make use of tiny 3×3 convolutional filters and were pretrained on the ImageNet dataset. DenseNet121 and DenseNet169 have designs with dense connections that improve gradient flow and feature reuse. Their 121 and 169 layers, respectively, enable them to record intricate patterns that are essential for recognizing motor impairments associated with PD in drawings. InceptionNetV3 boosts computing performance by utilizing techniques like label smoothing and factorized convolutions. Xception improves on the Inception architecture and boosts its capacity to extract fine-grained data by utilizing depthwise separable convolutions. All models use their pretrained data from ImageNet to enhance the classification of drawings to detect PD. By examining several models, the study seeks to determine which architecture is most suitable for this task.

VGG16 model consists of 16 learnable weight layers, including three fully connected layers and 13 convolutional layers. Small 3×3 filters are used in each

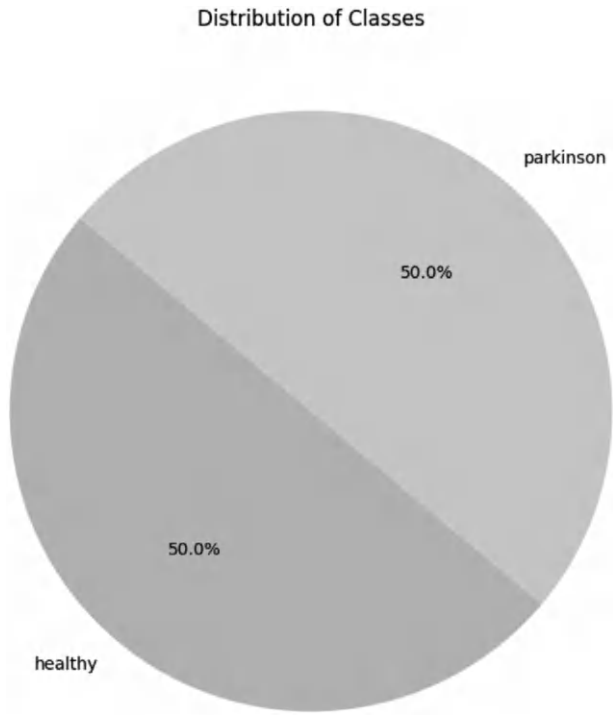

FIGURE 18.1 Data distribution plot.

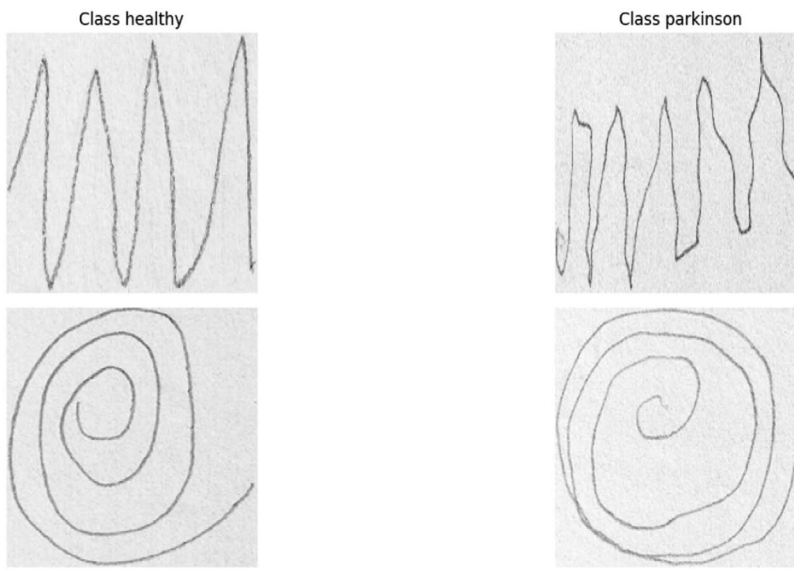

FIGURE 18.2 Sample images from the dataset.

convolutional layer, and they are stacked to increase the network's depth while catching intricate characteristics. The architecture is symmetrical, with many convolutional layers followed by spatial dimension-reducing max-pooling layers. Predictions are made using the final three layers, which are fully integrated. With around 138 million parameters, VGG16 is a deep model with a lot of parameters. The VGG19 structure, which has 19 layers with learnable weights, is an expansion of the VGG16 architecture. It has three fully connected layers and 16 convolutional layers; in comparison to VGG16, it has more convolutional layers, which enables more intricate feature extraction. Similar to VGG16, VGG19 makes use of multiple max-pooling layers and 3×3 convolutional filters. Classification uses the completely connected layers at the end. Because VGG19 has more layers than VGG16, it has somewhat more parameters, that is, about 144 million. DenseNet121 is comprised of 121 layers, which are arranged into dense blocks where each layer gets input from all layers that came before it in that chunk. The pattern of dense connectedness encourages feature reuse, which leads to a large reduction of parameters. Dense blocks make up the architecture, which is followed by transition layers that manage the network's complexity and shrink its spatial dimensions. These layers include pooling operations. Compared to conventional deep networks, DenseNet121 is significantly more efficient because it contains around eight million parameters. DenseNet169 extends the depth to 169 layers while adhering to the same architectural concepts as DenseNet121. Additionally, it makes use of dense blocks, which connect every layer to every layer before it, improving feature propagation and lowering the number of parameters. To control feature map expansion and avoid overfitting, the network has multiple transition layers. With almost 14 million parameters, DenseNet169 strikes a fair compromise between model complexity and parameter efficiency. The modular architecture of InceptionNetV3 includes "Inception modules" that employ parallel convolutional layers with various filter sizes (e.g., 1×1, 3×3, 5×5) inside the same module. This makes it possible for the model to efficiently capture multiscale characteristics. To lower computational costs, the network additionally uses factorized convolutions, which divide bigger convolutions into smaller ones (e.g., 7×7 into 1×7 and 7×1). With over 23 million parameters, InceptionNetV3 strikes a balance between efficiency and depth throughout its several layers.

The foundation of Xception is the concept of depthwise separable convolutions. These convolutions drastically reduced the number of parameters by splitting the typical convolution operation into two parts: a depthwise convolution (spatial filtering) and a pointwise convolution (channel combination). The architecture is composed of several depthwise separable convolutional layers, with fully connected layers for classification at the end. With over 23 million parameters, Xception is a very efficient model with an architecture that is both simple and robust.

18.4 PROPOSED RESEARCH METHODOLOGY

This section describes the systematic procedure that was employed in this work to use pretrained DL models to identify PD using drawing images. The preparation of

the input, data preprocessing, data splitting, model training, and assessment are the five primary processes in the approach.

The first step involves collecting drawing images from the dataset, which includes drawings from both healthy individuals and patients with PD. The dataset contains a total of 204 images, evenly divided between the two classes. Secondly, the raw spiral images were preprocessed, such as resizing them to 224 × 224 pixels to meet pretrained model requirements, converting them to red, green, and blue (RGB) for consistent input data format, and shuffling them randomly to prevent training biases and ensure good model generalization. Then these preprocessed data were split into training (80%) and testing (20%) sets. The pretrained models are trained using the training set, which consists of 163 images split evenly between the classes for PD and those for healthy people. Each of the six pretrained DL models (VGG16, VGG19, DenseNet121, DenseNet169, InceptionNetV3, and Xception) was trained separately on the preprocessed drawing images. The training data were used to fine-tune the models so that they precisely target the goal of differentiating between people who have PD and others who are healthy. The performance of every trained model is evaluated using the testing data consisting of 41 images. A range of performance criteria, including the F1score, accuracy, precision, recall, and ROC curve, are used to assess the models' effectiveness.

- $$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \tag{18.1}$$
- $$\text{Precision} = \frac{TP}{TP + FP} \tag{18.2}$$
- $$\text{Recall} = \frac{TP}{TP + FN} \tag{18.3}$$
- $$\text{F1-Score} = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \tag{18.4}$$

The research methodology for detecting PD using pretrained DL models is illustrated in Figure 18.3.

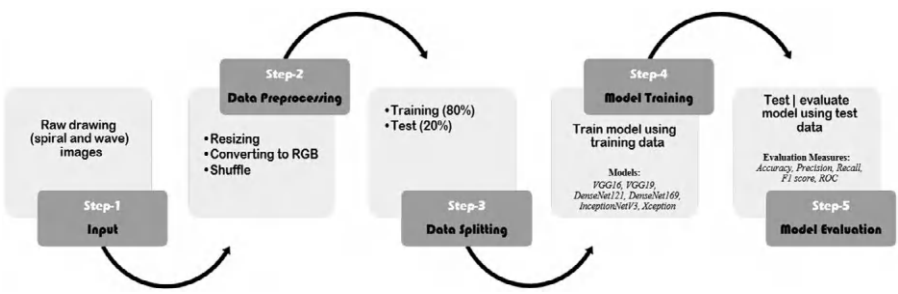

FIGURE 18.3 Proposed research methodology.

18.5 EXPERIMENT EVALUATION AND RESULTS

The experimental work used Jupyter Notebook within Google Colab, a cloud-based platform providing interactive computing resources. Depending on availability, Google Colab offers a free tier with graphics processing unit (GPU) support, specifically utilizing NVIDIA Tesla K80, T4, or P100 GPUs. In addition, the hyperparameter tuning involves using the "sigmoid" activation function and "binary_crossentropy" loss function, optimized with "adam." For 50 epochs, the model is trained with a batch size of 32.

During training, the VGG16 model showed remarkable performance, attaining flawless metrics with 100.00% precision, accuracy, recall, and F1 score. It continued to perform well on the testing set, achieving an F1 score of 97.44%, accuracy of 97.56%, precision of 95%, and recall of 100.00%. These outcomes highlight how well VGG16 can categorize photos of drawings to diagnose PD. Figure 18.4 depicts the confusion matrix, Figure 18.5 shows the training and testing accuracy curves, and Figure 18.6 shows the ROC curve.

With an accuracy of 95.09%, precision of 91.21%, recall of 100.00%, and F1 score of 95.40%, the VGG19 model demonstrated strong performance. Testing results for the model showed 90.24% accuracy, 82.61% precision, 100.00% recall, and 90.48% F1 score. Figure 18.7 presents the confusion matrix for VGG19. Figure 18.8 shows the training and testing accuracy curves, and Figure 18.9 shows the ROC curve.

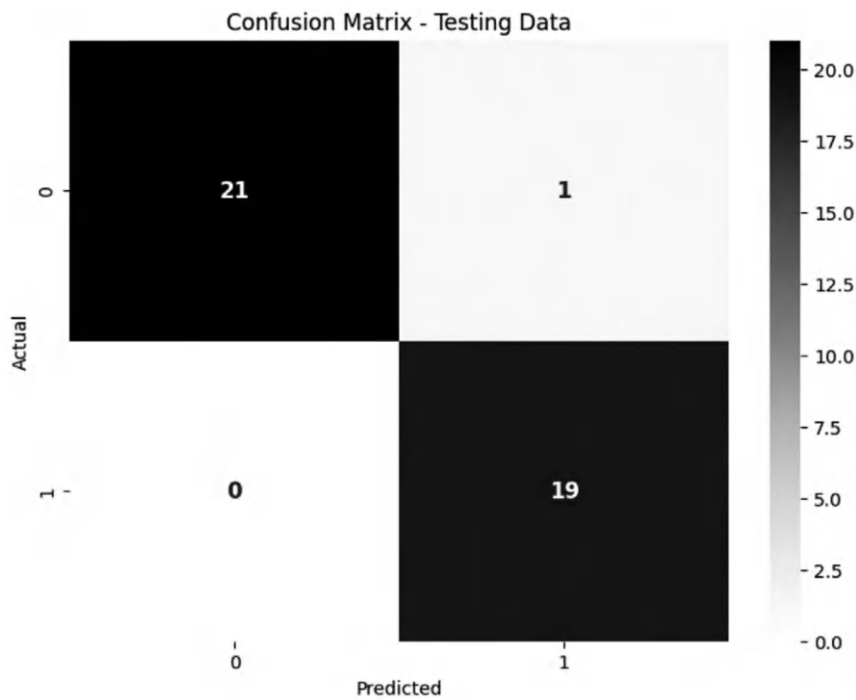

FIGURE 18.4 Confusion matrix (VGG16).

FIGURE 18.5 Training and test accuracy curves (VGG16).

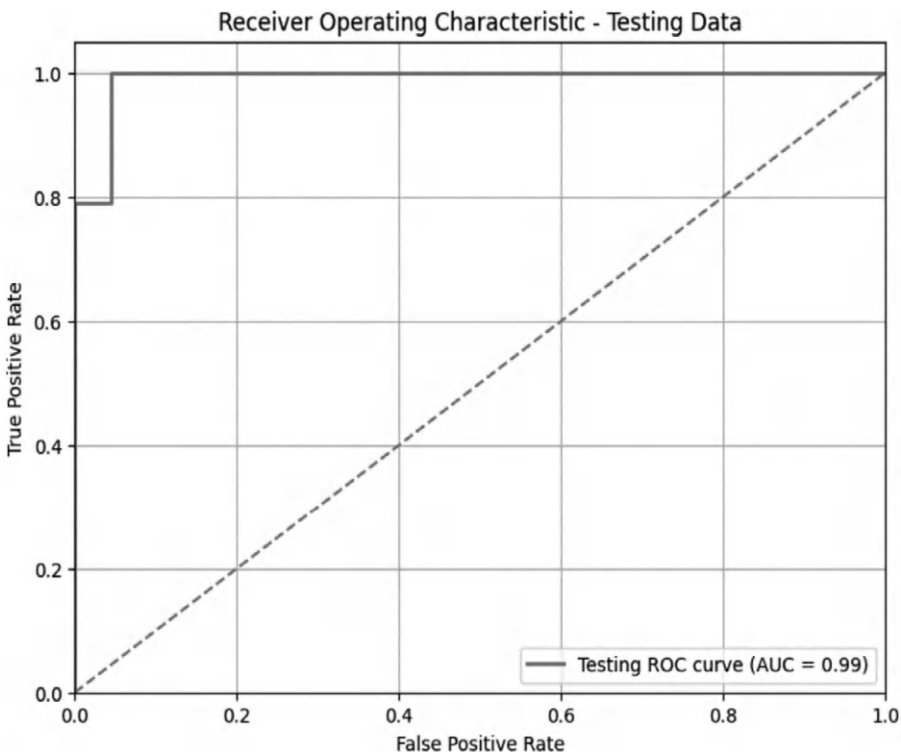

FIGURE 18.6 ROC curve (VGG16).

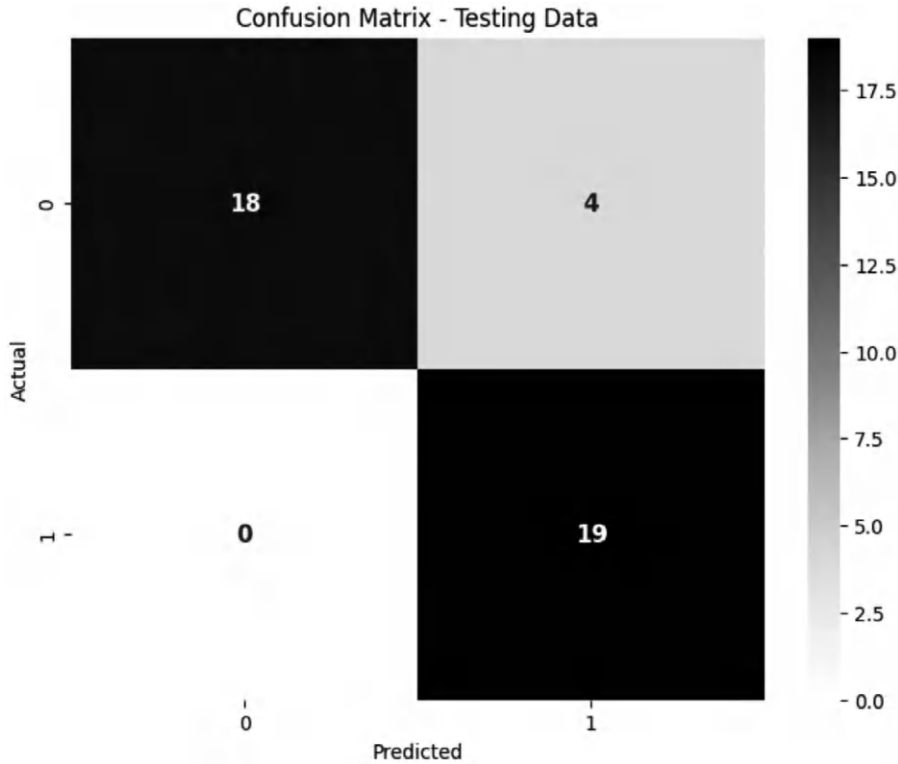

FIGURE 18.7 Confusion matrix (VGG19).

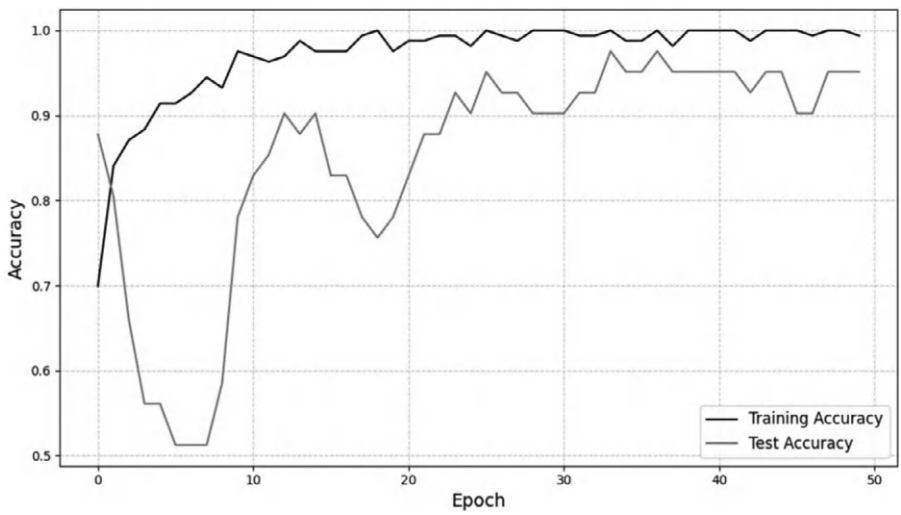

FIGURE 18.8 Training and test accuracy curves (VGG19).

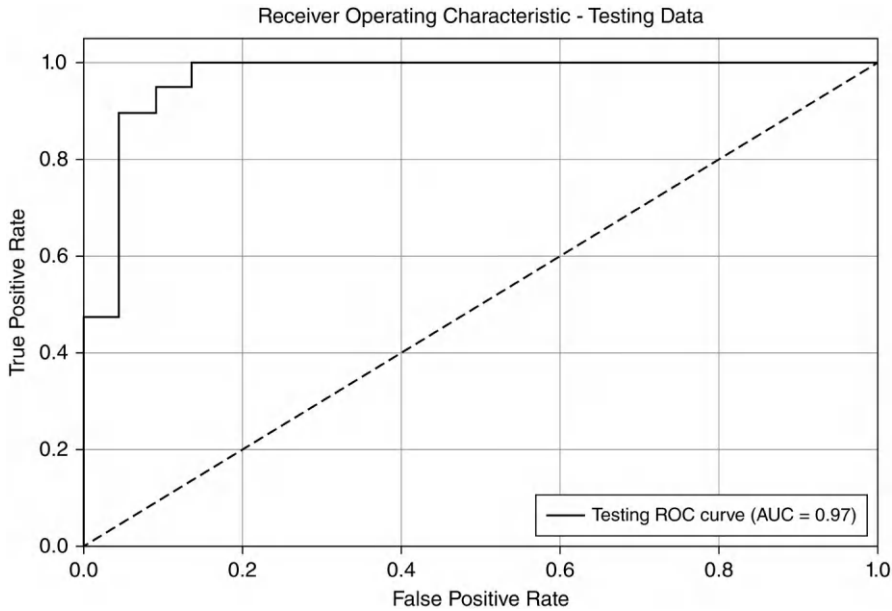

FIGURE 18.9 ROC curve (VGG19).

Training metrics of 99.39% accuracy, 100.00% precision, 98.80% recall, and 99.39% F1 score were attained by the DenseNet121 model. On the testing set, the model achieved 87.80% accuracy, 85.00% precision, 89.47% recall, and 87.18% F1 score. Figure 18.10 displays the confusion matrix, while Figure 18.11 shows the training and testing accuracy curves., and the ROC curve is presented in Figure 18.12.

The training metrics of the DenseNet169 model were 100.00% for accuracy, 100.00% for precision, 100.00% for recall, and 100.00% for F1 score. The model performed as follows on the testing set: 90.24% accuracy, 94.12% precision, 84.21% recall, and 88.89% F1 score. Figures 18.13 and 18.14 depict the training and testing accuracy curves, Figure 18.15 shows the ROC curve, and Figure 18.13 shows the confusion matrix.

Training metrics of 100.00% for accuracy, 100.00% for precision, 100.00% for recall, and 100.00% for F1 score were attained by the InceptionNetV3 model. It obtained 92.68% accuracy, 94.44% precision, 89.47% recall, and 91.89% F1 score on the testing set. Figure 18.16 displays the confusion matrix, Figure 18.17 shows the training and testing accuracy curves, and Figure 18.18 shows the ROC curve.

With training parameters of 100.00% accuracy, 100.00% precision, 100.00% recall, and 100.00% F1 score, the Xception model performed admirably. On the testing set, it produced an accuracy of 90.24%, precision of 85.71%, recall of 94.74%, and F1 score of 90.00%. The confusion matrix is shown in Figure 18.19, the training and testing accuracy curves are illustrated in Figure 18.20, and the ROC curve is presented in Figure 18.21.

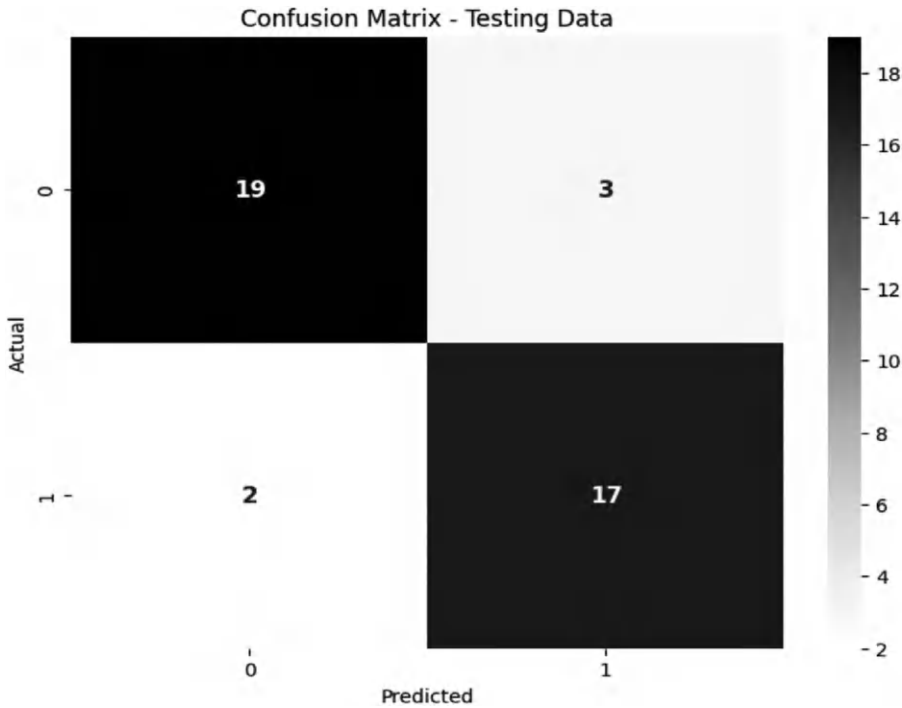

FIGURE 18.10 Confusion matrix (DenseNet121).

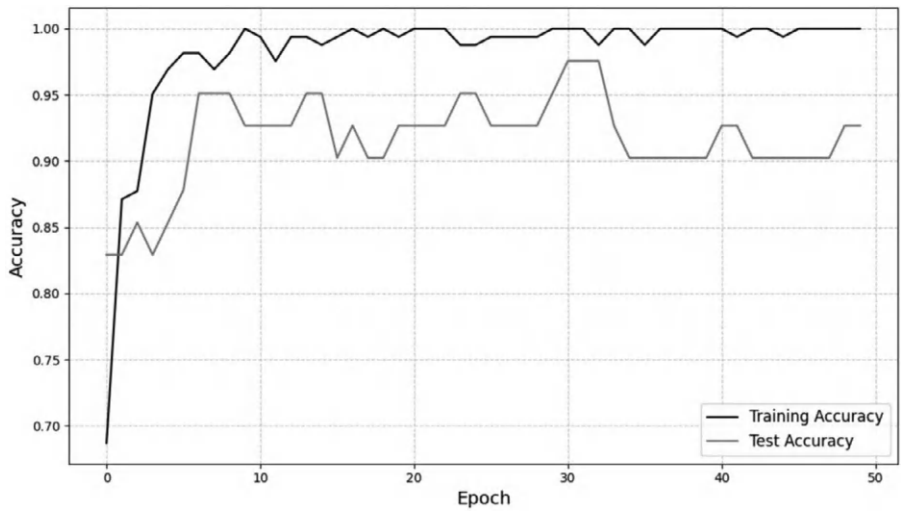

FIGURE 18.11 Training and test accuracy curves (DenseNet121).

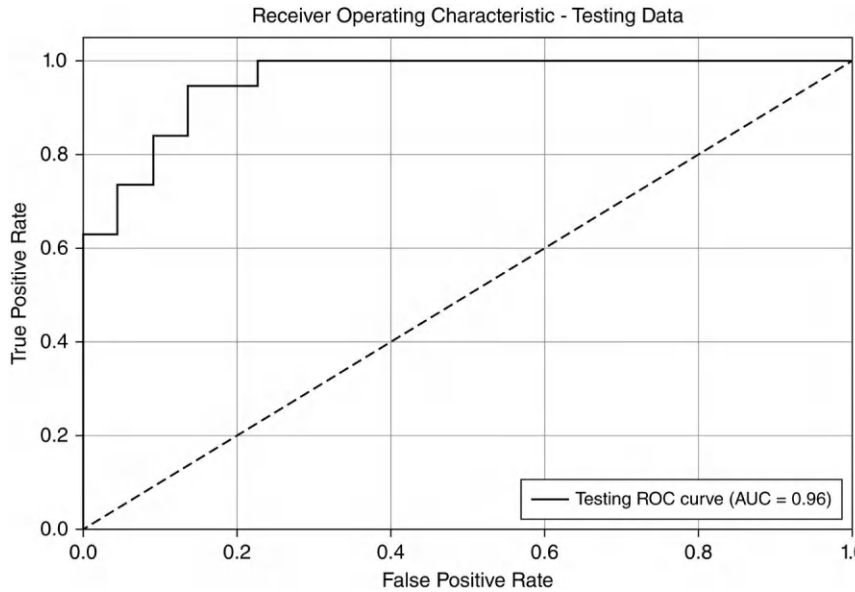

FIGURE 18.12 ROC curve (DenseNet121).

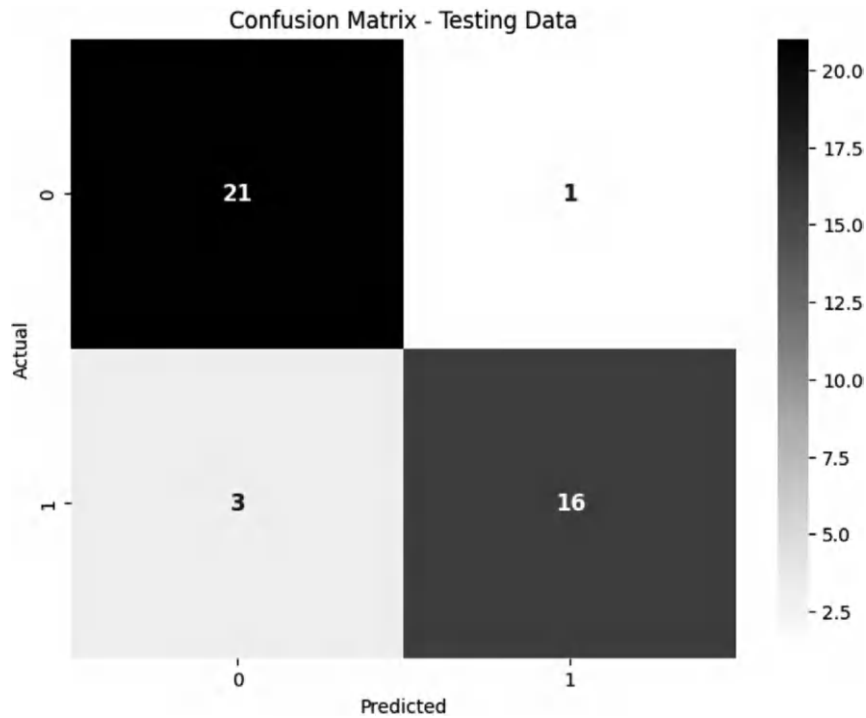

FIGURE 18.13 Confusion matrix (DenseNet169).

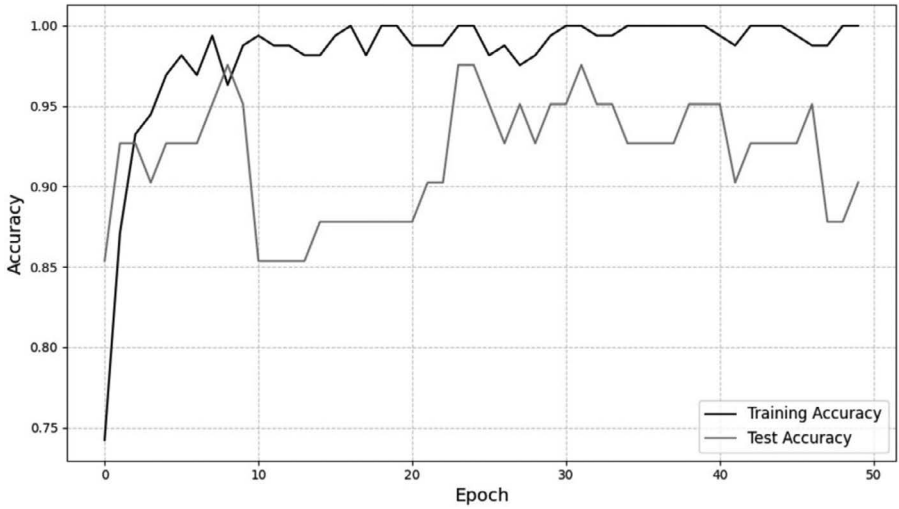

FIGURE 18.14 Training and test accuracy curves (DenseNet169).

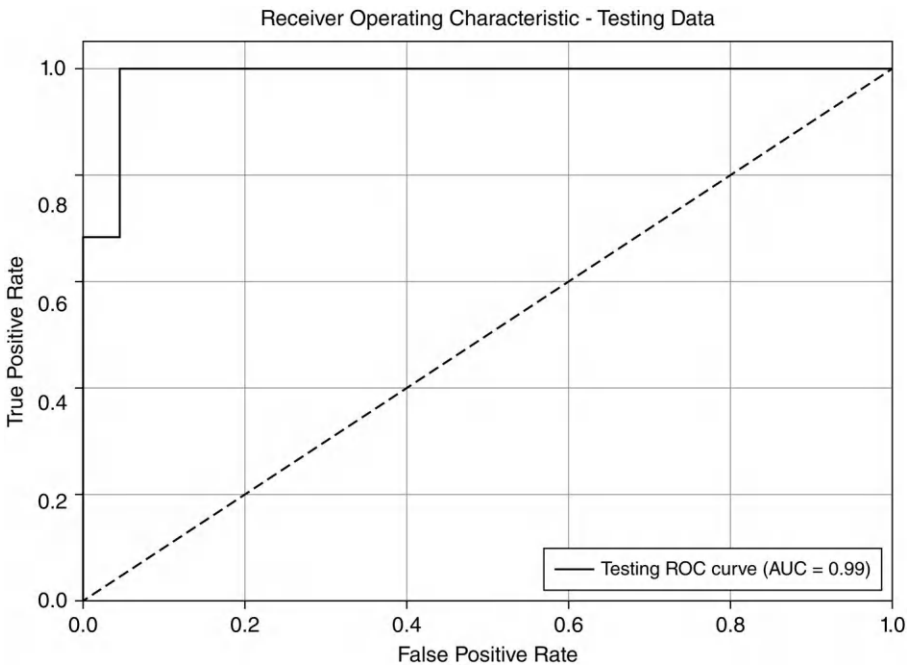

FIGURE 18.15 ROC curve (DenseNet169).

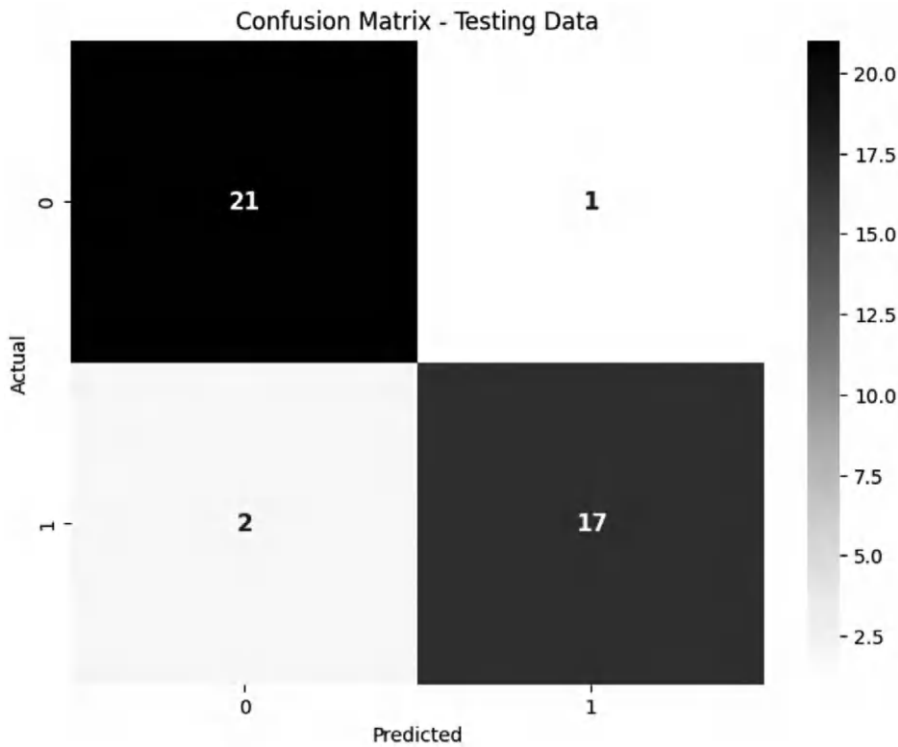

FIGURE 18.16 Confusion matrix (InceptionNetV3).

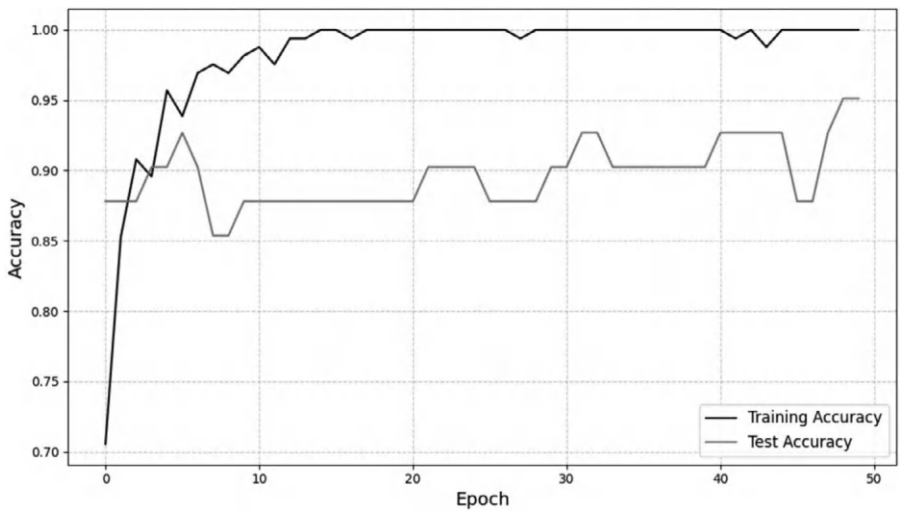

FIGURE 18.17 Training and test accuracy curve (InceptionNetV3).

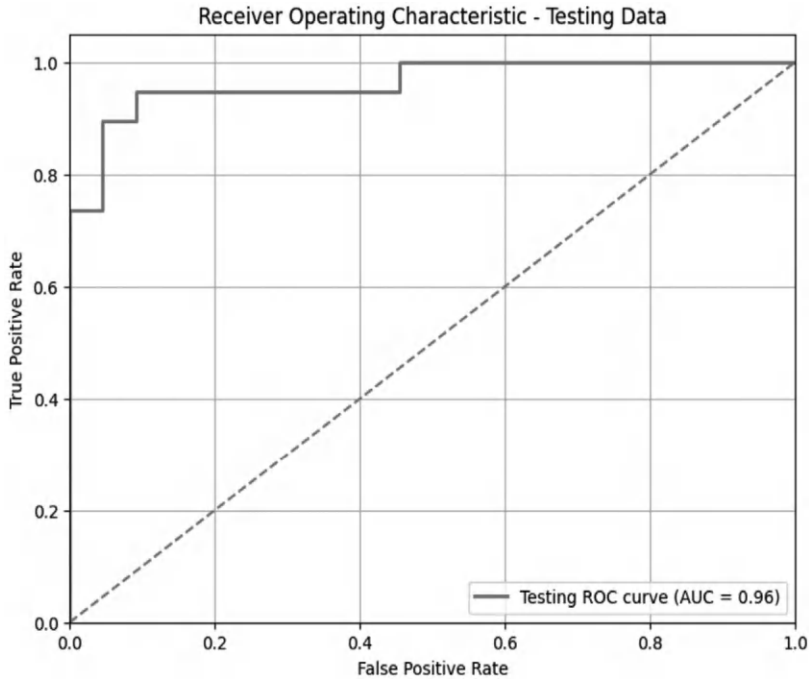

FIGURE 18.18 ROC curve (InceptionNetV3).

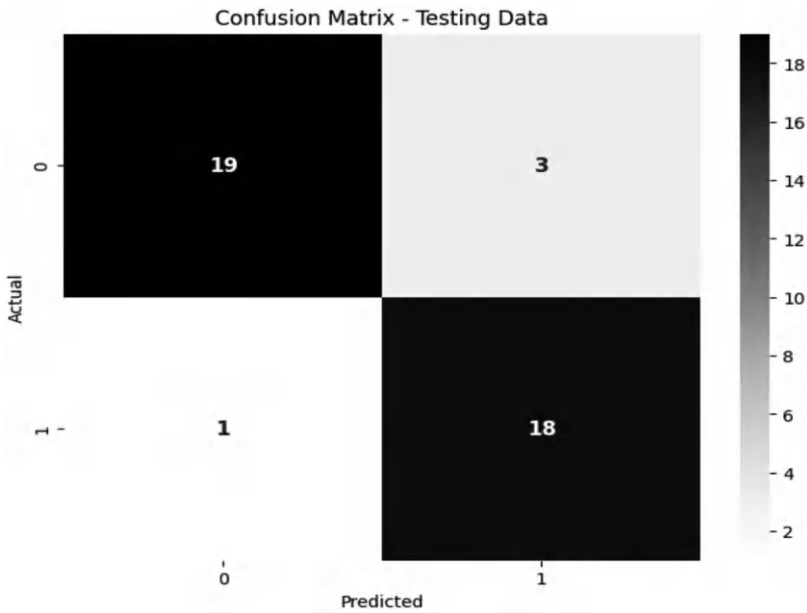

FIGURE 18.19 Confusion matrix (Xception).

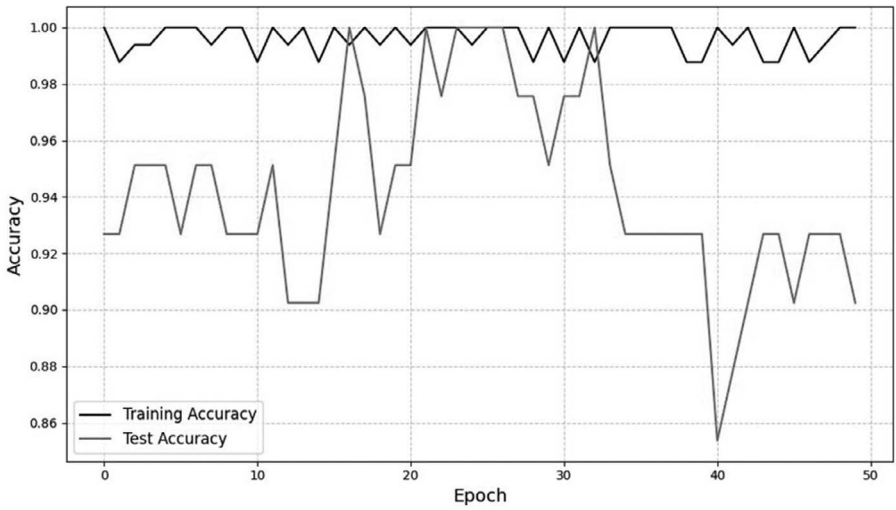

FIGURE 18.20 Training and test accuracy curve (Xception).

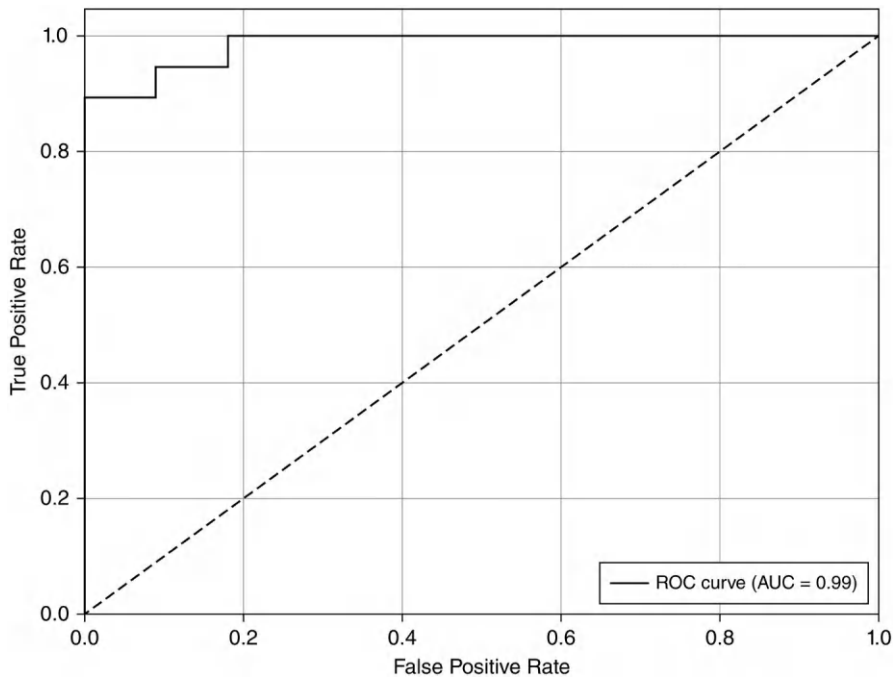

FIGURE 18.21 ROC curve (Xception).

The performance metrics for each model are detailed in Table 18.1. Notably, VGG16 surpassed all other models in training and testing outcomes, with exceptional performance across accuracy, precision, recall, and F1 score.

Various researchers have worked on neurological disorders like AD, PD, schizophrenia, epilepsy, ataxia, Huntington's disease, and so forth. Among them, PD is the second most prevalent neurological disorder after AD. To diagnose PD patients accurately and early, researchers used a variety of ML and DL approaches to work on datasets including both motor and nonmotor symptoms. The reason behind this study is to frame a prediction system for classifying healthy individuals and PD patients based on handwritten drawings. A comparison of related works on the handwriting datasets is shown in Table 18.2.

Extensive research is currently under way to detect the cause and cure of PD and to develop state-of-the-art preventive measurements. The development of more precise and effective diagnostic models may lessen the morbidity and mortality rate.

TABLE 18.1
Performance Metrics of All Pretrained Models

Model	Metric	Training (%)	Testing (%)
VGG16	Accuracy	100.00	97.56
	Precision		95.00
	Recall		100.00
	F1 score		97.44
VGG19	Accuracy	95.09	90.24
	Precision	91.21	82.61
	Recall	100.00	100.00
	F1 score	95.40	90.48
DenseNet121	Accuracy	99.39	87.80
	Precision	100.00	85.00
	Recall	98.80	89.47
	F1 score	99.39	87.18
DenseNet169	Accuracy	100.00	90.24
	Precision		94.12
	Recall		84.21
	F1 score		88.89
InceptionNetV3	Accuracy	100.00	92.68
	Precision		94.44
	Recall		89.47
	F1 score		91.89
Xception	Accuracy	100.00	90.24
	Precision		85.71
	Recall		94.74
	F1 score		90.00

TABLE 18.2
Comparative Analysis

Reference	Best Method	Dataset (Type)	Precision (%)	F1 Score (%)	Recall (%)	Accuracy (%)
[19]	CNN + HOG	Sinusoidal and spiral handwritten drawings	–	–	85.4	83.1
[20]	Logistic regression	Digitized spiral drawing	66	80	100	91.6
[21]	CNN	Wire cube and pentagon spiral drawing	–	–	–	93.5
[22]	VGG19 model	NIATS dataset	–	–	–	96.67
[25]	DT	Arabic online handwriting	–	–	–	92.86
[27]	Transfer Learning	NewHandPD	98	–	86	95.29
[32]	SVM	Spiral	–	–	–	83
[30]	CNN	HandPD dataset	–	–	–	95
[25]	CNN	PD spiral drawings using digitized graphics tablet dataset	–	97.7	–	96.5
[24]		Archimedean spiral drawings	–	95	–	94
Our work	**VGG16**	**Drawing images**	**95**	**97.44**	**100**	**97.56**

Moreover, DL techniques are flexible to perform better in terms of performance in healthcare.

18.6 CONCLUSION AND FUTURE WORK

Using the spiral and wave-based PD drawing dataset, six pretrained DL architectures – VGG16, VGG19, DenseNet121, DenseNet169, InceptionNetV3, and Xception – have been used for the automated and early detection of PD. To determine which of these six pretrained models is the best classifier for distinguishing PD patients from healthy persons, a comparison of the models has been conducted. With accuracy, precision, recall, and an F1 score of 97.56%, 95%, 100%, and 97.44%, respectively, VGG16 outperformed the others. The suggested model may be able to help with the early diagnosis of PD and act as a tool for healthcare stakeholders, depending on the performance attained. In the future, other datasets including audio voice features, gait data, MRI, EEG, and EMG should be used along with state-of-the-art DL models to accurately detect the early stage of PD with better performance.

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19 Optimizing Digital Healthcare for Alzheimer's Disease

A Deep Federated Learning Convolutional Neural Network Scheme (DFLCNNS)

Swathi Sambangi, T. Kusuma, D. Srinivasa Rao, G. Lakshmeeswari, and Rakhee

19.1 INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disorder that is a major concern of cause for dementia. The starting stage of this disease effects the cognitive abilities of the patient. A patient with AD has impairment or abnormality of ventromedial temporal lobe, which is important for episodic memory and the ability to recall past events or experiences [1]. Further progress of AD can affect the patient's physical activities by interrupting their day-to-day basic actions. This causes the patient to depend on other persons even for use of washroom, dressing, eating, etc. [2]. All over the world, 60–70% of dementia cases are caused by the progressive neurodisease AD. In 1906, Alois Alzheimer described the disease characteristics as it begins with experiencing episodic memory loss and gradual diminishment in cognitive functions that even effect day-to-day activities [3]. This chapter discusses the various methods and innovative approaches for early detection to fulfill and improve AD patients' quality of life.

Currently the detection process of AD depends on clinical assessments and behavioral cognitive abilities of patient's history, which can be influenced by the experience of doctors or physicians [4]. The digitization of detection of AD involves integration with electronic health records [5], which allow the patients to share the data to healthcare providers for further suggestions and curative treatment therapies. Although sharing such records has advantage over other methods, privacy and security are major concerns for safeguarding the confidentiality and integrity of the patient's data from unauthorized access [6] The AD disease detection and diagnosis and its management can be done by integrating several advanced technologies like deep learning algorithms, cloud

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computing, and fog computing. These technologies provide cutting-edge solutions to improve the detection rate and provide better treatment therapies and continuous monitoring of a patient's well-being and recovery from the disease.

19.2 RELATED WORK

M.S. Bhargavi [7] stated that AD causes brain shrinkage and cell destruction and is the primary cause of progressive dementia. Early identification can help limit the course of the disease, especially in those with mild cognitive impairment (MCI). To address AD diagnosis, the EfficientNetB0 model is fine-tuned on a Kaggle dataset using transfer learning (TL) by Pallawi et al. [8]. In multiclass classification, the model outperforms current methods with an accuracy of 95.78%. AD must be promptly diagnosed and treated, as stated by Singh Chhabra et al. [9]. They presented a deep learning (DL) method that combines structural magnetic resonance imaging (sMRI), functional magnetic resonance imaging (fMRI), and diffusion tensor imaging (DTI) to provide an extensive feature set for the purpose of identifying AD from multimodal neuroimaging data. With state-of-the-art findings of 93.5% accuracy, 92.3% sensitivity, and 94.6% specificity, the suggested model – which uses a three-tiered architecture of sMRI convolutional neural network (CNN), fMRI recurrent neural network (RNN), and DTI based Graph convolutional network (GCN) – strongly suggests its generalizability and potential for clinical application. Elgendy, O et al., [10] suggests ways to categorize brain MRI pictures into four phases of AD. The proposed method by authors outperformed 90% accuracy and 90% F1 score in every class.

One of the main causes of death in industrialized nations is neurological illness, such as AD, as stated by Trivedi et al. [11]. With a distributed client-server architecture and independent and identically distributed (IID) datasets, the framework displayed increased capabilities for early-stage detection and classification of AD, achieving 98.53% accuracy with Alex Net. Sampath et al. [12] offered a superior method by using an optimized DL model and improving MRI image processing for more accurate biomarker discovery. The approach of S.S, G.M et al., [13] improved accuracy by 0.66% and decreased detection errors by 0.0345% when compared to previous methods by merging the cuckoo search optimizer with a deep belief network (DBN). Arya et al. [14] uses an artificial semantic segmentation algorithm based on the Segnet architecture to classify hippocampal atrophy in brain MRI data. Prabhakar et al. [15] have worked to cultivate a machine learning (ML) model that can discover AD early and perchance result in prompt intervention and more effective therapy by utilizing nonamyloid blood markers. Moorthy et al. [16] have studied recent innovations in ML approaches for prompt AD identification and shows how they could develop patient aftermaths and diagnostic exactitude. The study determines by what means K-nearest neighbors (KNN) containers develop early conclusions and treatment methods by overtaking support vector machines (SVM), with 98.98% accuracy in AD diagnosis using MRI brain images. The amalgamation of cerebrospinal fluid (CSF) and plasma proteins with SVM earn the highest accuracy in AD diagnosis. The effectiveness of this technique by Luz et al. [17] in AD diagnosis and assessment features perfect, gainful biomarkers. Khadatkar et al. [18] have estimated numerous classifiers through metrics such

as accurateness, fastidiousness, recall, and F1 score to expedite transfer wisdom. The authors discovered alternatives to MRI, such as positron emission tomography (PET) scans, to advance diagnostic accuracy. Lu et al. (2023) investigated AD and attained an F1 score of 96.2% using handwriting analysis and voice patterns from more than 15,000 samples using ML. The authors research has created the "revoAD" smartphone app, which serves as an effective tool for that facilitates better communication with healthcare professionals with ten times closer diagnosis and 97.6% training exactitude. Irfan et al. [19] presented major developments in DL for AD recognition, proving its higher performance over customary ML, and tackles current challenges with preparation processes and dataset convenience.

AD causes subtle mild brain changes before symptoms were appear, early diagnosis of the disease can be subtle challenge stated by Saxena et al. [20]. The Computer-Aided Alzheimer's Disease Diagnosis (CAADD) [21] structures from 2017 to 2023 are thoroughly analyzed in this study using both ML and DL. The study estimates the ML and DL procedures pragmatic to neuroimaging data as well as show indicators to afford likely directions for supplementary study. Mandawkar et al. [22] recommends a Hybrid Cuttle Fish−Grey Wolf Optimisation (CUF-GW)−tuned Ensemble Classifier model that enhances uncovering precision by using optimized combination parameters and predictable ML classifiers. The model completed 97.205% recognition accuracy using exercise data from the Alzheimer's Disease Neuroimaging Initiative (ANDI) database, and 97.665% exposure accuracy in k-fold evaluation. Highlighting CNNs and vision transformers (ViTs), Hcini et al. [23] offered a thorough valuation of DL methods for AD classification by means of brain imaging data.

The ML ideal offered by Uddin et al. [24] comprises Gaussian NB, decision tree, random forest, XG Boost, voting classifier, and gradient boost to predict AD. The voting classifier with the best validation accuracy of 96% using the Open Access Series of Imaging Studies (OASIS) dataset shows how ML algorithms may greatly enhance early diagnosis and lower the death rates from AD. Table 19.1 offers a survey of these studies.

TABLE 19.1
Literature Survey of Existing Methods for Detection of AD Using DL and Federated Learning (FL)

S. No.	Author	Datasets Used	Methodology	Key Findings
1	Zhang, L., et al. (2024)	ADNI, OASIS	Multimodal FL model combining MRIs and PET scans	Detection accuracy improvement by 7%
2	Gomez, A., et al. (2024)	ADNI	Personalization of FL models to individual patient data using TL	Diagnostic accuracy improvement by 90%
3	Smith, J., et al. (2023)	ADNI, AIBL	Optimization of communication costs in FL models using model pruning and quantization	Reduced communication costs by 30% with a 2% drop in accuracy (from 88% to 86%)

(*Continued*)

TABLE 19.1 (*Continued*)
Literature Survey of Existing Methods for Detection of AD Using DL and Federated Learning (FL)

S. No.	Author	Datasets Used	Methodology	Key Findings
4	Rahman, H., et al. (2023)	ADNI, UK Biobank	Applied cross-silo FL with decentralized institutions sharing their models	Detection accuracy of 89%.
5	Li, M., et al. (2023)	ADNI	Utilized edge computing in FL to process data locally before sharing with the central server	Reduced latency
6	Li, X., et al. (2022)	ADNI	Implemented privacy-preserving techniques using differential privacy in FL	Accuracy 85%, data privacy
7	Shen, W., et al. (2022)	ADNI, NACC	Applied TL techniques in a federated setting to predict disease progression	Prediction accuracy 83% using pretrained models
8	Kim, J., et al. (2022)	ADNI	Addressed the challenge of imbalanced datasets in FL using synthetic data augmentation	Improvement in minority class performance.
9	Kumar, R., et al. (2021)	ADNI, AIBL	Developed an ensemble method combining FL models from different institutions	Balanced accuracy 88%
10	Zhang, H., et al. (2021)	ADNI	Introduced adaptive learning rates in FL models for AD detection	Improved convergence speed, accuracy
11	Zhao, Y., et al. (2021)	ADNI, OASIS	Applied FL to combine data from multiple institutions without sharing sensitive data	Accuracy of 87%
12	Wang, T., et al. (2020)	ADNI	Focused on early detection using lightweight FL models	Accuracy 82%
13	Patel, S., et al. (2020)	ADNI	Implemented FL using MRI data for AD detection	Accuracy 84%
14	Liu, Y., et al. (2020)	ADNI, AIBL	Developed scalable FL models for discovering biomarkers related to AD	80% precision using biomarkers dataset
15	Xu, L., et al. (2020)	ADNI	Applied differential privacy techniques in FL models for secure AD detection	Accuracy 83%, protecting patient data

19.3 CHALLENGES IN DIGITAL HEALTHCARE IMPLEMENTATION FOR AD

Providing solutions for AD with digital healthcare systems undergoes substantial difficulties like privacy of data, security and integrity of the systems, validations, ethical concerns, and cost. The author Pyrrho et al. [25] stated that to protect the sensitive data of AD patients, there is a need for securing electronic health records and digital health platforms. Merging previous healthcare systems also faces challenges; for example, many digital devices do not rely on outdated digital platforms that cannot be integrated easily with modern devices and systems. These complexities in achieving effortless integration were discussed by Herrmann.T et al. [26] and have highlighted the necessity of benchmarked protocols for improving interoperability. As stated by Doll et al. [27], stakeholders have to collaborate collectively and follow to common data standards in order to achieve interoperability. Usability and accessibility are essential, particularly for AD patients who may experience cognitive impairment. User-centered design principles may enhance the effectiveness of digital health interventions for AD, according to a study by Dabbs et al. [28]. Grande et al. [29] discussed the importance of consistent standards along with the complexity of the standardized environment around digital health technologies.

19.3.1 Computational Complexity

To provide digital healthcare solutions for AD, dealing with computational complexity is a major concern, as it involves in dealing with large amounts of heterogeneous data that include clinical data, records, image data of scanned reports, genetic biomarkers information, and data from wearable devices and sensors. Liu, Y. et al. [30] have stated that computational complexity of integrating data from different devices is a significant challenge. Zhang et al. [31] have highlighted the challenges and difficulties in developing algorithms that deal with high processing power and are cost efficient.

19.3.2 Challenges in Fog, Cloud, and Deep Leaning Technologies

DL, fog computing, and cloud computing technologies bring various opportunities in treating AD. However, they face the following problems for detecting and diagnosing AD.

DL model training: For AD diagnosis and treatment, DL models must be trained on the data provided. In the words of Li et al. [32], the complexity and high dimensionality of AD data, like CT scan images and biomarkers data, require the use of complex neural networks that are computationally intensive.

Real-time processing: By bringing immediate information processing capabilities near to the information source, fog computing aims to reduce latency. However, due to their constrained processing capability, DL models are

hard to implement in fog nodes. The difficulty of implementing highly resource-intensive DL algorithms in fog environments without reducing performance has been brought into focus by Shen et al. [33].

Data Privacy and Security: Providing security for distributed servers in cloud and fog environments is a challenging task. Kim et al. [34] discussed the significance of deploying strong encryption techniques and protected communication protocols to secure patient data from security breaches and illegitimate access.

19.3.3 Network Requirements

Low latency requirements: The main goal of fog computing is to minimize the latency value by processing the data at edge level. Despite that, implementing complicated CNNs is a challenging task with respect to latency reduction. Kumar et al. [35] has discussed optimization of DL algorithms for achieving minimum latency.

Bandwidth constraints: Transferring large amounts of data that are gathered from various sources, including edge computing devices, the fog environment, and the cloud layer, overburdens bandwidth. To establish uninterrupted data transfer and data processing, it is crucial to harness bandwidth effectively. Guo et al. [36] have highlighted the necessity for effective data compression and transmission techniques to resolve bandwidth limitations.

19.3.4 Infrastructure Requirements

Resource allocation: Efficient resource allocation in distributed environments, especially in cloud computing and fog computing, plays a major role in supporting computational need and support for running complex DL algorithms. Chen et al. [37] have discussed various challenges of dynamic resource allocation and load-balancing techniques to achieve optimal efficiency and resource efficiency.

Scalability: AD-related data are huge, and to adjust to an increase in the volume of data, scaling up cloud and fog infrastructure is challenging task. Li et al. [38] focused on the need for scalable and elastic system designs that can manage large-scale applications without deteriorating performance. By carrying real-time data processing abilities near to the data source, fog computing seeks to lower latency. However, because of their constrained processing power, DL models are difficult to implement in fog nodes. The challenge of implementing resource-intensive DL algorithms in fog environments without sacrificing performance is brought to light by Wen et al. [39].

19.4 DEEP LEARNING NETWORKS AND OPTIMIZATION ALGORITHMS IN ALZHEIMER'S DISEASE

Due to its capacity to assess involved and high-dimensional data, DL networks emerged as a key element in studying and dealing with AD. Liu et al. [40] stated that by knowledge of the spatial hierarchies of brain pictures, CNNs have shown

auspicious results in recognizing early hints of AD, which are needed for detecting and tracing the disease's course. Research by Vaswani et al. [41] stated that RNNs can calculate exactly how AD patients' cognitive cost will progress, a strength that delivers significant evidence for individualized handling regimens. According to Schraudolph et al. [42], converters can be used to incorporate multimodal data, such as inherent, imaging, and clinical data, to increase the accuracy of AD diagnosis and prediction. The optimization of DL models through iteratively changing model constraints to minimize the loss function is a joint application of gradient descent and its derivatives, such as stochastic gradient descent (SGD), minibatch gradient descent, and adaptive techniques of Adam. Snoek et al. [43] emphasized the success of optimization procedures in circumstances with profuse adding resources. Zhang et al. [44] illustrated how Bayesian optimization can be used in hyper parameter tuning of DL models, with which significant improvements can be achieved in accuracy..

19.5 METHODOLOGY

This section illustrates the proposed methodology for detecting AD.

19.5.1 Dataset Description

In 2004, to investigate AD, the ADNI research project was launched. The dataset consists imaging files, including fMRI, sMRI scans, and PET scans. It has three classes, namely cognitively normal (CN), MCI, and AD.

19.5.2 Deep Federated Learning CNN Scheme (DFLCNNS)

This chapter demonstrated the architecture for classifying AD, as shown in Figure 19.1. The architecture has three different layers, namely the edge computing layer, the fog computing layer and the cloud computing layer. Initially, the AD patient's data (blood samples, ECG, and MRI scan) are collected from various local laboratories such as at individual clinical hospitals. These data are maintained in an individual electronic health record database for further processing. The entire process of data offloading is carried out at the edge computing layer with several diagnostic tools and bio medical instruments used for diagnosis. As far as the FL is concerned, the collected data must be trained locally with DFLCNNS at the individual hospitals, which are connected to a centralized cloud server present at the main hospital that acts as a head for AD detection. The local training is done at the fog computing layer.

As it is depicted in Figure 19.1, the local clinics that have undergone training generate weights for the aggregated model, which is trained at the main hospital that is directly connected to the cloud server. With this local training and aggregation, FL is implemented for achieving optimality by training smaller sample datasets received at the edge devices. Training models with smaller sample datasets at local processing nodes results in reducing processing time at the aggregated model when it is dealing with large samples of data. Local training is done at

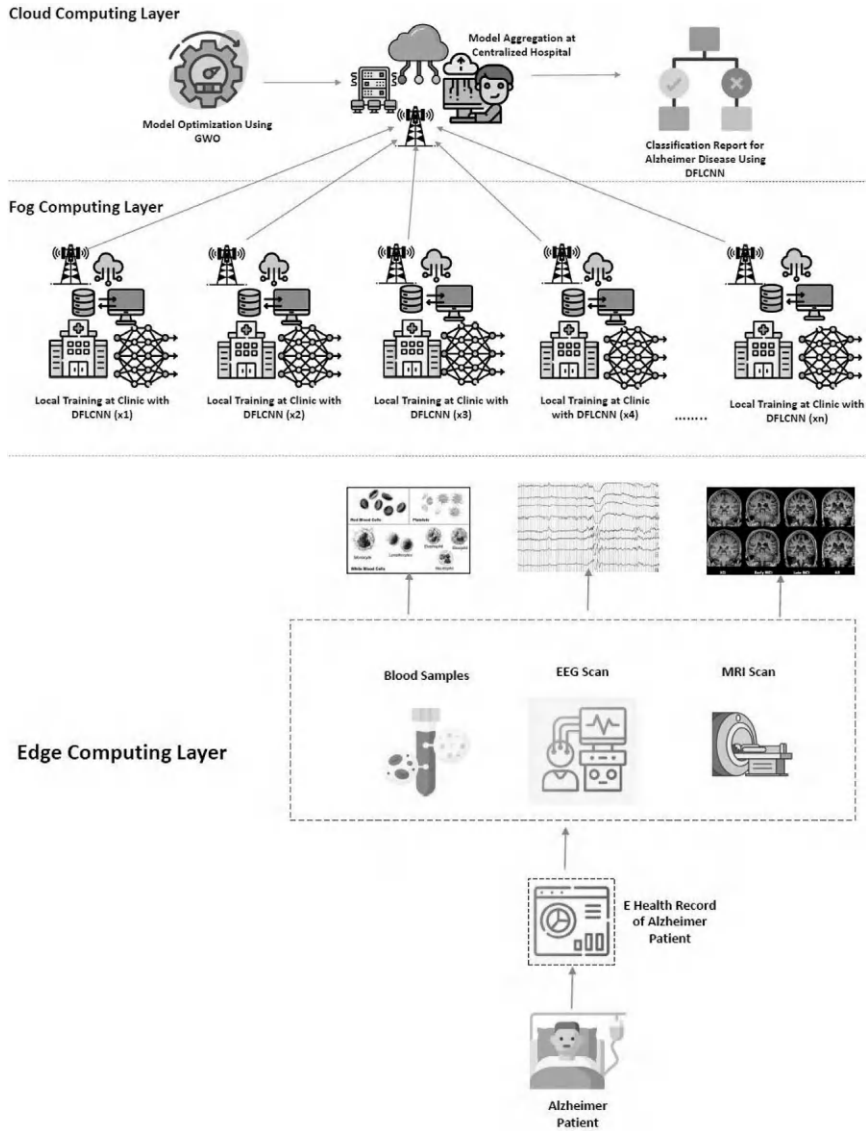

FIGURE 19.1 Architecture for Alzheimer's disease detection using deep federated learning with optimization.

the fog computing layer, which is near to edge devices, and model aggregation is carried out at the cloud computing layer. This architecture DFLCNNS uses an EfficientNetB2 DL model for classification of AD. To achieve better accuracy and other performance metrics, the architecture uses the Grey Wolf Optimizer (GWO) optimization algorithm for feature extraction at local training and model aggregation.

19.5.3 EfficientNetB2 Architecture for Alzheimer's disease Classification

Implementation and effectiveness are enhanced via the CNN architecture known as EfficientNetB2. The graphical representation is shown in Figure 19.2. The layers and functions of the architecture can be expressed quantitatively:

- *Input layer*: Receives an picture of size $H_{ght} \times W_{dth} \times C_{lr}$, where H_{ght} and W_{dth} are denoted by height and width and also C_{lr} represents the number color channels (E.X. $280 \times 280 \times 3$).
- *Stem block*: $2D\ Convolution \rightarrow Batch\ Normalized \rightarrow Rectified\ Linear\ unit$

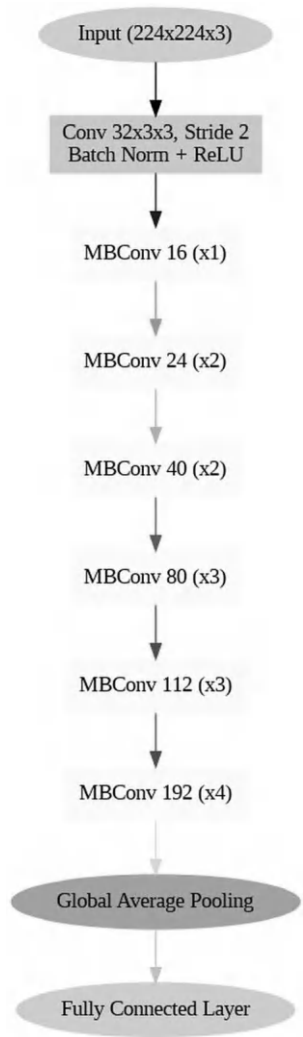

FIGURE 19.2 Efficient B2 architecture.

Accurately, for a convolution process,

$$OP_{a,b,c} = \sum_{p,q} In_{put_{a+p.b+q.d}}.ker_{a,b,c,d} + bias_c$$

where OP is the output features map, In_{put} is the input image, and ker is the convolution kernel.

19.5.3.1 Mobile Inverted Bottleneck Convolution Blocks

Batch normalization, residual connection, depthwise convolution, and pointwise convolution are included in every mobile inverted bottleneck convolution block. With input M, for a mobile inverted bottleneck convolution block,

$$M_{Input} = Rectified\ \ Linear\ \ unit\Big(Batch\ \ Normalized\big(Depthwise\ \ Conv(M)\big)\Big)$$
$$\rightarrow Pointwiswe\ \ Convoulation \rightarrow Rectified\ \ Linear\ \ unit$$

19.5.3.2 Global Average Pooling (GAP)

GAP decreases each feature map to a single value:

$$OP_a = \frac{1}{H_{ght} \times W_{dth}} \sum_{H_{ght1}}^{m} \sum_{W_{dth1}}^{n} M_{H_{ght},W_{dth},a}$$

This is the fully connected layer:

$$OP = softmax(W_m.M + Bias)$$

Here, W_m is the weight matrix.

19.6 GREY WOLF OPTIMIZER (GWO)

The GWO algorithm imitates the chasing behavior of gray wolves. It is used to improve hyperparameters of the model. In this work, GWO is used for optimizing performance of EfficientNetB2. The design of GWO algorithm is shown in Figure 19.3.

The accurate stages involved are

19.6.1 Position Update

Gray wolves apprise their locations constructed on the place of w_1, w_2, w_3 wolves:

$$U_{w_1} = \left|C_{w_1}.w_1 - G_i\right|$$

$$U_{w_2} = \left|C_{w_2}.w_2 - G_i\right|$$

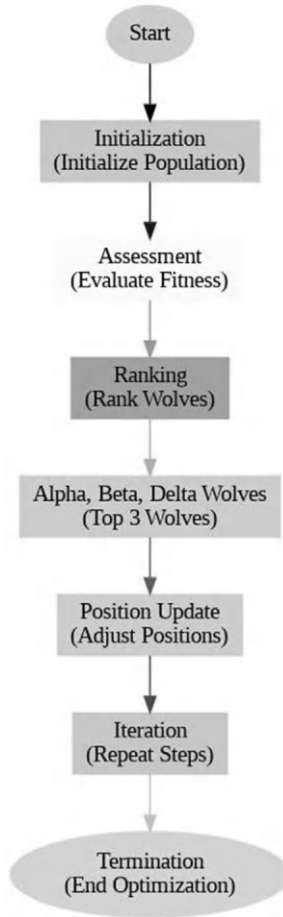

FIGURE 19.3 Grey Wolf Optimizer architecture.

$$U_{w_3} = \left| C_{w_3}.w_3 - G_i \right|$$

$$G_i^{new} = \frac{w_1 + w_2 + w_3}{3} - A.U$$

where $A = 2l.v_1 - l$ and $C = 2.v_2$ are coefficient.

l decreases linearly from 2 to 0, and v_1, v_2 are random vectors in [0, 1].

19.6.2 Objective Function

Classically, the objective function is the performance of negative metrics.

For hyperparameter optimization:

$$h(G) = Accuracy(G)$$

19.7 RESULTS AND DISCUSSIONS

The following bar plot provides an accuracy comparison of four different DL models: ResNet, DenseNet, Inception v3, and Efficient Net.

From Figure 19.4, it is observed that 92.2% highest accuracy is achieved by EfficientNetB2. An accuracy 89.0% is achieved by DenseNet, and ResNet has achieved 88.5% accuracy. Inception V3, when applied to the dataset provided, has recorded accuracy of 87.8%. This analysis shows that EfficientNetB2 is the most efficient of the models.

Figure 19.5 illustrates the loss comparison values for ResNet, DenseNet, Inception v3, and EfficientNetB2. The plot in the figure shows that EfficientNetB2 attained the lowest loss value of 0.29, which is effective for minimized prediction error and contributes to the performance improvement and efficiency. Inception v3 achieved 0.39 loss value, which is highest among the four DL architectures, showing poorer performance than the other models. ResNet and DenseNet have attained 0.35 and 0.32 loss values, respectively. Thus, Figures 19.4 and 19.5 show that EfficientB2 has the highest accuracy and lowest error values.

Figure 19.6 depicts the values of F1 score for different DL architectures for classification of the AD dataset. For the ResNet DL architecture, 0.87 is the F1 score, DenseNet achieved 0.88, Inception v3 slightly slower than previous two architectures with a value of 0.86, and finally EfficientNetB2 got a 0.89 value F1 score. The results shows that EfficientNetB2 as the most efficient model in terms of the F1 score, demonstrating its capability in balancing precision and recall. Interpretation of the results shows that ResNet with 0.87 value and Inception v3 with 0.86 are less efficient when compared with the other two architectures.

Figure 19.7 highlight EfficientNetB2 with ten hours training time as the most efficiently designed model for training, succeeded by DenseNet at 12 hours, Inception v3 takes 14 hours, and ResNet takes 15 hours for training. For cloud computing

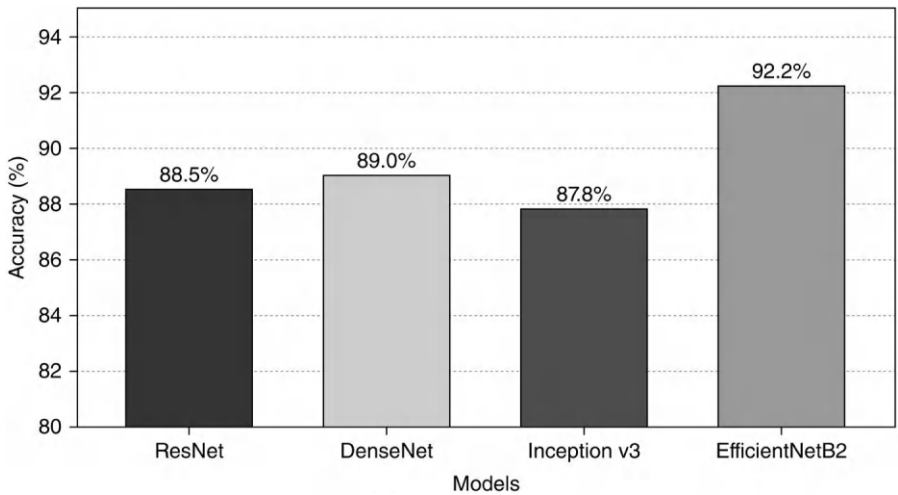

FIGURE 19.4 Accuracy of EfficientNetB2.

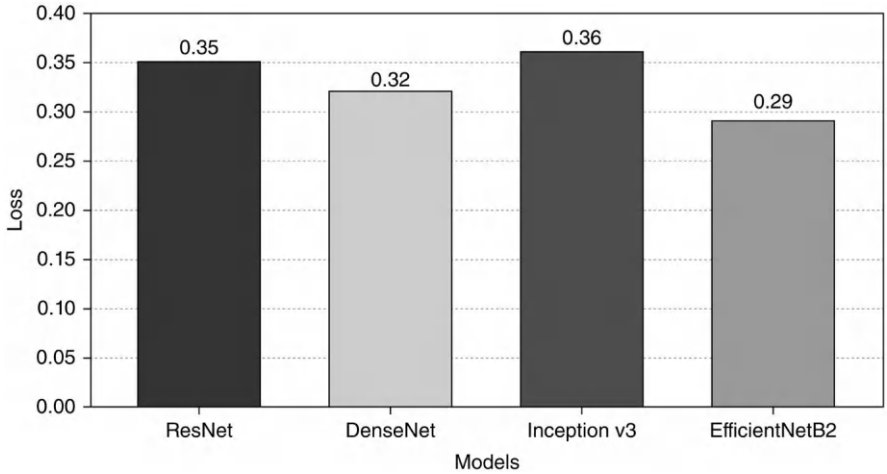

FIGURE 19.5 Loss comparison of EfficientNetB2.

and fog computing environments, it is preferable to choose EfficientNetB2 with less training time. These results highlight the balancing factors between EfficientNetB2 model complexity and training time.

The bar plot shown in Figure 19.8 presents testing times (in hours) for four DL models: ResNet, DenseNet, Inception v3, and EfficientNetB2. EfficientNetB2 has achieved the least testing time of 4.0 hours, which shows that EfficientNetB2 is not just efficient in training but also outperforms with its testing speed.

Figure 19.9 depicts the model communication cost for the federated DL model. When DL models are used in FL, the data are communicated between the central

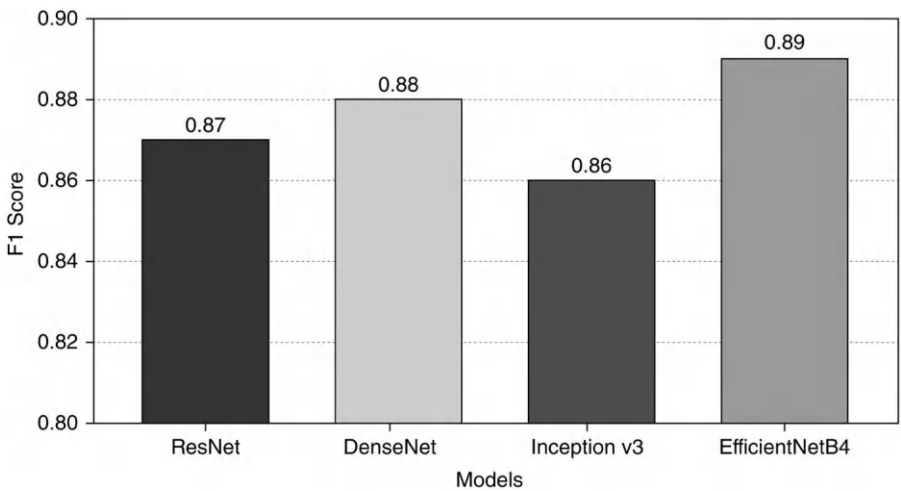

FIGURE 19.6 Comparison of F1 score values.

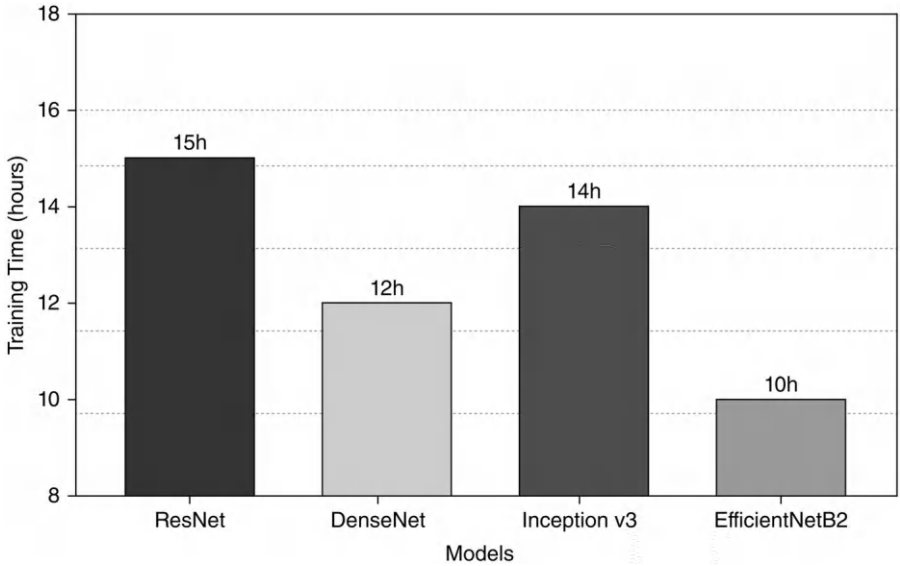

FIGURE 19.7 Comparison of training time.

server and distributed clients. This communication includes parameter updates and training details. As this communication affects the system's performance, there is a cost incurred with the process of communication. The plot shown in Figure 19.9 illustrates comparison of communication cost for the selected DL models. Due to the concise architecture of EfficientNetB2, 0.9 GB is the cost associated with the

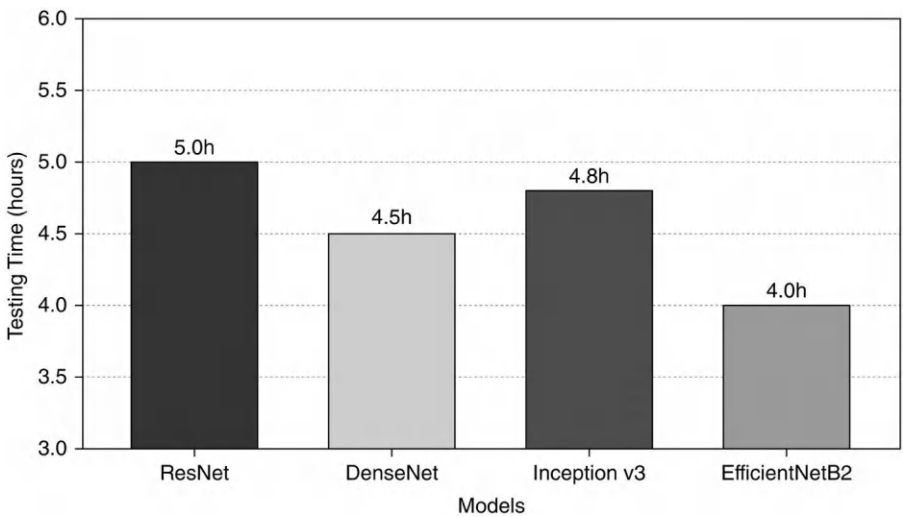

FIGURE 19.8 Comparison of testing time.

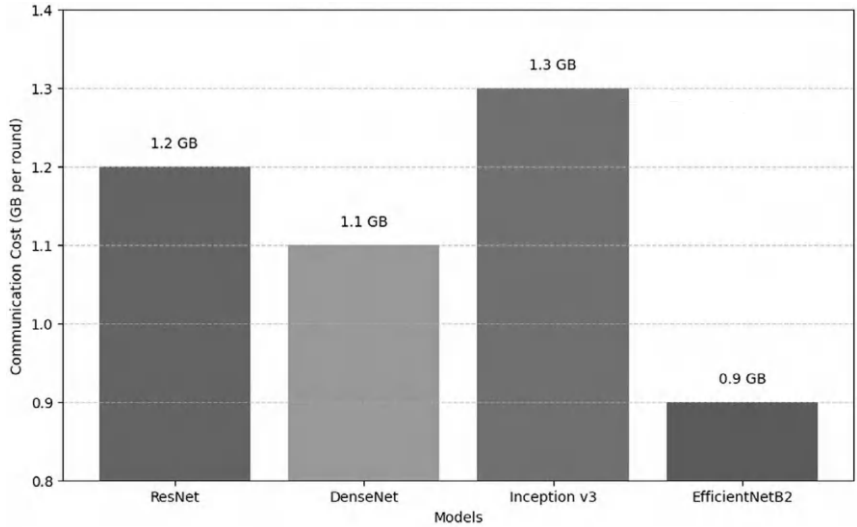

FIGURE 19.9 Model communication cost comparison.

communication. However, DenseNet requires higher data transfer of 1.1 GB per round, and ResNet communicates at 1.2 GB. Among the four models, Inception v3 has the highest communication cost of 1.3 GB per round, as it has a complex architecture. The plot in Figure 19.9 shows that EfficientNetB2 is more advantageous to consider for training models for deep FL for detecting AD classification.

Figure 19.10 illustrates the efficiency of different optimization algorithms applied in FL with the combination of EfficientNetB2. GWO attained good federated

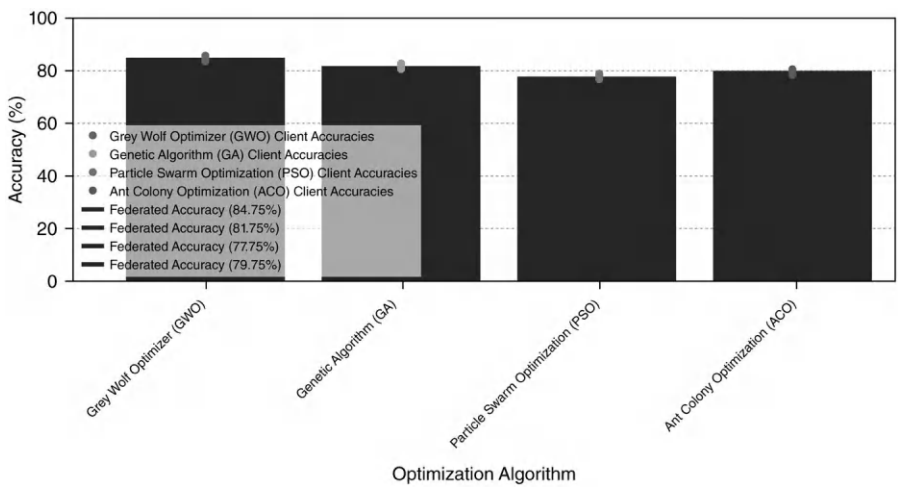

FIGURE 19.10 Comparison of Federated Learning accuracies of EfficientNetB2 with different evolutionary algorithms.

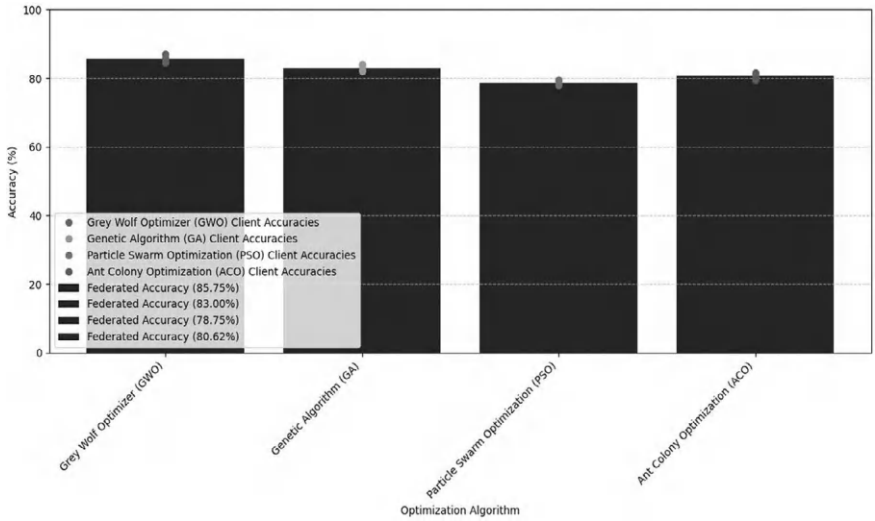

FIGURE 19.11 Comparison of federated learning accuracies of ResNet with different evolutionary algorithms.

accuracy at 84.5% among other algorithms with client results. These observations show that GWO is the most efficient optimization algorithm.

The above Figure 19.11 shows the results for optimization algorithms for ResNet in FL, where GWO has achieved the highest federated accuracy of 85.5%. Figure 19.12 shows DenseNet with various optimization algorithms and their federated accuracies.

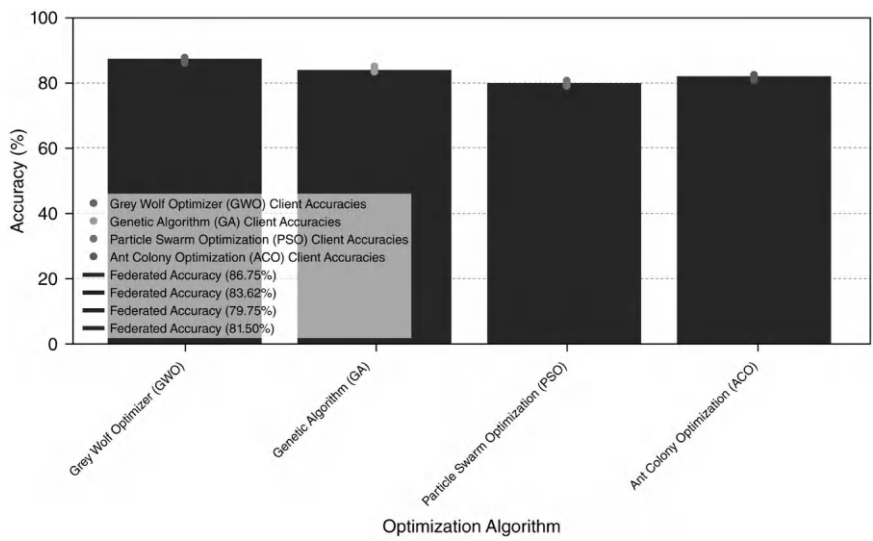

FIGURE 19.12 Comparison of federated learning accuracies of dense net with different evolutionary algorithms.

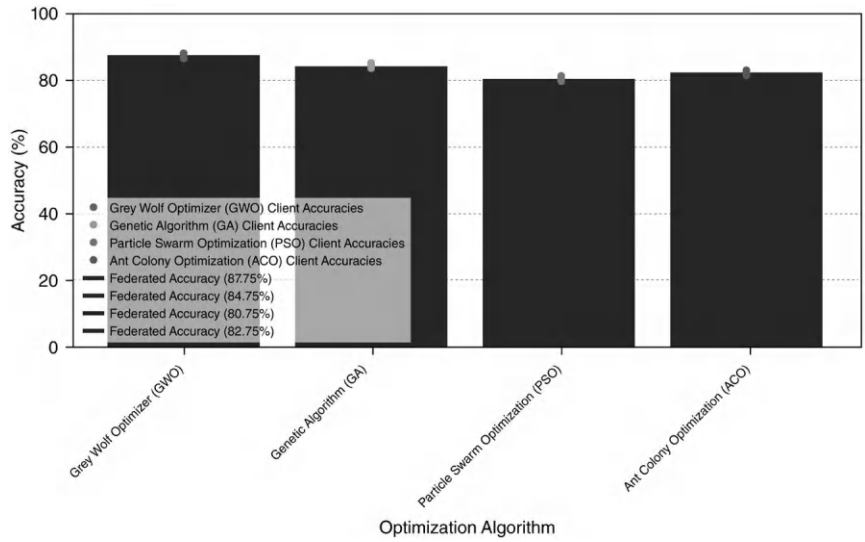

FIGURE 19.13 Comparison of federated learning accuracies of inception V3 with different evolutionary algorithms.

Figure 19.13 shows the federated accuracy results for optimization algorithms for Inception v3 in FL with various evolutionary optimization algorithms.

The bar plot depicted in Figure 19.14 displays the accuracy comparison of different federated DL models from various studies from previous reseach, including a proposed model. The data comprise four entries: Li et al. (2022) with CNN,

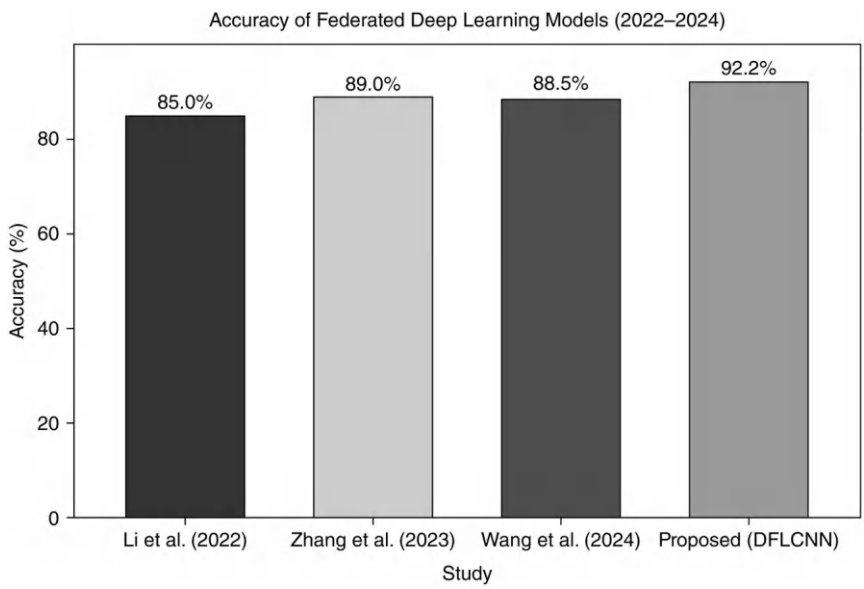

FIGURE 19.14 Comparison of existing methodologies with proposed DFLCNN.

Zhang et al. (2023) with MobileNet, Wang et al. (2024) with VGG, and the proposed DFLCNN model. It shows that DFLCNN achieves the highest accuracy of 92.2%, significantly outperforming the other models. MobileNet follows with an accuracy of 89.0%, VGG at 88.5%, and CNN at 85.0%.

19.8 CONCLUSION

In this chapter, we have explored the applications of federated DL models for classification of AD, specifically applying EfficientNetB2 and optimizing the model with the GWO algorithm. The obtained results demonstrated that this scheme yields better performance metrics, where accuracy is 92.2%, a loss is 0.29, and achieved an F1 score with value of 0.89. In addition, the cost of model communication is effectively managed at 0.9 GB, which highlights its efficiency in a deep FL environment. These findings specify that by optimizing advanced neural networks with dense layers, we can achieve high accuracy and lower model communication cost, which is an encouraging solution for real-world applications in distributed environments, like cloud and fog environments that receive data from various digital healthcare systems. Despite these results, DFLCNNS is limited to a specific dataset. Future research can be focused on applying evolutionary optimization algorithms to different datasets with different parameter settings. Additionally, the research can be elaborated by validating model performance on biomarkers datasets.

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20 Artificial Intelligence
A Game-Changer in Parkinson's Disease Neurorehabilitation

Nabeela Rehman, Arshya Anwar, and Sahar Zaidi

20.1 INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative, extrapyramidal, progressive, chronic disorder of movement characterized by a reduction of dopamine-producing neurons [1, 2]. Recent epidemiological research has provided new insight into the rising incidence and pattern of this debilitating condition around the world. According to the Global Burden of Disease (GBD) report, the number of people with PD increased by 118% to 6.2 million between 1990 and 2015. It is expected that this concerning pattern will persist, with over 12 million people worldwide estimated to have PD by 2040 [3, 4]. Notably, the disease is associated with motor symptoms like rigidity, tremors, bradykinesia, postural instability, muscle stiffness, and coordination issues, all of which can limit a patient's movement and independence [5].

Artificial intelligence (AI) has shown significant potential in the diagnosis and treatment of disease. With high accuracy rates ranging from 93.88% to 96.27%, many AI models, including a support vector machine, random forest, and decision tree, are used to assess PD. Early and precise prediction is essential, and these models help with that [6, 7].

Furthermore, AI methods assist in evaluating disease severity and stage, producing reliable evaluations necessary for PD patients' appropriate treatment and monitoring [8]. Automated assessment of motor and gait impairments is one such use; this is an important first step toward early identification of the disorder [9]. Researchers can now examine and compare walking patterns between PD patients and healthy individuals owing to the development of autoregressive algorithms that can extract information from gait signals [10].

By accurately classifying patients based on their speech and language patterns, AI – especially deep learning – also helps develop speech biomarkers for the assessment of disorders and provides efficacy for speech rehabilitation [11–13]. Several studies have emphasized the practical importance of AI methods, like computer vision and machine learning algorithms, in precisely detecting PD based on small variations in motor control in handwriting patterns [14]. These AI-driven methods extract information from handwriting photos, such as spectral properties, pressure

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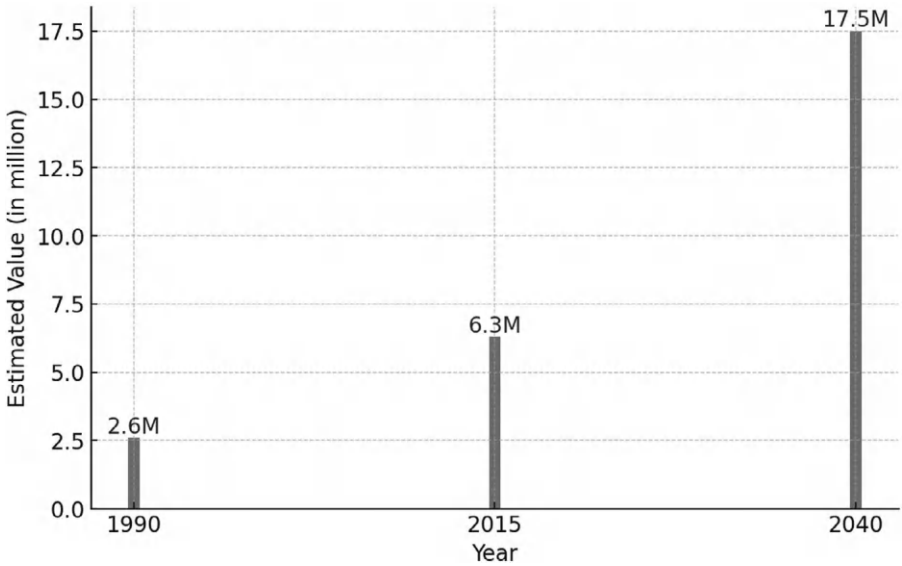

FIGURE 20.1 Projected global burden of Parkinson disease, 1990–2040.

data, and kinematic parameters to precisely differentiate PD patients from healthy individuals [15]. Current machine learning techniques have demonstrated encouraging outcomes in accurately diagnosing PD, offering a useful adjunct to traditional clinical evaluation approaches. AI allows for proactive intervention in the management of the disease and greatly improves diagnostic precision by integrating clinical data with machine learning algorithms [6]. Additionally, AI-powered rehabilitation programmers can be very helpful in assisting people with PD to regain and maintain their independence and mobility. The development of specialized rehabilitation programs that are tailored to the particular needs of every individual can be provided.

This chapter will talk about AI-based evaluation and treatment strategies along with robotic rehabilitation for gait management, machine learning models for speech rehabilitation, and the role of virtual reality in maintaining a healthy diet and sleep and performing an adequate amount of physical activity to improve the quality of life of people with the disease. Figure 20.1 shows projections for the growth in the use of these strategies.

20.2 INTRODUCTION OF INTELLIGENCE IN PARKINSON'S DISEASE

20.2.1 AI-Based Gait Evaluation and Rehabilitation

A modern instance of technological innovation is the virtualization of rehabilitation. In the evaluation and management of PD, AI-based technologies have become increasingly important in recent years [16, 17]. Furthermore, PD biomarkers for analysis of posture during the gait cycle can be used by various devices with machine learning and deep learning features to carry out automated detection [18]. Numerous AI models, including

machine learning techniques, smartphone applications, sensory-based technology, and data on nocturnal breathing, are utilized to study and identify PD [19]. Gait analysis and assistive technology have been combined, allowing sensor-equipped devices to recognize and predict risks associated with falling (freezing of gait) to prevent falls or reduce their impact [18, 20]. Excellent outcomes have been observed when using inertial measurement units (IMUs) to observe the advancement of PD and identify specific gait anomalies in individuals (see Figure 20.2). Research has shown that IMU-based models of gait assessment are capable of quantifying a wide variety of gait factors, such as spatiotemporal parameters, joint kinematics, variability, asymmetry, and stability, and can accurately distinguish between healthy controls and early-stage PD [21]. Wearable IMUs have also been used to track motor characteristics of PD, identify fluctuations in motor performance, dyskinesia, and freezing of gait, and evaluate treatment responsiveness in outdoor environments, demonstrating its potential as a tool for ongoing monitoring and disease rehabilitation [22]. One well-known disorder that frequently harms a person's quality of life is gait festination. The pooling techniques have been heavily utilized by convolutional neural networks (CNN) in particular for their deep learning strategies. In fog prediction, recurrent neural networks (RNNs), CNNs, and other distinct neural network subtypes have also been extensively used [23].

AI models like the hybrid ConvNet-Transformer architecture can accurately diagnose PD severity stages from gait data, leveraging the strengths of CNNs and transformers to capture both local features and long-term spatiotemporal dependencies in the data [24]. Levodopa administration combined with any type of implantable pulse generator (IPG) stimulation results in a significant improvement on posture and also average step height and step length on each side [25].

Also, in terms of PD gait evaluation and rehabilitation, random forest outperformed naïve Bayes, which had an accuracy of 84.6% in diagnosing the disease, while random forest performed exceptionally well in identifying its stages [26].

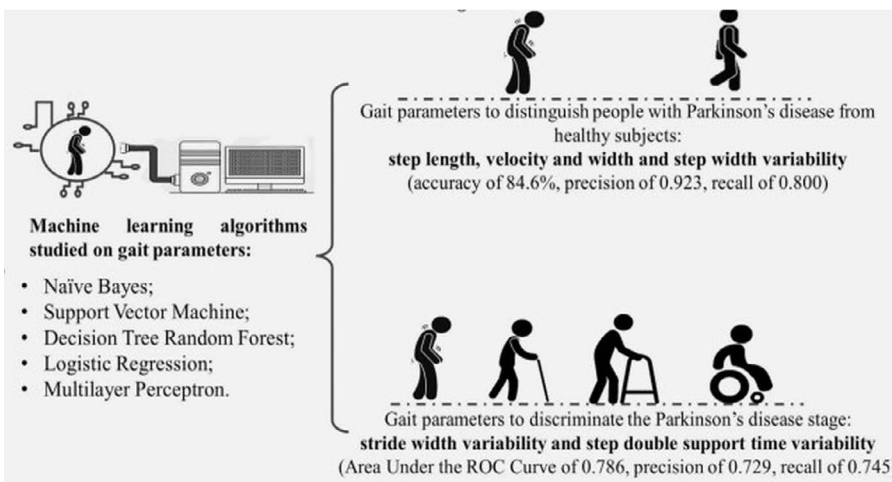

FIGURE 20.2 Significance of ML algorithms for PD diagnosis and stage identification by analysing gait parameters.

K-Nearest Neighbors (KNN) helps identify Parkinson's disease symptoms early and facilitates prompt treatment [27]. There is a significance of machine learning models for PD classification based on selected spatial-temporal parameters, which include step length, step width, and velocity. Two relevant gait features, stride width and step double support time, are used for quantifying the disease stage. Different algorithms like naïve Bayes (NB), support vector machine (SVM), decision tree (DT), random forest (RF), logistic regression (LR), and multilayer perceptron (MLP) can be used to assess different variables of gait [26]. The procedure for gait analysis includes a collection of data with nonwearable or wearable devices that is preprocessed and subsequently classified using different algorithms for the automatic recognition of gait, detection of spatiotemporal variables, PD diagnosis, and staging [18].

20.2.2 Robotic Rehabilitation

Robotics and AI integration has become a viable treatment strategy for PD patients in recent years. Robotic rehabilitation systems have the ability to offer tailored, rigorous, and repetitive training – a strategy that has been demonstrated to be successful in promoting functional recovery and improving motor abilities [28, 29].

One of the main benefits of robotic rehabilitation is that it accurately measures and monitors a patient's motor abilities as it makes it possible to customize training regimens to meet the demands of each person. Exoskeletons and end-effectors are two popular robotic devices used for motor training; each has advantages of its own. Exoskeletons (devices where a particular joint's movement is regulated, such as an ankle, knee, or hip joint) or end-effect robots, in which equipment is located at the extremity of the limb (for example, the feet are set on a footplate) [30, 31].

Robotic-assisted rehabilitation showed marked improvement in balance confidence, fatigue, and lower limb motor performance [32]. Virtual reality in conjunction with robotics is the best possible application, and it should be encouraged [33]. The use of robotic exoskeletons has been proven to be beneficial for PD rehabilitation by maintaining joint mobility, stimulating motor units, and standardizing wrist movements, thereby improving patient care and increasing the efficiency of wrist rehabilitation [28].

The Honda Walking Assist (HWA), a portable robotic exoskeleton device (EXOD) for single joints, is utilized in gait training, demonstrating potential benefits for those with more severe motor impairments. Moderately advanced PD patients experience immediate enhancements in cadence, step length, hip flexion, and extension range while using the device along with improved walking endurance during unassisted walking following ten half-hour sessions of gait training at home [34].

Memory, walking endurance, and engagement in high-intensity exercise have shown enhancement through the application of exoskeletons. Therefore, incorporating robotic exoskeletons and end-effector robots in PD rehabilitation programs can be beneficial for enhancing motor function and overall quality of life [35].

20.3 ROLE OF MACHINE LEARNING FOR SPEECH EVALUATION AND REHABILITATION

Machine learning algorithms can recognize dysarthria resulting from PD and evaluate the parameters of speech like phonation, prosody, and articulation through voice assessment accurately [36]. Its ability to evaluate minor changes in voice features is far better than that of audiologists and speech therapists [37] and helps in the early recognition of PD [38]. Generally, vowels like \a\, \e\, and \u\ are used for sustained phonation [39]. The algorithm consists of getting speech data from the microphones, which is characterized by the articulation involving tongues, jaws, lips, and other movements of vocal muscles. Then the phonetic sequence is generated for mapping the articulation features to phonetic sequences or texts, and in the final step, the sequences/texts are converted to speech using language processing techniques based on desired rhythm, syntactic information, and intonation [40]. Nowadays, smartphones are also equipped with high-performing processors and sensors, which are used for remote assessment and can screen large populations effectively and facilitate the rehabilitation of PD patients.

The neuro-fuzzy system (NFS) and SVMs are used for the evaluating total Unified Parkinson's Disease Rating Scale (UPDRS) using a sustained phonation of vowels [41]. In the neuro-fuzzy system, the output shows a continuous value between 0 and 1, which can be acquired by applying different rules to the input values, which can vary in different neurons. The estimated score is useful for remote assessment of severity [42].

The SVM is a biomedical decision support system [43]. It works by extracting signal features from speech samples and classifying the speech symptom severity levels under the UPDRS [44]. It is the best method, with an accuracy of 86% [45], and allows for early management.

RF is a simple method and works on the DT concept [46] with an accuracy of 96.8%. It is like a flowchart that consists of different speech features [47]. Vaiciukynas et al. proposed a method to detect PD by extracting the phonation of the /a/ vowel from short sentences and classifying them according to different individual feature sets and decision-level fusion sets [48].

20.4 ROLE OF VIRTUAL REALITY IN MANAGING PARKINSON'S DISEASE

Sustenance of lifestyle modifications is immensely challenging for motor and nonmotor signs associated with PD. The advancements in digital therapeutics provide us with various scopes to increase engagement in healthy lifestyle behaviors, such as exercising regularly, a healthy diet, and better sleep hygiene habits. Strategies like cognitive behavioral change therapy are effective in improving behavior [49] by goal setting, action planning, self-evaluating, and providing social support, positive feedback, and rewards.

These are achieved with the help of relational agents that are computational artifacts designed to entrench social-emotional relationships with users. A relational agent can be in the form of an animated virtual coach that has video conversions

with users through a touch screen on a tablet or computer [50]. Recent advancements in virtual coach technology also allow recognition of written or spoken language enabling user-oriented and distinctive communications and have increased the scope for more complex dialogues and flexibility in conversations [51]. The virtual coach guides them through an educational session, regarding different things like step counts and customized diet patterns and is available 24/7 to interact with users. With various advances in AI, virtual coaches have tremendous prospects to promote self-evaluation and management across myriad domains like physical activity, healthy diet, and optimal sleep [52].

20.5 ADVANTAGES AND DISADVANTAGES OF EXISTING AI METHODS FOR THE CLASSIFICATION OR DETECTION OF PARKINSON'S DISEASE

20.5.1 Advantages

The classification of PD symptoms has been significantly improved by AI-based machine learning algorithms, which also improve early detection and individualized treatment. To find patterns suggestive of PD, these algorithms examine a variety of data types, such as voice, EEG signals, and motor activities.

- Voice analysis, which identifies minor speech abnormalities connected to the illness, is one type of information that machine learning models can use for predicting PD symptoms [53].
- AI-based machine learning methods enable better PD classification by evaluating electroencephalography (EEG) data, leveraging extended empirical mode decomposition (EEMD) for feature extraction and deploying models like RF, gradient boost, SVM, CNN, and deep neural networks (DNNs) for accurate detection [54].

20.5.2 Disadvantages

- The classification in supervised machine learning is prone to error due to labeling by clinicians in classifying the disease stages and quantification [55].
- The "black box" nature of machine learning is a common challenge. New deep learning models, also known as DNN models, usually consist of millions of parameters that increase the complexity and render the models incomprehensible to clinicians for accurate classification of results [55].
- The training of numerous AI models is based on restricted datasets, possibly failing to encompass the complete range of PD symptoms. This could result in overfitting and a lack of robust generalization. Additionally, AI models may encounter challenges in selecting features and relying on subjective data interpretation, consequently affecting their accuracy and clinical relevance [56].

20.6 CONCLUSION

AI is regarded as a successful therapeutic alternative for the recovery of individuals with neurological conditions like PD. It supports the creation of novel assessment and rehabilitation procedures. It has demonstrated encouraging outcomes in terms of motor and nonmotor symptoms, improved the quality of care, and reduced the cost for patients and healthcare systems. The intersection of AI and neuroscience is making significant future advancements, and emerging technologies have the potential to drastically change the way of managing PD.

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21 Targeting Upper-Limb Sensory Gaps
New Rehab Insights for Chronic Neck Pain

Sahar Zaidi, Sohrab Ahmad Khan, Charu Chhabra, Habiba Sundus, and Irshad Ahmad

21.1 INTRODUCTION

Chronic neck pain (CNP) is one of the major musculoskeletal health problems worldwide. Seen in the general population, the prevalence of neck pain worldwide ranges from 0.4% to 86.8% with a mean prevalence of 23.1%. Higher prevalence was estimated among women, in higher-income countries, and in urban areas [1]. In the Global Burden of Diseases (GBD) 2010, neck pain ranked 21st on the global burden and fourth in terms of disability among the 291 conditions that were considered [2]. Global prevalence of neck pain of greater than three months duration has increased to 21% in the ten years between 2005 and 2015 [3] (GBD 2016). When quality of life (QOL) of CNP was measured, it was found that longer duration of symptoms results in negative effects on the mental health status of the patients [4]. Moreover, certain cognitive factors seen to be related to higher intensity of pain are mainly pain catastrophizing and greater vigilance toward pain [5].

Furthermore; sleep quality disturbances in CNP have been reported. It has been demonstrated that 68% of mechanical neck pain patients reported poor quality of sleep with a Pittsburgh Sleep Quality Index (PSQI) score of >8. Sleep disturbances should be taken into account while treating neck pain patients [6]. Additionally, greater intensity of pain was reported to be one of the risk factors of insomnia in CNP in addition to depression, female gender, older age, and any other comorbid musculoskeletal conditions [7].

The recent evidence emphasizes the dysfunction of scapular stabilizers in CNP patients. The work of Cagnie et al. (2014) and Cools et al. (2013) signified the scapulothoracic muscle's role in CNP patients [8, 9]. Secondly, upper-limb repositioning acuity, i.e., position matching, was found to be reduced in CNP patients [10]. Zabihhosseinian et al. (2015) postulated that neck muscle fatigue alters upper-limb proprioception [11]. Yilmaz et al. (2024) suggested that target-controlled goal-directed training should be incorporated into rehabilitation [10].

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Raizah et al. (2023) reported that disruptions in cervical spine proprioception are frequently associated with impairments in functional balance in individuals with CNP [12]. Balance disorders can also be aggravated by misalignment between cervical, visual, and vestibular reflex pathways, which may cause inappropriate sensory integration within the CNS.

These sensory deficits emphasize the need to address proprioceptive deficits to improve CNP patients' functional outcomes. Thus, this review aims to implicate these findings in the rehabilitation of CNP patients and raise awareness about these treatment regimens among rehabilitation clinicians.

21.2 SCAPULAR DYSFUNCTION AND CHRONIC NECK PAIN

CNP is defined as pain experienced in the posterior region of the cervical spine, which persists for more than three months with any generalized neck and/or shoulder pain where symptoms can be detected by cervical spine movements, with sustained postures of neck, or on deep palpation of the cervical spine muscles [13, 14]. However, scapular dyskinesia is defined as any alteration in the movement of the scapula during upper-limb movements or its position at rest [15]. Helgadottir et al. (2011) in their study revealed that in CNP patients, there is an alteration in the alignment of the shoulder girdle and cervical spine with reduced clavicular retraction and scapular upward rotation during upper-limb movements and decreased cranial angle [16]. The work of Cagnie et al. (2014) and Cools et al. (2013) further emphasizes scapulothoracic musculature [8, 9]. These muscles have some common attachment points with cervical muscles, and thus any alterations result in abnormal strains in cervical regions [8]. They provide major stability as well as mobility to the cervical spine The main scapular muscles involved in chronic neck pain are the upper, middle, and lower trapezius and the serratus anterior, pectolaris minor, levator scapulae, and rhomboids [9] (Figure 21.1).

Biomechanically altered activity of these muscles was reported. For instance, Castelein et al. (2016) postulated that patients with neck pain were found to have lower control of the middle trapezius when compared to healthier counterparts, and this reduced ability of the trapezius to retract results in abnormal position of the scapula [17]. Moreover, increased tension in the levator scapulae leads to compressive forces on the cervical spine [18]. Serratus anterior delayed activation of lesser duration was also postulated by a study [17]. Thus, it is evident from the aforementioned studies that altered activity of scapular muscles in CNP patients results in scapular dysfunction, which subsequently leads to the development of mechanical chronic neck pain. Scapular stabilization exercises are the mainstay of chronic neck pain patients. Current evidence implicates retraining scapular muscles with selective activation of muscles. By definition, stabilization means the ability of a system to resume its orientation after any perturbations or movement [19]. To restore the purposeful movement of the scapula, exercise training should be in a manner that should be specific to the pattern evaluated and target the patient's functional deficit [8]. As suggested by Cools et al. (2013), these training regimens should be focused on the patient's daily life limitations, which can eventually bring significant changes in their symptoms [9].

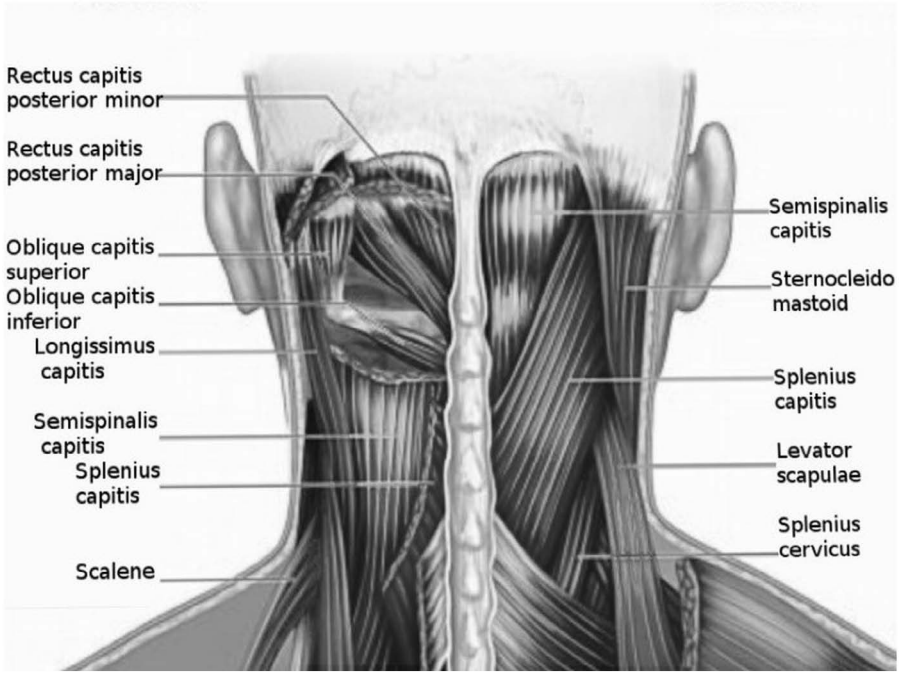

FIGURE 21.1 Muscles of the cervical spine.

21.3 SENSORIMOTOR SYSTEM AND PROPRIOCEPTION

Dr. Vladimir Janda, during the 1950s and 1960s, advocated that sensory and motor systems cannot be taken as two different, separately working systems; instead, he integrated them in his approach to manage chronic pain syndromes[20] (see Figure 21.2). Janda and VaVrova (1996) developed rehabilitation of the lower extremities as well as the spine [21]. It was recommended that there are three locations in the body where enormous amounts of proprioceptors are present, which are mainly the foot, sacroiliac joint (SI), and the cervical spine. The aim was to increase proprioception of these sites to facilitate a smooth, well-coordinated movement pattern.

Proprioception was first devised by Dr. Charles Sherrington (1906). It was defined as a sense of position, posture, and movement. Freeman and Wyke (1966) did further research and declared that proprioceptive receptors were found in the nerve endings of the joints of cats, and if these receptors were disconnected from the CNS, cats were incapable of walking correctly [22]. To describe proprioception includes afferent information arising from joint mechanoreceptors that are responsible for postural control, joint stability, and other conscious sensations. Thus, it includes subsystems: joint position sense (posture of segment), kinaesthesia (which can be active or passive), and resistance to movement as described by Sherrington [23, 24]. Contrary to this, Somatosensory System is a broader term that encircles

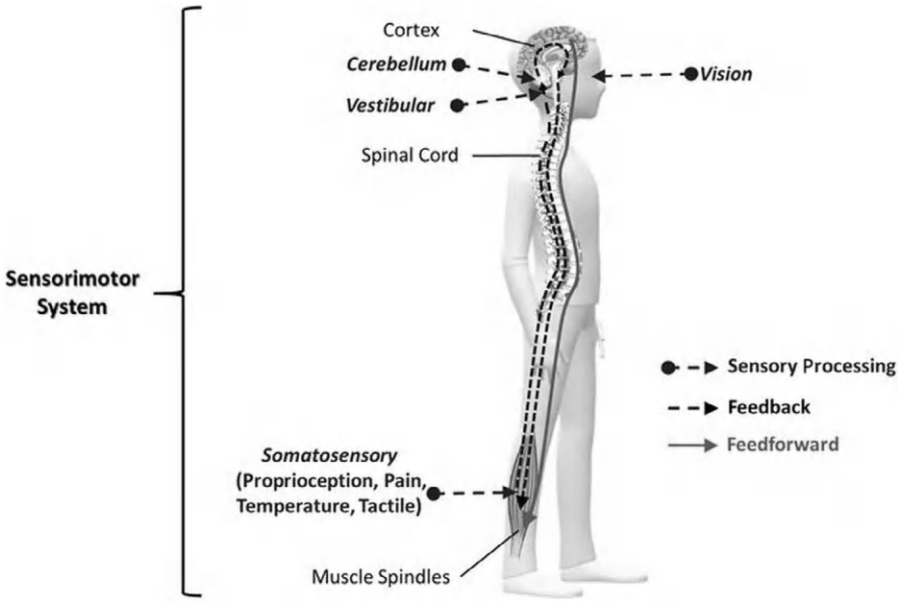

FIGURE 21.2 The sensorimotor system.

mechanoreceptors, thermoreceptors, and nociceptors [24]. Proprioceptors are present in muscle, tendon, ligament, and capsule, while other mechanoreceptors are also found in deep skin and fascia [25]. Those located in the musculotendinous junction are known as Golgi tendon organs (GTOs), whereas muscle spindles are found in muscle tissue. The main function of GTOs is to cue for active muscle tension, i.e., during the state of contraction, and not during an inactive or passive state [26]. Any goal-directed movement requires feedback through mechanoreceptors and feed-forward control, i.e., anticipating change [24].

21.4 ALTERED PROPRIOCEPTION IN MUSCULOSKELETAL DISORDERS

Altered proprioception can be related to various clinical findings like pain, muscle fatigue, and effusion [27]. Cervical spine disorders can lead to the development of impaired proprioception, as stated [28].

21.5 ALTERED PROPRIOCEPTION AND ITS CONSEQUENCES

Consequences such as changes in motor control strategies were observed. For instance, decreased activation of deep cervical flexors was observed during upper-limb tasks [29]. Painful musculoskeletal disorders alter load sharing among muscles and result in various neuromuscular adaptations and decreased repositioning acuity in performing movement tasks [10, 30]. These dysfunctions

result in clinical symptoms of disrupted coordination and smoothness of movement [28].

21.6 UPPER-LIMB PROPRIOCEPTION IN CHRONIC NECK PAIN

Cervical muscles of the spine have abundant proprioceptive receptors, which have an association with central and peripheral reflexes, including the vestibular system, postural control, and visual systems [31]. Additionally, the suboccipital muscles particularly own a high density of muscle spindles [27, 32]. The upper-cervical spine from C1 to C3 has direct connections to the vestibular nuclear complex and the superior colliculus, for synchronization between the head and neck movement with vision [33, 34]. It was seen in a handful of studies that position sense in arm movement, i.e., repositioning acuity, is reduced. Reduced repositioning acuity of the elbow in people with whiplash-associated disorder (WAD) and of the shoulder in CNP and WAD has been observed [10, 35]. Röijezon et al. (2009) hypothesized that CNP has decreased neck-shoulder proprioception due to reduced precision in fast pointing movements [36]. Moreover, CNP was found to have more jerky movements of the cervical spine with decreased smoothness of the movement, leading to poor motor control [28]. The head position has a major impact on the organization of sensory information for upper-limb proprioception [35, 36]. Furthermore, it was postulated that any change in the position of the head and neck with vision occlusion affects sensory information and elbow joint position sense in neck pain patients with WAD [35]. Thus, they demonstrated that the position of the head determines the position of upper-limb segments as CNS constantly matches the position of the head and neck with the upper limb; consequently, head movements and altered proprioception result in reduced accuracy of upper-arm movements [11]. It is suggested that the acuity tasks of pointing, especially endpoint acuity, were variably affected in CNP patients compared to healthier controls [10]. From a functional point of view, affected proprioception and goal-directed movements reduce the ability of an individual to carry out activities like carrying, reaching for objects, and lifting. If there is a small increase in endpoint variability, it will affect precision and timing, which will eventually compromise the performance of an individual whether in playing sports or any musical instrument [10]. Possible mechanisms as postulated by Yilmaz et al. (2024) are quite tentative. They include reduced acuity of signals from the muscle spindle system and injuries of the peripheral nervous system somewhere along the sensory pathways, although they argue that it is not a major factor, as there are no symptoms of paresthesia or sensory loss in their patient population [10]. Visual disturbances and oculomotor deficits have been found to affect those with chronic neck pain. A strong association between self-rated neck function and endpoint acuity was found. [37].

21.7 IMPLICATIONS IN REHABILITATION

The main objective of this analysis is to provide an update on the rehabilitation of CNP patients and to extend the knowledge of clinicians to develop a new treatment regimen of scapular stabilizers and upper-limb proprioception

training as an adjunct in the current exercise methods. Active joint repositioning technique for enhancing upper-limb proprioception is based on motor learning. Motor learning is defined as relative or permanent changes in behavior that are enhanced by the practice of movements [38]. The two main effects of motor learning are retention and transfer. Retention is when the changes last for a longer time due to neuroplastic changes in the CNS, and the transfer effect is when the transfer of this training is seen in other similar tasks or daily activity task requirements [38]. To enhance the training, the factors responsible are that we must ensure that exercise is not too easy or too difficult for the patient and should be adjusted accordingly to the patient's skills (challenge point framework). Secondly, it should include repetitive solving skills rather than repeating it only once [38, 39].

Each patient will encounter three phases of motor skills acquisition: the cognitive phase, the associative phase, and the autonomous phase (see Figure 21.3).

Cognitive phase: It involves making the patient understand what to do. This phase has inconsistent but large gains.

Associative phase: When the patient determines the strategy to perform the task. Here the gains are more gradual.

Autonomous phase: When less conscious is needed to perform the task and is simultaneously performed with other tasks [39, 40].

Looking at these aspects, we can determine whether motor learning improves after proprioceptive training. Ostry et al. (2010) postulated that teaching an individual to reach with a directional force will result in systematic change in the perception

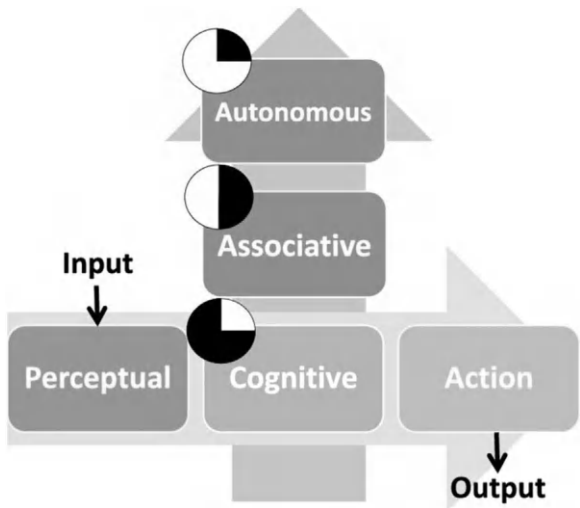

FIGURE 21.3 Phases of motor skill acquisition.

of hand position in space, and the perceptual change persisted for 24 hours even when the duration of training is as short as ten minutes [41]. Thus, learning to produce accurate movements is both sensory and motor [42]. Wong et al. (2012) experimentally concluded that motor learning is improved by proprioceptive training [43]. The observed motor learning improvement results from changes in motor cortical regions and subcortical regions. The other areas involved are the cerebellar cortex and dorsal premotor cortex [42].

21.8 CONCLUSION

There is a scarcity of research on the aforementioned concept, i.e., upper-limb proprioceptive training in CNP patients. Although the work of Cagnie et al. (2014) and Cools et al. (2013) signifies the scapulothoracic muscle's role in neck pain patients, literature still lacks any evidence-based study for upper-limb proprioceptive training to the best of our knowledge and skills [8, 9]. The prognosis of CNP is poor as indicated that 50−85% of patients who experience CNP report neck pain in the next five years [44]. Thus, it depicts that most of this patient population does not recover absolutely. A fine-tuned sensorimotor system is essential for various tasks that require precision. When the proprioception is the deficit, the vision outweighs performing movements [45]. Another method to improve accuracy in goal-directed movements is the co-contraction of antagonistic muscles or stiffening of the muscles to improve endpoint movement variability. Their hypothesis is based on neuromotor noise theory, which describes that prolonged and repetitive movements will result in increased muscle co-contraction [46]. This leads to greater stress on the head and neck and makes it more vulnerable to strains. Consequently, this co-contraction of the muscles reduces the error of the movement but results in wear and tear of small fibers [47].

Other than these large bodies of previous works, recent research is more focused on the kinetic chain. Abichandani and Parkar (2015) postulated that there is a repositioning error in the shoulder, elbow, and wrist joints in CNP patients as compared to healthier controls [48]. Zabihhosseinian et al. (2015) concluded in their study that altered or disrupted upper-limb proprioception due to neck muscle fatigue has negative implications in workplace settings as well as in sports and recreation by increasing the chances of upper-limb injuries [11]. Lastly, a recent study confirmed that in CNP patients with neck fatigue, wrist joint position sense is affected [49].

There is a need to understand these interconnections and their impact on the population of CNP. This will help clinicians identify the cause of the symptoms and treat patients with long-term goals to prevent reoccurrences. Integration of these systems should be the focus of all treatment regimens rather than treating the condition in isolation. The entire purpose of presenting this literature is to bring forward an insight into recent advances in the physiological basis of our treatment approaches. Regimens that are more focused on movement control and that integrate vision and proprioception of the neck and upper extremities should be a part or adjunct to the rehabilitation of CNP.

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