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Neuroimaging: Mapping and diagnosis of Neurodegenerative diseases

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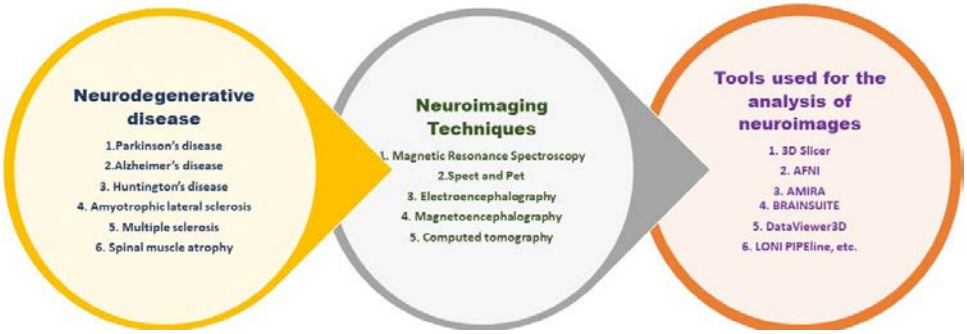
Review

ABSTRACT



Dementia is particularly difficult to diagnose in its early stages when family members and professionals frequently mistake the patient's symptoms for normal aging. Alzheimer's disease, Huntington's disease, Parkinson's disease, multiple sclerosis, and amyotrophic lateral sclerosis are the most common diseases linked to neurodegeneration. In the last twenty-five years, a number of advanced techniques have been established that permit precise viewing of organ structure and function. Neuroimaging technology examines in detail the functioning of different parts of the human brain and thus plays a vital role in clinical and scientific applications. The current opportunities for neuroimaging techniques in the diagnosis and differentiation of neurodegenerative illnesses are presented in this review. This paper also provides a review of the bioinformatic tools that have been used to analyze these structures. Additionally, it offers an exceptional understanding of the available neuroimaging devices, enabling better decision-making in selecting instruments for specific research purposes. Lastly, this paper discusses the implemented methodologies, system requirements, strengths, and weaknesses of the instruments broadly used to visualize the structures and functions of the nervous system.

Keywords: Neuroimaging, Neurodegenerative Diseases, Central Nervous System, Bioinformatics, Image Analysis.

INTRODUCTION

Neuroimaging is the study of the brain's various functions and has been gaining popularity among scientists. In the field of neuroimaging, pictures of the brain can be captured without causing any harm to the patient in order to study the anatomy and operation of the nervous system. It examines a number of systems, including cognition, information processing, and changes in the brain during the diseased condition. For medical research and diagnosis, neuroimaging has grown quickly in recent years and is now a potent tool. So it was developed to allow scientists to study the unusual features of human brains. Back then, it was very restricted to exploring the neurophysiological structure and functions of psychological processes. Because of this, the experiments and study of the brain could only be conducted in animal models and post-mortem examinations. To assess the most prevalent types of central nervous system diseases, many diagnostic procedures are employed. Different neuroimaging methods, such as high-

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resolution magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission tomography (SPECT), etc. have been developed in recent years. These have greatly aided in identifying the anatomical and functional elements that underlie mental illnesses. Neuroimaging methods have recently made significant contributions to the diagnosis and treatment of anxiety disorders.[1] Despite the significant progress in neuroimaging techniques for evaluating central nervous system diseases, there is no definite pattern of pathological changes in neurodegenerative disease has been observed. To diagnose moderate cognitive impairment and Alzheimer's disease, however, it is possible to employ tools like MRI and functional neuroimaging to examine the brain's metabolic activity and blood flow. No longer used to study changes in the brea-th, ultrasounds. Instead, new techniques have replaced them, that allow the study of changes without an autopsy. Some molecular imaging techniques have been described as biomarkers for the diagnosis.[2] MRI, DST, and MIBG scans are commonly used as potential biomarkers for assessing the clinical diagnostic criteria for people with the disease. Neuroimaging was defined as a potential biomarker for progressive supranuclear palsy. Other criteria for the diagnosis of neurodegenerative diseases refer to only characteristic findings from neuroimaging. They do not consider the role of imaging as a biomarker.[3]

Neuroimaging tools are complex and require extensive coding expertise. Prior to 2016, neuroimaging tools were usually standalone. Only black and white images of the nervous system were intended for them. This technology has allowed us to create tools that are more accurate and precise in their approach. The present article provides an overview of the methods that have been employed to produce representations of the human nervous system's composition and operation. Each tool comes with a thorough source, link, and function explanation.we have discussed some of the bioinformatic tools that help us in analyzing the neuroimage. Also, the system requirement as well as the benefits and drawbacks of using these instruments on the neurological system were revealed.

NEURODEGENERATIVE DISEASE

The heterogeneous group of diseases which are represented by the progressive degeneration of structure and loss of function of the central nervous system or the peripheral nervous system is termed neurodegenerative diseases.

Parkinson’s disease:

Parkinson’s disease is a progressive and debilitating disorder of the peripheral nervous system. It is characterized mainly by motor and non-motor symptoms. The most common kinds of motor symptoms include tremors, muscle rigidity, and slowness of movements. Non-motor symptoms are of advanced stages at Parkinson’s disease. They include depression, anxiety, and cognitive dysfunction.[4] In people with Parkinson's disease, the cells that produce the chemicals known as dopamine in the brain become damaged or die. This impairs their ability to communicate with each other. When these cells fail to produce enough dopamine, the brain's basal ganglia lose its ability to control body movements. This impairs the function of the nerve cells that supply the chemical.[5]

The disease is also commonly recognized by psychiatrists and other health care professionals. It has been observed that a high percentage of people with Parkinson’s disease are misdiagnosed when their diagnosis is based on clinical criteria.[4] Another method that can help to detect the illness is functional imaging. Numerous methods have been employed to investigate the severity of neuronal loss in humans. They can also be carried out in real time utilising nuclear medicine. In addition, MRI and cranial computed tomography scans are usually utilized for the diagnosis of progressive brain changes. MRI scans can be used for the mild to moderate phases of the condition. For the diagnosis of diseases of the central nervous system, MRI is superior to CT. It can also be used to evaluate periventricular white matter anomalies, which are often associated with dementia.[6] MRI has been used in the treatment of atypical and differentiated forms of Parkinson's disease. PET and SPECT can be used to detect subtle changes in the pathophysiological brain.[7,8] These are the various methods that are used to detect early stages of cognitive impairment. This procedure can detect the level of positron-emitting radios at a spatial resolution of 3 to 5 mm. Through positron emission tomography, it is possible to monitor the changes in cerebral blood flow, oxygen, and dopa metabolism in real-time. A commonly employed procedure for determining the emission of particle emission tomography, or ET, is single-photon emission tomography, or SPET.[9] Structural imaging is used to detect changes in the brain structure. It is also used to examine changes in the brain's metabolism and receptor binding. For the assessment of the dopaminergic terminals in the striatum, neuroimaging investigations of the nigrostriatal dopaminergic pathways are crucial. There are three ways to estimate the function of dopamine terminals. The activity of dopa decarboxylase is regulated by the presence of adenine decarboxylase. It is also involved in the availability of presynaptic dDP and VMAT2.[10]

Alzheimer’s disease:

Alzheimer's disease is a progressive illness that usually affects the elderly. Memory loss and other cognitive problems like difficulty with abstract thought, planning, and motor tasks are defining characteristics and key symptoms. These areas of the brain are distinguished by pathological structures called amyloid plaques and neurofibrillary tangles.[11,12] The progression of Alzheimer's disease is characterised by a hierarchy, which means that information about the disease stage is related to the density and spatial distribution of its symptoms.[13,14] Alzheimer's disease's precise cause is still unknown but, at a fundamental level, the brain's proteins don't function properly, which can harm the cells that regulate emotion and behavior. The most common changes in Alzheimer's disease occur in the parts of the brain that affect learning and memory while these changes can manifest in various forms of behavior and mood hence, it can also lead to worsening memory loss and other severe symptoms. In Alzheimer's disease, computerized tomography and magnetic resonance imaging may reveal non-diagnostic cerebral atrophy.

Although, novel neuroimaging techniques are being developed to improve the accuracy of diagnoses and the discovery of new treatments. These tools can also measure the levels of certain neurotransmitters and the tau tangles in the brain. Two approaches

are used to detect AD, automatically by EEGs. In the first approach, DWT is applied to the signals to obtain major EEG sub-bands, and then the PSD of each sub-band is calculated using Burg's method. The second method computes interhemispheric coherence values [15]. MRI and CT scans may detect non-invasive cerebral atrophy in patients with AD so, magnetic resonance imaging is a commonly used method to study the various features of the brain. It can detect vascular pathology and white matter abnormalities as well as the structures in the temporal lobe, which are crucial for normal memory, can be measured using MRI.[16] Both techniques can also help identify Alzheimer's disease because amyloid plaques are the most common characteristic of Alzheimer's disease and they are insoluble deposits of the beta-amyloid protein. Amyloid fragments are commonly used as AD biomarkers so it can inform us of the pathophysiological processes involved in AD.[17,18] Tau tangles are pathological proteins that are primarily found in the axons of neurons. The degenerative process in AD usually appears around 20 to 30 years before the symptoms of the disease appear hence, biomarkers are useful tools that can help diagnose AD in the early stages.[19,20] These instruments are used for the evaluation of safety and efficacy of drugs in AD in addition they are capable of offering objective and trustworthy assessments of disease-modifying treatment in AD.[21]

Huntington's disease:

Huntington's disease is a neurodevelopmental disorder characterized by various motor and cognitive abnormalities. It usually appears during middle age and is triggered by various genetic defects. HD is a group of motor, cognitive, and psychiatric abnormalities. It can cause various symptoms, such as motor and cognitive decline.[22] Huntington's disease (HD) is defined by the presence of mutated huntingtin in the form of intranuclear inclusions within the brain. These aggregates have a negative impact on the function of various transcription factors, leading to the decline of GABAergic medium spiny neurons (MSNs) both in the striatum and cortical regions.[23] The condition is caused by a single inherited defect in the gene. In order to develop it, the affected individual only needs one copy of the defective gene.[24] The first symptoms of hereditary diabetes usually appear in middle age. This is, when patients typically give birth and pass the genetic defect to the following generation. In most cases, the diagnosis of HD is relatively simple in patients who have a known family history of choreiform movements or cognitive dysfunction.[25] Besides, MRI and computed tomography scans are usually not able to reveal any structural changes in the brain during the early stages of HD. However, they can help evaluate the atrophy of the frontal and caudate cortex during the later stages of the disease. Despite extensive research, there is still no validated biomarker for HD, no cure, and the disease will ultimately result in death, usually occurring 15 to 20 years after the onset of symptoms. The exact causes of the clinical symptoms and the progression from pre-symptomatic stages to full-blown symptoms are not yet fully understood.[26]

Numerous studies have demonstrated that functional imaging techniques like oxygen emission triangulation (ET) and single atom emission tomography (SEAT) can be used to assess cerebral blood flow and local brain metabolism.[27] PET is a type of imaging technique that uses radionuclides that have short half-lives. These radionuclides can be used for various applications such as quantitative analysis and monitoring physiological processes. Although both MRI and CT can detect changes in the brain caused by Huntington's disease, they cannot diagnose the disorder in its early phases. Instead, they are only able to provide information about the disease's symptoms. SPECT is a procedure that uses radionuclides, which are half-lives of which are longer than 3 h. Since they do not require a cyclotron, they are more widely used.[27,28]

Amyotrophic lateral sclerosis:

Amyotrophic lateral sclerosis is a progressive disorder that manifests itself through the degeneration of the central nervous system and the progressive degeneration of the corticospinal tract, brainstem, and anterior horn cells of the spinal cord. Amyotrophic lateral sclerosis (ALS) causes the motor neurons in the brain to gradually deteriorate. This causes the motor neurons to die and limit voluntary muscle movements. When the motor neurons are damaged, they can't send and receive messages to the muscles. This causes the muscles to fail.[29] Motor neuron disease may manifest with the progressive degeneration of the pure upper motor neuron (UMN), the pure spinal lower motor neuron (LMNs), or the bulbar motor neuron (MN).[30] The main symptoms of this condition are progressive muscle atrophy, muscle twitching, and spasticity. A person with Amyotrophic lateral sclerosis (ALS) is usually not able to cure or treat the illness. It progresses to death within 3 to 5 years. Although MRI scans of patients with amyotrophic lateral sclerosis (ALS) can show signals of changes in the corticospinal tracts, but these are usually not confirmed by other researchers. There have also been reports of mild to moderate cortical atrophy in some individuals. fMRI is a diagnostic tool that can identify focal neuronal activation due to increased blood flow and oxygen extraction.[31,32] However, it lacks the specificity and sensitivity that are necessary for distinguishing abnormal features from healthy individuals. SPECT imaging shows a decrease in the blood flow to the frontal and the parietal cortex during an evaluation of brain perfusion using the 99mTc-ethyl cysteinate dimer. Studies using FDG-PET have shown that disturbed glucose metabolism and rCBF can occur in the basal ganglia and the sensorimotor cortex.[33]

A multi-modal neuroimaging study was performed on a group of 25 individuals diagnosed with Amyotrophic Lateral Sclerosis (ALS) and compared to a group of healthy control subjects. The neuroimaging techniques utilized included T(1)-weighted imaging, diffusion-weighted imaging, and resting-state functional magnetic resonance imaging. This combination of techniques allowed for an evaluation of both the structural and functional connectivity in the brain. The results showed that there was a dichotomy in the failure of the cerebral network in ALS, characterized by increased functional connectivity in areas with reduced structural connectivity. Interestingly, patients with a slower rate of disease progression had connectivity measures that were closer to those of healthy controls, suggesting that the increase in functional connectivity might not be solely a result of reduced structural integrity.

Multiple sclerosis:

Multiple sclerosis is a chronic illness that occurs when the central nervous system's demyelination causes lesions to form. Although the link between MS and viral infection is not yet clear, it has been theorized that an autoimmune disorder could be causing the condition. Multiple sclerosis is a very unpredictable condition. Multiple sclerosis is a disease that occurs when the body's immune system unintentionally attacks its own tissues. This inhibits brain and spinal cord function.[34] It can vary significantly between cases while the usual symptoms of depression include anxiety, fatigue, and depression. They can also change their personality, experience unilateral loss of vision and almost half of the cases of MS involve cognitive impairment.[35] The symptoms of Multiple Sclerosis (MS) are characterized by demyelination and inflammation resulting from the damage to the protective myelin sheath, and the lesions associated with MS can change and worsen over time. As with all diseases, brain atrophy can affect all parts of the brain.

Diagnosing multiple sclerosis (MS) often involves the use of neuroimaging techniques, including magnetic resonance imaging (MRI).[36] This imaging tool provides in-depth images of the central nervous system, allowing the detection of MS-related changes. MS is a chronic autoimmune disorder that affects the myelin sheath surrounding nerve fibers in the central nervous system. The immune system attacks and damages the myelin, leading to scarring, which is known as sclerosis. MRI can also detect new or active areas of inflammation, which are indicative of a relapse or exacerbation of MS.[37] This information is crucial for monitoring the progression of the disease and evaluating the efficacy of treatment.

In conclusion, MRI and other neuroimaging techniques are key for detecting and monitoring MS, offering a non-invasive way to visualize changes in the central nervous system and track the progression of the disease over time.

Spinal muscle atrophy:

The nerves that manage the upper and lower portions of the spinal cord are impacted by spinal muscular atrophy, a deadly condition.[38] SMA, a neuromuscular disorder with a frequently fatal outcome until recently, with those affected never being able to sit, stand, or walk, children now achieve these motoric abilities and almost age-based development when treated pre symptomatically.[39] It is characterized by weakness in the trunk and limb muscles that affect the proximal and lower limbs. It is also known to manifest as limb and trunk weakness. The main clinical features of SMA are evaluated by a neurologist. They may also be backed up by a person's favorable family background.[40] The onset of respiratory problems caused by scoliosis significantly reduces the risk of SMA, an autosomal recessive hereditary disease. It is hypothesized that continuing to walk would significantly reduce or delay the appearance of related complications, thereby increasing life expectancy and improving quality of life. SMA Reduced expression of the ubiquitously expressed SMN protein causes infantile or childhood mortality. The SMN protein is a component of a multiprotein complex that is required for the cellular assembly of ribonucleoprotein particles involved in various aspects of RNA metabolism.[41] In general, diagnosing spinal muscle atrophy (SMA) involves the use of neuroimaging techniques, including magnetic resonance imaging (MRI) and computed tomography (CT) scans.[42] These techniques allow for a comprehensive evaluation of the spinal cord and surrounding muscles. MRI provides clear images of the muscles, which enables the assessment of their size and volume.[43] In cases of SMA, the muscles in the spinal cord may appear smaller and thinner than normal, demonstrating muscle atrophy. MRI can also reveal changes in the spinal cord and related structures that are characteristic of SMA, such as an enlarged spinal canal or degeneration of the nerve roots. CT scans provide cross-sectional images of the bones in the spinal column and can demonstrate a reduction in the size of the vertebral bodies and an enlarged spinal canal, additional signs of muscle wasting.[44] However, the primary clinical features of SMA are usually evaluated along with a family history. SPECT imaging reveals areas of hypoperfusion in the brain. This method is usually used for detecting CNS lesions in SMA diagnosis [45], [46]. In addition some previous investigations described three patients with SMA 0 who had bMRI abnormalities that were widespread and progressive over time: supratentorial brain atrophy with severe white matter reduction, severe hippocampal atrophy, and thinned corpus callosum.[26] In conclusion, neuroimaging plays a crucial role in diagnosing SMA by presenting visual evidence of muscle wasting and weakness, as well as other changes in the spinal cord and surrounding structures.

NEUROIMAGING TECHNIQUES

Neuroimaging is a technique used for studying the human brain in terms of healthy and impaired individuals. Neuroimaging is a type of technology that provides visual representations of various parts of the central nervous system and the brain. It is mainly used for the diagnosis of intracranial disease and structural abnormalities [47]. Besides these, it also studies the effects of metabolic and physiologic factors on the brain. Walter Dandy was a neuroradiologist who discovered the use of pneumoencephalography in 1918. He used air bubbles to stimulate the lateral ventricles of the brain.

Neuroimaging falls into two broad categories:

1. **Structural imaging**: is a type of imaging that focuses on the structure of the brain. It helps identify diseases such as tumors and aneurysms. The properties of the brain are studied utilising structural imaging techniques in this field. This method can also be used to locate structures and analyse their geometric properties. It can also determine a structure's size and volume.
2. **Functional imaging**: is a type of diagnostic imaging that focuses on processes related to metabolic diseases and cognitive disorders. The goal of these methods is to detect the presence of biochemical activities in cells or tissues. Some of the often employed techniques are functional magnetic resonance imaging (FMRI), oxygen emission tomography (ET), and electro-encephalography. Various types of neuroimaging techniques that were used to review this study are as follows,

MRI:

Functional magnetic resonance imaging and magnetic resonance imaging are the most commonly used methods for studying psychology.

Structural MRI: T1-weighted structural MRI is a method of choice for the analysis of the gray matter. It provides good tissue

contrast and is commonly used for the study of gray matter. The most basic approach to evaluating the impact of a disease process is to identify a region of interest (ROI) based on the acquired images. Several tools are currently available that allow automated segmentation of brain structures.[48] These techniques can also reveal differences in surface area and thickness of structures [49]. Automated segmentation tools can help minimize manual delineation, improve interrater variability, and provide good accuracy. Additional automated post-processing tools, like voxel-based morphometry, can aid in the visualization of grey matter density maps.[50,51]

Intensitometry derivatives of VBM can be used to diagnose ALS white matter pathology.[52] However, diffusion tensor imaging is the approach that is most frequently utilised. In white matter, the distribution of water molecules is elliptical. It is due to the constraints imposed by membranes on the movement of these molecules. The diffusion tensor model can be used to describe the behaviour. This model shows the elliptical displacement profile using mathematical formalism. The diffusion tensor model can be used to describe the behaviour.[53] The concept of diffusion tensor metrics is often misunderstood due to the complexity of their measurements and their dependence on underlying microstructural causes.[54] For instance, they are influenced by the presence of multiple fiber species in a single MRI voxel. Due to the lack of the diffusion tensor model's description of fully multivoxel fiber bundles, the concept of high-angular resolution diffusion imaging has been developed. DTI metrics can be analyzed using various methods, such as ROI, tract-based spatial statistics, or whole-brain voxel-wise analysis. There are also various applications related to brain connectivity.[55,56,57]

Magnetic fields are uniform and strong enough to require a few parts per million across a wide scan volume. The field strength is measured in teslas. The field strength of a magnet is measured in teslas, and while many systems operate at a 1.5 T, commercial ones can be used up to 7 T. Permanent magnets can be used to achieve lower field strengths, which are used in MRI scanners for patients with claustrophobic conditions. In the ultra-low fields, MRI has been demonstrated using prepolarization and Larmor precession methods. This procedure can provide sufficient signal quality for MRI in microtesla-tomillitesla ranges.[58]

Functional MRI: The most widely used technique for functional MRI is based on the response that is dependent on blood oxygen levels. It assumes that firing neurons cause a spike in blood oxygen levels. Deoxygenated and oxygenated hemoglobin have different properties that make them detectable by MRI. A task that is repeated several times can affect the patterns of MR signal variations in the brain. These variations can be used to determine the areas of the brain that are affected by the task's effect on the brain. A resting-state fMRI is an advanced technique that enables the study of the brain's functional organization at rest [59]. This procedure allows the exploration of the brain's signals when the brain is not performing an explicit task. While studying the resting-state connectivity of brain regions, researchers have found networks that are similar to those that are involved in certain tasks.[60] The most popular method for analyzing resting-state fMRI data is seed-based or independent component analysis.[61] To calculate late signal correlations with other pre-defined voxels in the braid or vice versa, a pre-defined voxel, or RI, is used. The focus of this hypothesis-driven approach is on identifying the seeds within and between patients that can be utilised to predict the progression of their illness. An ICA-based approach is mostly observer-independent and can be fully automated.[62] However, it can also be hard to interpret and may not always relate to a particular research context.

Magnetic Resonance Spectroscopy:

Magnetic resonance spectroscopy is a method used to study the metabolites of brain tissue in vivo. The study involves measuring the nuclear magnetic sensitivity of the nucleus. The proton MRS can identify various markers of physiological integrity, such as N-acetyl aspartate, choline, and creatine. G- and glutamine-related metabolites can be measured separately or as a composite of these metabolites in the brain depending on their field strength and signal-to-noise ratio.

A non-invasive diagnostic that analyzes the metabolic alterations in the brain is MRI spectroscopy. It can be used to diagnose brain tumors. MRI scans the anatomical location of a tumor. However, instead of identifying the location of the tumor, it uses spectroscopy to analyze the chemical composition of the brain. In individuals with epilepsy and stroke, this test can be done to find out if there are any tissue abnormalities. An in vivo method used to research the brain is magnetic resonance spectroscopy. This procedure can detect neurochemicals that are relevant to certain processes in the brain. Many methods are used to detect compounds that contain phosphorus and hydrogen. These include 1H-MRS and 31P-MRS. These studies show that the concentrations of neurochemicals, such as N-acetyl aspartate, can affect the performance of tests related to cognitive function. Neurometabolite values are often linked to the extent of cognitive dysfunction in people with neuropsychiatric disorders.[63]

The same machine that is used for MRI is used for this treatment. To produce precise images, it employs a strong magnet and radio waves. This procedure uses spectroscopy to measure the metabolic activity of a tumor in the brain. It can be done on MRI scans. spectroscopy is a type of molecular analysis that uses focused beams of protons or hydrogen ions. It can detect the presence of other molecules. Different metabolites can be measured to identify different tumor types: Amino acids, Lipid, Lactate, Alanine, N-acetyl aspartate, Choline, Creatine, Myoinositol.

Different meteorites' frequency is measured in units referred to as "parts per million." They are plotted on a diagram. The neuroradiologist can determine the type of tissue being investigated in the brain by measuring the ppm of metabolic markers.

To identify the type and aggressiveness of a tumor as well as to differentiate between a recurrent tumor and a radiation necrosis, an MR scan can be performed. Different metabolite indicators include:

- Glioma: lower than normal N-acetyl aspartate levels, elevated choline and lipid levels, and lactate peaks.
- Radiation necrosis: does not have elevated choline levels.
- Meningioma: elevated alanine levels.

Spect and Pet:

Techniques related to neuroimaging have been used in the field of neurodegenerative disease to study the various aspects of

cerebral blood flow and oxygen metabolism. Neuropathology studies reveal those patients with neurodegenerative disease exhibit lesions in the temporal lobe, the parietal neocortex, and the hippocampus.[64] This laboratory investigation uses SPECT to evaluate cerebral perfusion. It has been used to evaluate the function of the brain in people with dementia. Both SPECT and PET can detect and quantify the presence of amyloid in vivo. They can also be used in conjunction with radioligands.[65–67]

This concept is based on the brain uptake of radionuclide-L,L-ethyl cysteinate, or NME, which is a tracer containing technetium 99mime. These compounds can help determine the severity of dementia since they are sensitive markers of cerebral blood flow. The administration of 99mTc-HM is done intravenously. It can be taken up to 2 minutes after the injection. Brain blood flow and oxygen utilization are also measured using Tc-HMPAO SPECT scans. A radiotracer that can be used for the measurement of cerebral blood flow is 123I.IMP-SPECT. SPECT is mainly used for patients with suspected Alzheimer's disease.[68] This imaging method's primary drawback is that it cannot be used in real time.

A more sensitive technique known as PET can be used to detect abnormalities in the brain before it is killed. In a study, patients with neurodegenerative disease exhibited a sensitivity of 94% and specificity of 73%. The metabolic uptake of fluorine 18 and 2 fluorodeoxyglucose in dementia patients has been studied using this method.

It is thought that calcium ions accumulate in damaged nerve cell bodies and that degeneration of axons occurs as a result of a passive flow. ^{57}Co and ^{55}Co are analogues of Ca^{2+} that reflect the influx of Ca^{2+} in chemically damaged cerebral tissue. These methods can be used to gauge how different situations affect the brain. They may also be used for estimating the severity of various diseases such as neurodegenerative disease.[13,69–71]

Electroencephalography:

A convenient and clear window on the brain is provided by EEG. It permits observations of actions related to the electrical circuits that run beneath the bridge. The outside breazier is responsible for most of the cognitions that people experience. For instance, memory is linked to the activities and thoughts of people. The cortical processes involve the electrical signaling between neurons in a given region. The temporal resolution of EEG is the only reliable technology to follow the quick dynamic changes that can happen in response to stress .

Electrode placement inside the skull can be used to study brain function in humans. Internal accountings provide significant measurements of the dynamics of the heart in tiny spatial scales. They can also be used to study behavior and cognition. Intracranial recordings are usually only made for patients with intractable epilepsy.[72] They are typically used for brain surgery. Electrocorticography (ECoGs) are recordings that are made. ECoG recordings are usually only obtained in a limited portion of the cortex. They can be guided by electroencephalogram recordings of epileptic activity.

Electrodes are commonly placed on the scalp to record EEG. It is typically recorded from the electrodes located on the head. Each scalp electrode measures electrical activity in cortical tissue, which contains up to 500 million neurons.[73] These estimates provide important data on the brain's dysfunction for various scientific studies. Human mind measurements can be easily obtained by a large-scale collection of scale reportings. EEG is a monitoring device that measures the state of consciousness of subjects in clinical work or experimental studies. The effects of voltage on the brain are known to affect sleep and behavior. For instance, slow EEG oscillations are associated with deep sleep or anesthesia states. Modern signal analyses enable the identification of various sleep phases and the depth of anesthesia. The findings of these experiments reveal strong connections between cognitive events and physiological signals.[74]

In addition, the spatial EEG resolution is not as good as MRI or PET. These methods do not provide detailed information about the dynamics of neural circuits due to their temporal resolutions. Magnetoencephalography is a type of brain imaging technique that uses magnetic field recordings to study the brain. MEG is a high-resolution digital video recorder that uses electroencephalograph (EEG) technology. The sulcal walls and gyri are the sources of the tangential current in the brain, which is where MEG is sensitive to. Radial sources can affect EEG as well.

Magnetoencephalography:

Magnetoencephalography is a procedure that measures the magnetic fields produced by electric currents inside the brain. The timing of neuronal activity is measured by the MEG test. It is a non-invasive test. MRI and MEG are usually combined to get a better structural view of the brain. This procedure is called magnetic source imaging. Currently, its use is approved for both epilepsy surgery and for mapping of the brain. Most clinical trials for MEG's are conducted at centers for epilepsy treatment.[74]

The brain generates magnetic fields using electric currents. The fields are recorded in the MEG database. The magnetic field of biological tissues is not distorted by the distance between the skull and the scalp. When activated synchronously, neurons produce electric currents and magnetic fields.[75] The MEG outside the skull then records the resulting magnetic field. Similar to electroencephalography, the dendritic currents of pyramidal neurons produce the magnetic fields. The magnetic fields that the brain normally produces have very modest amplitudes. The magnetic field on Earth is between 104 and 105 T. The typical MRI is 1.5 to 3 T.

In order to record the magnetic fields in the field, engineers have a unique engineering dilemma. There are two basic issues with recording magnetic fields: one is to keep track of them, and the other is to protect them from the Earth's magnetic fields. This technology can detect minute magnetic fields. Superconductors need to be maintained in an extremely cold environment. This can be achieved by using liquid helium, which is 3 degrees Celsius lower than absolute zero.

The MEG is housed in a magnetically shielded room. A magnetometer is a type of sensor that measures magnetic fields while a gradiometer is used for measuring liquid magnetic fields. They can be generally used with deep brain sources.

Although the radial dipoles are not detected on the MEG, tangential dipoles are. This is because the radial dipoles' magnetic field is still contained within the cranial cavity. The primary challenge in identifying the source of information in the brain is

that it is not possible to determine the active site of the brain using magnetic fields outside the head. The solution to this problem is not a unique one. Instead, it uses approximations that are based on certain assumptions. An assumption that is commonly used to model neural generators is that the generators are equivalent to current dipoles.[76]

Without distortion, the fields of MEG pass through the head. This benefit of the field allows the brain to function properly. The magnetic field's decrease depends on distance as well. This decay is more sensitive to superficial activity than electric fields. MEG and MRI Brain data are always co-registered to provide Magnetic source imaging (MSI).

Computed tomography:

X-rays are used in computed tomography (CT) to produce cross-sectional images. It should not be used to treat acute radiation sickness or to keep kids from being exposed to radiation. Current paediatric neuroimaging is only capable of evaluating potential cerebral calcifications or acute trauma. Fast and easy to perform, CT is commonly used for the evaluation of various conditions. It is superior to MRI in terms of assessing internal bleeding and osseous structures. Cranial CT can be performed with a helical or sequential technique.[77] Typically, this procedure is carried out with a thin collimation layer and a section thickness of 5 millimetres. The thinly coloured spiral has greater image quality than the thinly coloured sequential one. Additionally, it is possible to get improved visualisation of the brain tissue close to the skull as well as the reduction of skull-basing artefacts.

Primary indications for CT include acute head trauma, stroke, aneurysm, and calcifications. CT is a useful tool for assessing the status of various acute and chronic neurological deficits. It can also be utilized for determining the severity of acute migraines and non-acute headaches. In addition, cranial computed tomography with intravenous contrast can be used in patients with suspected neoplastic or infectious conditions.[78]

Early diagnosis of acute stroke is important to determine if there is bleeding and other mimics of the condition. Non-enhanced computed tomography is also commonly used to rule out hemorrhage and other complications of a stroke. It can also identify signs of acute ischemia.

With the introduction of spiral scanners, the use of CT angiography has become widely used in stroke protocols. This procedure allows for the evaluation of intravascular Thromb, arterial dissection, and vascular malformations. With multisection CT, the number of sections can be simultaneously registered during each gantry rotation, which enables faster and more accurate data acquisition. This procedure also allows the use of very thin sections to improve contrast resolution and minimize motion artifacts. The methods for computed tomography that are most frequently used for post-processing Angiography includes multiplanar reconstruction, maximum intensity projection, and three-dimensional reconstruction. These procedures assist in visualising the vessel's course and its numerous components. Cerebral blood volume, cerebral blood flow, and mean transit time may all be quantitatively evaluated using a resuscitation CT scan. Additionally, it permits the qualitative evaluation of the cerebral blood flow and the cerebral blood volume of the brain. The chemically salvable tissue shows increased MTT, decreased BT, and normal or increased BV in acute stroke. Radiated tissue has decreased BT and BV.[79]

A complex plane or multiple planes can be constructed from the data set to aid in the diagnosis of various disorders. 3D reconstruction can also be used to visualize instruments used in spine and cranial examinations. Mini-, micro and nano-CT scanners are used for in-vivo imaging of small animal tissues and organs.[80] They can provide high spatial resolution and detailed information about disease status and anatomical features. Due to the high-resolution imaging demands, the use of contrast agents is difficult. Instead, mini-CT systems can provide a decrease in scan time and lower applied X-ray dose.

TOOLS USED FOR THE ANALYSIS OF NEUROIMAGES

This section describes the various tools used to research the neural architecture of the nervous system and the connections between behaviour and brain function in humans.

3D Slicer: A 3D slicer is a tool that enables users to visualize and analyze medical images. It works with various platforms such as macOS. A 3D slicer is a programming language that simplifies the process of multi-modality imaging. It works seamlessly across various imaging modalities such as MRI, computed tomography, and nuclear medicine. In addition to taking screenshots, it also enables users to see images in 4D thanks to its adaptable user interface. This software package provides various functions such as 3D surface model creation, manual segmentation, and 3D mesh creation. A 3D slicer is a powerful tool that enables users to easily visualize and interact with data. A guided tour is provided to help users easily learn the software. This feature is usually used by developers and new users.[81] By letting the biomedical researcher concentrate on the implementation of the algorithm and offering abstractions for the typical tasks of data communication, visualization, and user interface development, 3D Slicer serves as a programming platform that facilitates the translation and evaluation of the new quantitative methods.

AFNI: AFNI is a program that provides 3D functional MRI data analysis and visualization. This program can run on Unix workstations. It is written in the C programming language. Color Effects is a program that allows users to transform neural activation maps into high-quality anatomical scans. Users of this application can simultaneously view the slices of each conventional plan.[82] AFNI can also transform functional and anatomical scans to stereotaxic coordinates. A manual automatic database can also be converted into a translated functional database using the software.

AMIDE: AMIDE is a tool that enables the analysis and registration of volumetric medical image data sets. It works seamlessly with all major operating systems. AMIDE is a programming language that uses GTK+. AMIDE is an accessible tool that allows developers to make their own software solutions that avoid the drawbacks of previous packages. It is possible to access the datasets and areas of interest using a tree structure, which can concurrently show and edit a variety of items.[83] It allows users to create 3D models of the objects within their environment, register their rigid bodies, and draw and analyze 3D regions of interest. AMIDE is a non-orthogonal user interface that allows for

a smoother alignment while viewing multiple medical images simultaneously.

AMIRA: A software programme called AMIRA allows users to visualise, modify, and evaluate medical imaging data. A MIRA is a multi-purpose programme that can carry out a variety of image processing and analysis functions. AMIRA accepts 2D/3D image data from a variety of sources, including medical scanners, optical microscopes, and electron microscopes.AMIRA is a tool that provides users with fast, easy, and precise visualization techniques. Techniques such as clipping, probing, and slicing enables high-quality rendering. They also contribute to the ability to perform various tasks such as clipping, slicing, and probing. This software can also be used to analyze medical images by measuring the distance between objects and the surface.[84] It can also perform various tasks such as cell, neuron, and fiber tracking. Movie clip Maker is a utility that enables users to create and share movie clips and animations with their computers. It also supports various video formats.

BioImage Suite: In the areas of registration, segmentation, and FMRI, medical image analysis is made possible by the software package known as BioImage. It features a robust algorithm that enables the analysis of complex medical images. This software is used for creating and maintaining databases. It is also available as a standalone software. The Mosaic Multiple Slice Viewer and the Orthogonal Viewer are the two additional viewers for the BioImage viewer.It features a variety of tools that allow users to draw and process complex shapes.[85] These tools include surface decimation and smoothing, histogram and image processing, and segmentation controls.

BRAINSUITE: BRAINSUITE is a tool that can analyze magnetic resonance images. It can generate spherical representations of the cortex based on the magnetic resonance pictures of the brain.[86] This tool could help improve the accuracy of brain segmentations in clinical trials. The tools featured in this section are used for various applications. Some of these include skull and scalp removal, tissue classification, and rendering. The tool features a graphic user interface. Users with little experience may use it to do a variety of tasks, including filtering pages, registering volumes, and processing diffusion-weighted images.

BrainVoyager: Users can visualise and analyse brain imaging data with the help of the software package known as BrainVoyager. The various data sets utilised for the analysis of electroencephalograms and magnetic resonance images are included in this section.The ability to provide a 3D environment is very useful for people who are graphic designers. The software features an interface that is designed to work seamlessly across various platforms. It is built using the cross-platform .NET framework. The software allows users to easily transfer and exchange data across various platforms. This tool can allow the transfer of data between various platforms. It can also be used to transfer data without errors.[87]

Camino: A software toolkit called Camino makes MRI diffusion processing possible. It offers numerous techniques for fitting a variety of terms, including diffusioin tensor fitting and mean diffusivity. The user documentation is often found in Unix manual pages, and the majority of programmes have a shell scripter. The data pipeline allows you to import and export data. Java-based software for Unix.[88]

COIN: COIN is a web-based collaborative neuroimaging suite. The software suite provides various features such as data upload and sharing, query and exporting, and reporting. The software allows users to easily export data to various popular formats, such as Excel and SPSS. The simple user interface known as COIN enables smartphone users to quickly become familiar with the software's fundamental features [89]. The software suite is built using PHP 5.5. It supports various features and functions. The software package is web-based and may be accessed by web browser plugins on any platform.

CONN: CONN is a software that compiles and displays functional connectivity in fMRI. It works seamlessly across various platforms. The region-of-interest connectivity metrics, graph properties of connectivity networks, and seed-to-voxel connectivity maps are among the connectivity measures. CONN is a platform that enables users to control various physiological or movement effects. It also allows them to perform other dynamic connectivity analysis. It has a graphic user interface that makes it simple for users to modify battle options. CONN is available on various platforms from MATLAB.[90]

DataViewer3D (DV3D): DV3D is a neuroimaging data visualization tool that combines multiple data sources into a single, multi-modal data visualization. DataViewer3D is a Python programming language-based tool that enables users to create interactive data displays. It works seamlessly across various platforms such as macOS. DV3D is a result integration tool that enables you to integrate your results into DV3D. Results from multiple analysis tools and methods can all be integrated. Users of the tool can output 3D models in both 2D and 3D. They can also see the effects of different methods and techniques thanks to it. It makes it possible to produce excellent animated and graphic projects for data exchange.[91]

Explore DTI: Explore DTI, which is a data processing framework that provides functions related to data reconstruction, motion correction, and quality assessment. This package allows you to easily identify and track the output of other tracking packages. It also provides a convenient way to navigate through these outputs. This software helps in creating a quick learning environment for the users. Explore DTI is a programming language that can be used to develop interactive displays on various platforms.[92]

FreeSurfer: FreeSurfer is a software suite that aims to study the human brain. It offers features connected to the volumetric segmentation of the human cerebral cortex representation. Additionally, it encourages the creation of models for the surface of the human cerebral cortex. FreeSurfer is a tool that enables automatic volume segmentation. This feature can also be used to detect and prevent volume overwriting.[93] This feature generates regions of interest for both locals and tourists. The tools include Tkmedit and Tksurf, which are designed to provide high-quality images and visual interactions. C++ is the language used for this software.

FSL (the FMRIB Software Library): FSL is a collection of tools that focuses on the functional and structural MRI brain

imaging data. Most of the tools may be used from the command line, although some can also be used as graphical user interfaces (GUIs). FSL permits the quantification of resting perfusion in axial magnetic resonance imaging. This device can also be used to correct psychological errors in psychological data. A straightforward graphic user interface called Command Line allows users to interact with the underlying command-line utilities [94]. FSL is a utility that compiles C++ code into Perl. It can run on various platforms such as Windows and Linux.

ISAS (Ictal-Interictal SPECT Analysis by SPM)-

ISAS is a tool that can be used to evaluate the results of SPECT scans conducted by SPM. The Ictal SPECT is a tool that measures the onset of seizure onset in patients undergoing surgery for epilepsy. ISAS is a unique tool that compares the interictal and ictal SPECT scans of a patient. This procedure will compare the differences between a healthy database and a random database to identify the normal variation in the database.[95] Any significant effect on CBF will be detected for further evaluation. The utility can be used on a variety of systems and was created in Matlab.

LIPSIA: LIPSIA is a software that enables users to perform functional magnetic resonance image processing on the human brain. It provides functions to visualize and analyze the various parts of the brain, as well as support the rendering of normalizations and registrations. It can also convert data into a variety of formats. LIPSIA is a quick and efficient implementation process for a variety of applications. This tool was tested to handle the raw data from a test subject in less than 10 minutes.[96] C and C++ text can be written using the LIPSIA language. It can only be used with Unix systems.

MIPAV: MIPAV is a medical image processing and analysis system. It is a standalone system that can run smoothly on various platforms. It is compatible with most major operating systems. This tool is a free and licensed JavaScript tool.[97] It permits the analysis and visualisation of images obtained using numerous medical technologies, including MRI, PET, and positron emission tomography. Researchers can easily share their research findings and analyses with the public thanks to this tool.

LONI PIPEline: LONI is a pipeline system that was developed by Ivo and his colleagues. It is compatible with various platforms.[98] This environment is a graphical representation of the steps and procedures involved in validating and constructing neuroimaging data analysis programs. This utility supports the conversion of automated data into grid computing.[99] It also provides a simple user interface and a variety of computational tools. This framework supports the development and deployment of decentralized computational systems for neuroimaging data analysis. This software collects data from the Alzheimer's Disease neuroimaging Initiative.[100] This tool can be used to create a simple and effective XML-based template for the presentation of the text in various formats.

MRIcro: MRtrix is a standalone system that can run on various operating systems. It is compatible with most major platforms. This tool performs weighted MR tractography with robust crossing protocols. It achieves its objective by constraining the spherical deconvolution (CSD) and the probabilistic streamlines.[101] This app is a free version of C++ language that works seamlessly with any device. This tool uses the latest data sets and statistical techniques to analyze and interpret the data.

Mango: The multi-purpose graphical user interface for mango was created by Saeed et al. It is a stand-alone system that can be used with various platforms. It is a non-profit tool that enables users to view and analyze medical images [102]. This device supports various formats such as NIFTI, NAG, NEMA, and DICOM. It can also load and save 3D, 2D, and 4D images. It provides tools that enable users to create regions of interest within the images, layer rendering, surface rendering, and histogram analysis. It can also be used for scientific neuroimaging.[103] The data from these maps are presented in a visualized format.

MRVision: High-end images can be visualised with the aid of the image analysis and visualisation software known as MRVision. This system is a standalone computer that only works with Linux. This tool is intended to assist you in organising and cleaning up your layout. It works seamlessly with any layout. MRVision is a portable MRI scanner that can be used for various applications. Some of these include biomedical and non-medical imaging.[104] This tool can detect the presence of different brain cells with the help of rat brain data. It can also identify different regions of the brain. This tool was created in C++ and is both free and licenced.

Mrtrix: The MRtrix was developed by the Tournier et al. It is a standalone system that can run smoothly on most major operating systems.[105] It performs diffusion weighted MR tractography with a robust approach that allows robust cross-referencing of complex white-matter tracts.

PyMVPA: Python is the language used for multivariate pattern analysis. This program is called PyMVPA. It is a standalone computer system that can be used with various platforms such as Windows, Linux, and Mac OS X. PyMVPA is a Python framework that allows the analysis of multivariate patterns in fMRI data [106]. This framework features a variety of algorithms for various tasks such as classification, regression, and feature selection. This programme is designed to work well with a variety of software packages such as scikit/learn, shogun, and others. Python is an open-source programming language that enables developers to create their own libraries and run them in various environments. Python is a programming language that can be used to create interactive objects.

NITRC: The acronym NITR stands for Neuroimaging Informatics Tools and Resources learninghouse. It is a repository of information related to neuroimaging informatics, including magnetic resonance imaging, SPECT, and computed tomography. It is a repository of neuroimaging data that can be accessed through a web browser.[107] It is also a computing environment built on the cloud. It is a free tool that integrates with HTML and MySQL.

NeuroLens: NeuroLens is a free software that was developed by Cloherty and colleagues. It allows users to perform studies related to neuro-Lens. It provides an environment for the analysis and presentation of functional neuroimages.[98] Through an intuitive interface, this device is intended to offer quick and versatile picture processing. Users are able to alter their vision using NeuroLens, a stand-alone technology.

Olea Sphere: Olea Sphere is a tool developed by Schiff. It was created for commercial use.[106] This tool is used for image

processing and image archive. It can be used for processing various types of media such as text, audio, and image. It standardizes the capabilities of various third-party software vendors in the analysis and viewing of functional and dynamic MRI and computed to X-ray datasets. The Olea Sphere and DICOM standards are compatible. This Windows workspace can be utilised with any common off-the-shelf workstation. Seven different types of applications can be implemented in the local environment. This app is written in Java language. This tool is used for image processing, image archive, post processing and communication.

Shanoir : Shanoir is a resource sharing platform that enables users to share NeuroImaging resources. Shanoir is a web-based tool that enables users to share, archive, and search neuroimaging data. It was built by Neuroinformatics team intelligence. It features a secure web access and an easy-to-use interface to collect and retrieve neuroimaging data. It also offers a wizard to make the process of storing and retrieving the data easier.[108] Ontology-based data organization, Shanoir offers NeuroLOG, a platform that enables users to store and manage their data on an ontology. This framework enables the reuse of data and metadata, and it provides a way to integrate processed data into an evolutionary approach.

AIR: AIR is an automated image registration system that was developed by Woods et al. It is a stand-alone system that can run both locally and remotely. It is compatible with most major platforms.[109] AIR is a type of automated registration that enables the simultaneous registration of three-dimensional and 2-dimensional images. It is a free tool that enables you to create a simple and effective web app.

SDM: The SDM was developed by Zilles et al. SDM is a 64-bit system that is compatible with various major platforms.[23] Using neuroimaging techniques, D Mapping is a statistical technique used for meta-analytic investigations on differences in brain structure and activity. This technique allows meta-analysis to be performed with studies that only have peak coordinates and SPM t-maps. This app is written in C language and can be downloaded for free.

SPM: For statistical parametric mapping, utilise this mapping technique. SPM is a web-based open-source system created by Penny and her companions. The statistical program SPM is used to determine the differences in brain activity in experiments. It utilizes a set of statistical processes that are designed to test different hypotheses.[110] This tool makes use of bear imaging data. SPM is a common tool used in libraries for neuroimaging.It is free and available in many languages. It is a powerful tool for creating C routines and functions.

TORTOISE: TORTOISE is a system that enables users to register and optimize their own Tensor Registration and Optimization software ensemble. It supports the processing of MRI diffusion data. This is a non-commercial, open-source project. DIFF PREP and DIFF CALC are modules that are used for image registration-based correction of motion and eddy current distortion. The software is very flexible and can be used to create various configurations and export both diffusion weighted and tensor quantities. It can also be used to export both DWIs and tensor quantities. This programme is developed in the programming languages C and C++ .[88]

GRAPHICS MOLECULAR SYSTEM TOOL: ADVANTAGES AND DRAWBACKS

Several programmes for molecular modeling and visualization have been developed based on various requirements. However, each software has its own set of advantages and disadvantages. Some programmes can only visualize protein molecules, whereas others can visualize proteins, DNA, and other molecules.[111] Additionally, most of them offer more than only visualization features, such as trajectory analysis, to fulfil the demands of a wide range of users.[112] Additionally, most tools create the specific image based on a supplied file, typically in PDF or cube format. However, other systems leverage the target molecule's existing database information for visualization.[113-114]

Numerous technologies for computer visualization and modeling of molecules are addressed in the preceding sections. However, there are several drawbacks to these molecular visualization methods. For starters, several of the programmes are unable of demonstrating dynamics, movements, and protein-protein or protein-ligand interactions. Furthermore, most of the tools could not illustrate horizontal and Vertical translation of molecules (same protein in several representations/renderings) (A protein in the context of biological organisation; molecules, cells, and organisms).[115] As a result, in the near future, we should anticipate increasingly effective computational tools for describing, analysing, and synthesising ever more complex chemical systems.[116] Increased interaction with the graphic design community will also lead to the development of rendering techniques that are more effective and understandable.[117] We anticipate that the majority of advancements in molecular visualisation will, however, be made in the fields of computer interfaces, human interaction, and novel approaches to representing and visualising non-spatial data.[118-120] We believe that as technology advances, molecular visualisation tools will be enhanced in the future, enabling greater quality visualisation and specialisation in fields like medication formulation.

CONCLUSION

To summarize, imaging with radiopharmaceuticals has been more and more popular in recent years for the evaluation of dementing deficits. The cognitive, dopaminergic, and sensory nervous systems are inseparable aspects of the pathological processes exhibited in cognitive disorders, and molecular imaging provides a unique view into them. Furthermore, these tools allow researchers to look at benzodiazepine receptors, opioid receptors, and glutamatergic receptors, which are all linked to dementia. Molecular imaging aids in the evaluation of drug treatment effects and may result in the development of novel drugs. It also enables researchers to understand the pathophysiology and mechanisms of dementing disorders. The development of new imaging modalities for the central nervous system, which is currently under investigation, is expected to significantly advance our understanding of the alterations in brain structure and function brought on by neurodegenerative diseases.

CONFLICT OF INTEREST STATEMENT

Authors declare that there is no conflict of interest. The study's design, data collection and analysis, and manuscript writing were all done independently of the funders.

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