WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 16, 1217-1233. Review Article ISSN 2277–7105

THE ROLE OF ARTIFICIAL INTELLIGENCE IN ADVANCING ALZHEIMER'S DISEASE DIAGNOSTICS: A REVIEW

Siju Ellickal Narayanan[1,2], Hariraj Narayanan[1,3] and Manju Sunder D.[1,2]*

[1]*Kerala University of Health Sciences, College of Pharmaceutical Sciences, Government Medical College, Kannur, Kerala-670503.

[2]Department of Pharmacology and Research Division, College of Pharmaceutical Sciences, Government Medical College, Kannur, Kerala-670503.

[3]Department of Pharmaceutical Chemistry, Kerala University of Health Sciences, College of Pharmaceutical Sciences, Government Medical College, Kannur, Kerala-670503.

Article Received on 02 July 2025,
Revised on 22 July 2025,
Accepted on 12 August 2025
DOI: 10.20959/wjpr202516-37999

***Corresponding Author**
Manju Sunder D.
Kerala University of Health Sciences, College of Pharmaceutical Sciences, Government Medical College, Kannur, Kerala-670503.

ABSTRACT

Alzheimer's disease (AD) is a leading cause of dementia, marked by gradual memory loss, cognitive deterioration, and behavioural changes. Traditional diagnostic approaches often identify the disease only in its advanced stages, limiting the effectiveness of available treatments. Recent developments in artificial intelligence (AI), especially in machine learning and deep learning techniques, have opened new avenues for the early and accurate detection of AD. These technologies can process and interpret complex biomedical data, such as brain imaging (MRI, PET), genetic markers, cerebrospinal fluid biomarkers, and cognitive test results, with remarkable precision. AI-driven systems have shown the ability to distinguish Alzheimer's from other neurological conditions and to forecast disease progression more effectively than some conventional methods. However, widespread clinical adoption is still hindered by issues like data variability, lack of model transparency, and integration challenges. This paper highlights the growing role of AI in enhancing diagnostic accuracy and stresses the importance of using diverse, high-quality datasets and interpretable models. Integrating AI into diagnostic workflows may lead to earlier interventions, better patient care, and progress toward more individualized treatment strategies in Alzheimer's disease.

INTRODUCTION

Alzheimer's disease is the leading contributor to dementia and is rapidly emerging as one of the most costly, deadly, and challenging health conditions of the 21st century.[1] Alzheimer's disease is a chronic illness with an average clinical duration of 8–10 years, together with long preclinical and developmental phases lasting up to 20 years.[2] The disease has an estimated prevalence of 10–30% in the population of people greater than 65 years of age with an incidence of 1–3%.[3] The combined presence of amyloid and tau continues to define the condition, but researchers are shifting slowly away from the original amyloid hypothesis, which suggested a simple linear causality.[4] An estimated 24 million individuals around the globe are affected by dementia, with the majority likely suffering from Alzheimer's disease.[5] As a result, Alzheimer's disease is a significant public health issue and has been identified as a priority for research. While licensed treatments exist to exaggerate the symptoms of Alzheimer's disease, there is an urgent need to enhance our understanding of its pathogenesis to support the development of disease-modifying treatments. Dementia is an acquired progressive cognitive impairment which is ancient to impact on activities of daily living, a major cause of dependence, disability, and mortality. Present estimates suggest that 44 million people live with dementia worldwide at present.[6] AD is the single biggest cause of dementia, accounting for 50%–75%, and is primarily a condition of later life; it could be doubling in prevalence every 5 years after age 65.[7] The primary features of Alzheimer pathology are amyloid plaques and neuro-fibrillary tangles (NFTs). In addition, neuronal threads, dystrophic neurites, associated astrogliosis and microglial activation are seen, and cerebral amyloid antipathy frequently coexists in AD. The downstream consequences of these pathological processes include neurodegeneration with synaptic and neuronal loss resulting in macroscopic atrophy. Mixed pathology frequently occurs, especially in older individuals, and includes vascular disease and lewy bodies.[8]

A fascinating aspect of artificial intelligence (AI) is that its exact scope and definition are surprisingly hard to pinpoint. Decades of research, both experimental and clinical, have helped uncover many mechanisms involved in the development of Alzheimer's disease (AD), yet the full picture remains elusive. While it may be assumed that there is no complete set of answers, the recent rise of open data-sharing initiatives, which collect lifestyle, clinical, and biological information from AD patients, has made vast amounts of data available, far surpassing human capacity to fully comprehend. Additionally, the integration of Big Data from multinomial studies opens new opportunities to investigate the pathophysiological processes across the entire biological spectrum of AD. In this regard, Artificial Intelligence (AI) presents a range of tools to analyze large, complex datasets, enhancing our understanding of AD.[9]

Deep learning models in the diagnosis of Alzheimer's disease

Convolutional neural network

A traditional Convolutional Neural Network (CNN) is a powerful deep learning framework that consists of three main elements: convolutional layers, pooling layers, and fully connected layers. Modelled after the human visual system, this architecture is designed to effectively interpret and analyze image data.[10]

The interpretation of two-dimensional brain MRI images by humans involves a sequence of visual processing steps. When pixel information enters through the pupil, the cerebral cortex identifies edges and the orientation of objects in the image. This initial data is then simplified into an approximate elliptical form, aiding in visual comprehension. Over time, the brain identifies the image as that of a human brain. In a similar manner, Convolutional Neural Networks (CNNs) process images through several layers to interpret them. The convolution layer detects features like edges, textures, and patterns using filters, breaking the image into smaller segments. The pooling layer follows, using methods such as max-pooling or average pooling to condense these features and reduce their spatial size. Finally, the fully connected layer integrates the gathered features to perform classification based on the input. Despite their strong performance in image analysis, CNNs face challenges such as loss of critical spatial details during pooling and limited depth in traditional architectures, which can hinder their ability to identify complex patterns. To enhance Alzheimer's disease detection, researchers have refined CNN models by introducing additional layers and advanced methods like residual connections and dilated convolutions. These improvements enable the models to better extract detailed features from brain MRIs, supporting earlier and more accurate diagnosis.[11]

Convolutional layers- The convolutional layer serves as the foundational component in the network architecture, where an input image is convolved with a filter to generate feature maps. Initial convolutional layers in deep CNNs capture important local features that remain consistent across scale and position.[12] In contrast, the final convolutional layers utilize these extracted features for classification tailored to the specific task. A major advantage of convolutional layers is the concept of shared weights within a feature map, which reduces the number of parameters and simplifies the model.[13]

Pooling layers - The pooling layer typically follows the convolutional layers and is responsible for down-sampling the input feature maps by substituting each region with either its maximum or average value.[14] This process reduces the number of parameters in the network while preserving the most critical features. Although average pooling was commonly used in the past, max pooling has become the preferred method due to its faster convergence and superior performance in classification tasks. Max pooling is more effective at capturing dominant invariant features, thereby enhancing the model's generalization ability.[15]

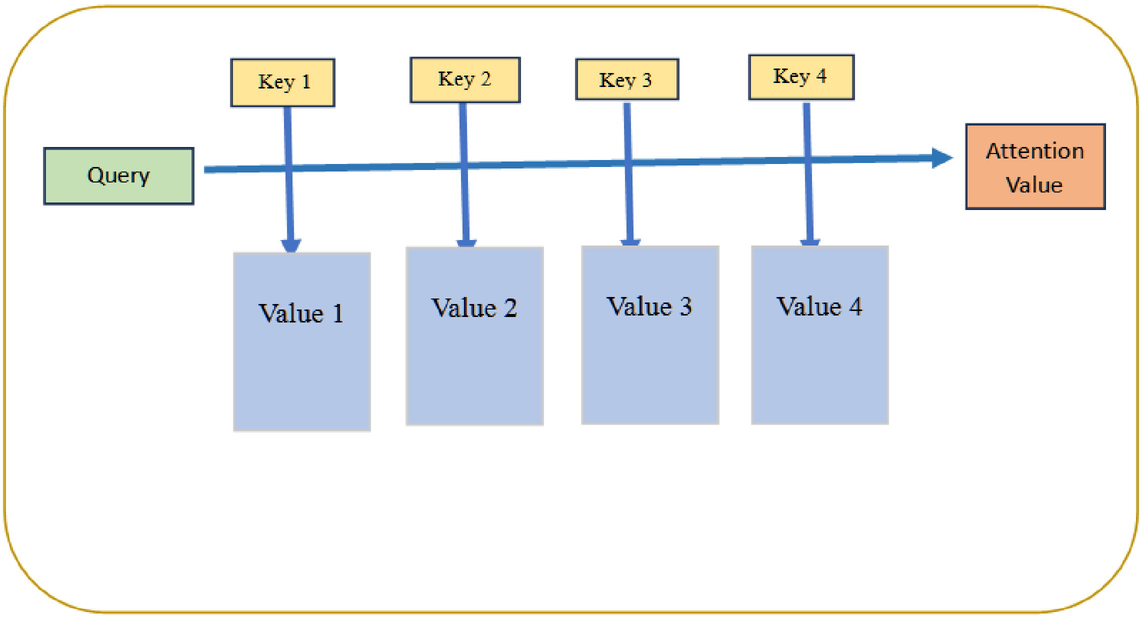
Fully connected layers represent the fourth type of layer and operate in a manner like traditional neural networks. It holds a significant number of the trainable parameters within a CNN. Following the initial layers, the feature maps are converted into a one-dimensional vector, eliminating their spatial arrangement. This vector is then passed to the fully connected layer, which links each node to the features from the previous layer. These layers play a crucial role in capturing complex non-linear relationships among the local features identified by the convolutional layers.[16]

Attention network

Deep learning models with attention mechanisms mimic this concept by selectively focusing on the most relevant parts of the input data.[17] To achieve this, a set of attention distribution coefficients, or weight parameters, is used to help the model assess the significance of each input region for a specific task. As illustrated in Figure 1, an example using an MRI image with multiple regions (values) is shown. A distinct numerical key is given to each region to facilitate efficient searching. When analysing a particular disease (query), it is not always necessary to examine every region in detail. Instead, attention is directed towards the areas that are most relevant to the disease being studied. The attention mechanism assigns higher weights to these important regions, allowing the model to focus more on them. This enables the model to capture both global and local relationships in the data simultaneously.[18]

However, attention mechanisms do have limitations. A significant challenge is their inability to retain spatial location information, which can hinder the detection of sequential patterns in the data (such as determining the order in which information should be learned).[19]

Overcoming this limitation may require combining the attention mechanism with other techniques or making adjustments to improve its effectiveness across different applications.



Source

Autoencoder

An autoencoder is a specialized neural network that transforms input data into a compact and informative representation, then reconstructs the input from this encoding in a way that closely resembles the original data.[21] An Autoencoder model is composed of two main elements: the encoder and the decoder. These components function in tandem to help the model extract key features from an image and recognize unique distribution patterns among those features, leading to efficient classification and diagnostic outcomes.[22]

During the encoding phase, the model compresses the input image by identifying and selecting critical features from a complex, high-dimensional space. The decoder then reconstructs the image by using the significant features obtained by the encoder, aiming to produce an output that closely resembles the original image.[23]

Through this two-step process, Autoencoder-based neural networks can not only extract important features but also distinguish between various feature distribution patterns. For instance, they can identify variations in pixel arrangements across different image categories. This ability enhances the model's performance in classification and diagnosis, making Autoencoders highly effective tools in deep learning and image processing applications.[24]

The advent of deep learning has introduced powerful methods capable of automatically identifying features in images without requiring prior knowledge of the underlying mechanisms.[25] In this study, we developed a deep convolutional autoencoder (CAE) architecture designed to carry out non-linear analysis on a large image dataset containing more than 2,000 samples. The features extracted through this data-driven approach showed strong associations with various clinical and neuropsychological metrics, including significant correlations (above 0.63) with factors such as patient age, tau protein accumulation, and cognitive assessment results. Moreover, this method proved effective in distinguishing Alzheimer's disease cases, achieving a diagnostic accuracy exceeding 84%. By visualizing the neural activation patterns and examining how these correspond to clinical indicators, insights were gained into the brain regions most impacted by the disease and their connection to cognitive decline. Consequently, our CAE model serves not only as a diagnostic aid for dementia but also enhances our understanding of how structural brain changes relate to cognitive performance, potentially guiding the development of novel imaging biomarkers for clinical use.[26]

Deep belief network

A Deep Belief Network (DBN) is mainly built using Restricted Boltzmann Machines (RBMs). As illustrated in Figure 5, its architecture includes one visible layer and several hidden layers. Importantly, connections are only present between adjacent layers—there are no links among units within the same layer. The visible layer handles the input data, while the hidden layers are trained to uncover relationships among higher-level features derived from the input. Due to this role, hidden layers are commonly known as feature detectors.[27]

When working with labelled training data, the top-level RBM should be trained using not only the primary neurons from the visible layer but also those representing the classification labels. Including label information during training enhances the model’s ability to learn more informative features and improves its classification accuracy.[28]

In contrast to conventional discriminative neural network models, a Deep Belief Network (DBN) operates as a probabilistic generative model. This approach allows the DBN to learn a joint probability distribution over the input data and their corresponding labels, effectively capturing both the data's internal structure and the interrelationships among categories. For classification purposes, a softmax layer is appended to the final hidden layer, transforming the learned distribution into class predictions.[29]

By learning a probability distribution across various classes, the model can generate predictions grounded in the associations it has identified between input features and their corresponding labels. This capability supports effective classification and diagnostic decision-making.[30]

Generative adversarial network

Generative Adversarial Networks (GANs) represent a major advancement in artificial intelligence, consisting of two neural networks—the generator and the discriminator—that compete in an adversarial setup. The generator is responsible for producing artificial data, while the discriminator assesses whether the data is real or generated. This ongoing interaction forms a minimax optimization process that helps in generating realistic synthetic data. Introduced by Ian Goodfellow in 2014, GANs have undergone significant evolution through various architectural innovations, such as Vanilla GAN, Conditional GAN (cGAN), Deep Convolutional GAN (DCGAN), CycleGAN, StyleGAN, Wasserstein GAN (WGAN), and BigGAN. These models aim to overcome issues like unstable training, lack of data diversity, and poor output quality.[31]

GANs have been adopted across many domains. In healthcare, they are used to create synthetic medical images, aiding diagnostic research while protecting patient confidentiality. In entertainment and media, GANs are utilized to improve the quality of images and videos and to generate highly realistic content. Despite their benefits, GANs face several obstacles, including mode collapse, instability during training, and difficulty in objectively measuring output quality. Moreover, they present ethical concerns, particularly regarding their potential use in creating deepfakes. Addressing these issues requires regulatory measures, advanced detection technologies, and increased public awareness.[32]

As shown in Figure 4, the generator continuously refines its parameters to produce outputs that increasingly resemble real data. At the same time, the discriminator enhances its ability to differentiate between genuine and synthetic inputs by adjusting its own parameters. This adversarial feedback loop fosters ongoing improvement for both networks.

During this process, the neural network's parameters are fine-tuned to identify shared features among data points within the same class and to highlight distinctive attributes across different classes. This capability aids in both classification and diagnostic tasks.

The powerful learning dynamics of GANs enable the production of realistic, high-fidelity synthetic data, which can be utilized in diverse fields such as image generation and data augmentation. Furthermore, the adversarial mechanism helps the network learn complex patterns within data, enhancing its effectiveness in diagnosis and categorization tasks by improving its ability to capture subtle variations between data classes.[33]

Graphical neural network

Graph theory provides a mathematical framework for representing systems made up of variables and the connections between them. In such models, variables—called nodes—are typically shown as geometric shapes, while their relationships are represented by edges or connecting lines. In functional MRI (fMRI) research, Graph Neural Networks (GNNs) are used to model brain connectivity and support the classification of Alzheimer's disease (AD). These models are particularly effective at handling complex data in a simplified, structured format.

GNNs offer several advantages: they support theoretical simulations such as lesion modelling, allow for the integration of diverse data types like neuroimaging, biomarkers, and demographic data, and are capable of processing multivariate information. Furthermore, GNNs can be paired with other neural networks, such as Convolutional Neural Networks (CNNs), for enhanced performance.[34]

Zhang et al. conducted a study using a Graph Convolutional Network (GCN) to classify AD by combining data from diffusion tensor imaging (DTI) and fMRI. The GCN was chosen because it can incorporate both the spatial detail found in fMRI data—similar to CNNs—and the structural connectivity captured by DTI. Their hypothesis was that integrating both spatial and temporal brain data would improve classification performance compared to using either modality alone.

In their approach, the research team used the Destrieux brain atlas to define brain regions and construct structural and functional connectivity graphs. The DTI-based structural network served as the initial layer for the GCN, while fMRI connectivity data were used to fine-tune the model. To evaluate its performance, they used data from 214 subjects obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI), including 116 cognitively normal (CN) individuals and 98 with mild cognitive impairment (MCI). The study employed fivefold cross-validation, and the model achieved a classification accuracy of 92.7% in distinguishing MCI from CN participants.[35]

Graph Neural Networks (GNNs) demonstrate significant adaptability by integrating effectively with different deep learning techniques and Alzheimer's disease (AD) biomarkers. This makes GNNs highly suitable for building comprehensive models of AD, such as combining fMRI data with other diagnostic indicators. In addition, GNNs are valuable tools for constructing and visualizing functional connectivity networks, offering a structured representation of brain activity and interactions.[36] Despite their advantages, Graph Neural Networks (GNNs) face certain challenges. These include the complexity involved in designing models, difficulties in capturing individual-level variations such as the severity of a participant's condition, and the typical noise issues associated with fMRI data. Nonetheless, advancements in research and technology are progressively addressing these limitations, improving the effectiveness and reliability of GNN-based approaches. Song et al. tackled several key limitations commonly associated with Graph Convolutional Networks (GCNs). They developed a model capable of incorporating disease severity, representing similarities between participants, and handling multimodal MRI data—specifically DTI and fMRI—for the classification of Alzheimer's disease (AD). To reflect disease severity, they linked nodes in the graph based on diagnostic labels provided by ADNI. Participant similarity was quantified by measuring correlated distances between graph nodes and applying ranking through a GCN. The multimodal MRI inputs were embedded into the model as graph connections (edges) and processed separately using two GCNs, each tailored to a specific MRI modality.

Their study involved 170 individuals from the ADNI database, categorized as 44 cognitively normal (CN), 44 with subjective memory complaints (SMC), 44 with early mild cognitive impairment (EMCI), and 38 with late MCI (LMCI). The model was evaluated using 10-fold cross-validation, and it successfully differentiated among the four groups with an average classification accuracy of 86.8%.[37]

Recurrent neural networks

Recurrent Neural Networks (RNNs) are a specialized form of deep learning models designed to process data that unfolds over time. They achieve this by feeding the output from one time step back into the model as input for the next, allowing the network to learn from sequential patterns. In fMRI studies, RNNs are particularly effective at capturing temporal variations in functional connectivity. They analyze a series of fMRI "snapshots" sequentially, using each one to inform the analysis of the next in the timeline.[38]

RNNs are often paired with Convolutional Neural Networks (CNNs) to enhance performance. For instance, when combined with a 3D CNN, RNNs enable the continuous evaluation of 3D fMRI images across time, creating a 4D model. A notable example is the work by Li et al.[47] who proposed a method for analyzing 4D fMRI data using a combination of a 3D CNN and a Long Short-Term Memory (LSTM) network—a popular variant of RNN designed for capturing long-term dependencies in sequential data. The 3D CNN handled the spatial components, while the LSTM managed the temporal analysis, allowing for comprehensive four-dimensional modelling.

Li et al. utilized ADNI datasets containing imaging data from 116 Alzheimer's disease (AD) patients, 99 individuals with mild cognitive impairment (MCI), and 174 cognitively normal (CN) participants. They compared their hybrid model's performance against other widely used 2D and 3D deep learning architectures.[43] The results demonstrated the superiority of the CNN-LSTM model, achieving classification accuracies of 91.1% for AD vs. MCI, 88.12% for MCI vs. CN, 97.37% for AD vs. CN, and 89.47% for multi-class classification (AD, MCI, CN). Their findings highlight the strong potential of 4D fMRI models integrating RNNs for accurate Alzheimer's disease classification.

fMRI and deep learning markers of AD

Deep learning and traditional fMRI analysis methods often share common preprocessing steps; they differ significantly in the types of data they handle and the features they extract. One key distinction lies in the dimensionality and complexity of the data each approach can process. For instance, conventional techniques often utilize Independent Component Analysis (ICA) to estimate functional connectivity, which typically results in time series and spatial activity maps. These outputs are frequently converted into Z-scores for subsequent statistical analysis in traditional workflows.[39]

In contrast, deep learning approaches can handle higher-dimensional data and make use of ICA outputs more directly. For example, the time series and spatial maps produced by ICA can be fed into 3D deep learning models for more detailed analysis. Additionally, combining both spatial and temporal data enables the creation of 4D models, enhancing the analysis of brain activity over time and space.

Beyond adapting existing methods like ICA, deep learning introduces entirely new techniques. For example, graph-based models are used to build functional connectomes, which represent the brain's network structure for further analysis. These methods are elaborated upon in sections discussing graph neural networks and emerging analytical techniques.[40]

Overall, deep learning offers powerful tools for exploring, transforming, and analyzing fMRI biomarkers associated with Alzheimer's disease (AD). Many studies in the field emphasize markers like hippocampal activity and alterations in the default mode network (DMN). By leveraging such advanced methods, deep learning combined with fMRI holds promise for delivering detailed and novel insights that can aid in the diagnosis of AD.[41]

IBM Watson health

IBM has played a prominent role in integrating artificial intelligence into healthcare over the past decade. In 2013, the company introduced an AI-driven lung cancer treatment tool—IBM Watson Oncology—at a cancer centre in New York.[42] Although the program faced financial and performance challenges, IBM continued to promote and test it across several hospitals (Strickland, 2019).[43] By 2016, IBM expanded its healthcare capabilities by acquiring Truven Health Analytics and rebranding the initiative as Watson Health, incorporating tools for data analysis, benchmarking, research, and services aimed at hospitals, insurers, physicians, and biotech firms.[44]

In 2022, IBM sold Watson Health to Francisco Partners for approximately $1 billion. The divested unit, renamed Merative, includes key components like Micromedex, a clinical decision support tool that delivers reliable and timely information for healthcare professionals.

Merative now offers a range of digital health solutions:

- Clinical Decision Support: Provides clinicians with drug databases and evidence-based medical information to support treatment choices.
- Data Management: Streamlines clinical trials through its Zelta platform, which includes tools for electronic data capture (EDC), trial planning, and regulatory document management.

- Imaging Solutions: Enhances diagnostic efficiency in radiology and cardiology using tools like Merge PACS, Merge Cardio, and Merge Hemo, all of which received high ratings in 2024 from U.S. healthcare authorities.

Furthermore, Merative supports modern clinical research with features such as:

- Electronic Clinical Outcome Assessment (eCOA): Allows patients to report outcomes digitally, improving accuracy.
- Electronic Consent: Enables participants to review and sign informed consent documents electronically.
- Electronic Trial Master File (eTMF): Ensures better organization and compliance in trial documentation.

The application of AI by companies like IBM and Merative has significantly enhanced healthcare delivery, particularly in areas like radiology, cardiology, and clinical research, and provides a model for future applications in fields such as Alzheimer's disease detection and management.[45]

CONCLUSION

Artificial Intelligence (AI) is playing an increasingly vital role in the early detection and management of Alzheimer's disease. Through the use of advanced techniques such as machine learning, imaging analysis, and predictive models, AI contributes to improved diagnostic precision, facilitates earlier identification of the disease, and aids in developing individualized treatment strategies. These innovative tools can recognize early biomarkers and cognitive changes that precede visible symptoms, allowing for prompt medical response. Despite existing obstacles—such as concerns over data security, transparency in AI processes, and integration into clinical practice—continued research and collaboration across disciplines are helping to address these issues. In summary, AI offers significant potential to transform Alzheimer's diagnostics by making them more efficient, accurate, and accessible, ultimately enhancing patient care and outcome.

REFERENCES

1. Scheltens P, Strooper BD, Kivipelto M, Holstege H, Chételat G, Teunissen CE, et al. Alzheimer's disease. Lancet Lond Engl., 2021 Apr 24; 397(10284): 1577–90.
2. Alzheimer's disease - PubMed [Internet]. [cited 2025 Jun 26]. Available from: https://pubmed.ncbi.nlm.nih.gov/27188934/.
3. Masters CL, Bateman R, Blennow K, Rowe CC, Sperling RA, Cummings JL. Alzheimer's disease. Nat Rev Dis Primer., 2015 Oct 15; 1(1): 1–18.
4. Scheltens P, Blennow K, Breteler MMB, Strooper B de, Frisoni GB, Salloway S, et al. Alzheimer's disease. The Lancet, 2016 Jul 30; 388(10043): 505–17.
5. Alzheimer's Disease: Symptoms & Treatment [Internet]. [cited 2025 Jun 26]. Available from: https://my.clevelandclinic.org/health/diseases/9164-alzheimers-disease.
6. Kamatham PT, Shukla R, Khatri DK, Vora LK. Pathogenesis, diagnostics, and therapeutics for Alzheimer's disease: Breaking the memory barrier. Ageing Research Reviews, 2024 Nov 1; 101: 102481.
7. Alzheimer's disease: risk factors and potentially protective measures | Journal of Biomedical Science | Full Text [Internet]. [cited 2025 Jun 26]. Available from: https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-019-0524-y.
8. Serrano-Pozo A, Frosch MP, Masliah E, Hyman BT. Neuropathological Alterations in Alzheimer Disease. Cold Spring Harb Perspect Med., 2011 Sep; 1(1): a006189.
9. Fetzer JH. What is Artificial Intelligence? In: Fetzer JH, editor. Artificial Intelligence: Its Scope and Limits [Internet]. Dordrecht: Springer Netherlands; 1990 [cited 2025 Mar 22]. p. 3–27. Available from: https://doi.org/10.1007/978-94-009-1900-6_1
10. Fabrizio C, Termine A, Caltagirone C, Sancesario G. Artificial Intelligence for Alzheimer's Disease: Promise or Challenge? Diagnostics, 2021 Aug; 11(8): 1473.
11. Teuwen J, Moriakov N. Chapter 20 - Convolutional neural networks. In: Zhou SK, Rueckert D, Fichtinger G, editors. Handbook of Medical Image Computing and Computer Assisted Intervention [Internet]. Academic Press; 2020 [cited 2025 May 7]. p. 481–501. (The Elsevier and MICCAI Society Book Series). Available from: https://www.sciencedirect.com/science/article/pii/B9780128161760000259.
12. Lopez Pinaya WH, Vieira S, Garcia-Dias R, Mechelli A. Chapter 10 - Convolutional neural networks. In: Mechelli A, Vieira S, editors. Machine Learning [Internet]. Academic Press; 2020 [cited 2025 May 8]. p. 173–91. Available from: https://www.sciencedirect.com/science/article/pii/B9780128157398000109.

13. Liu S, Liu S, Cai W, Pujol S, Kikinis R, Feng D. Early diagnosis of Alzheimer's disease with deep learning. In: 2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI) [Internet]. 2014 [cited 2025 Jun 3]. p. 1015–8. Available from: https://ieeexplore.ieee.org/abstract/document/6868045.
14. Liu S, Liu S, Cai W, Pujol S, Kikinis R, Feng D. Early diagnosis of Alzheimer's disease with deep learning. In: 2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI) [Internet]. 2014 [cited 2025 Jun 3]. p. 1015–8. Available from: https://ieeexplore.ieee.org/abstract/document/6868045.
15. Guo Y, Liu Y, Oerlemans A, Lao S, Wu S, Lew MS. Deep learning for visual understanding: A review. Neurocomputing, 2016 Apr 26; 187: 27–48.
16. Karwath A, Hubrich M, Kramer S. Convolutional Neural Networks for the Identification of Regions of Interest in PET Scans: A Study of Representation Learning for Diagnosing Alzheimer's Disease. In: ten Teije A, Popow C, Holmes JH, Sacchi L, editors. Artificial Intelligence in Medicine. Cham: Springer International Publishing; 2017; 316–21.
17. Ebrahimi A, Luo S, Initiative ADN. Convolutional neural networks for Alzheimer's disease detection on MRI images. JMI, 2021 Apr; 8(2): 024503.
18. Obeso AM, Benois-Pineau J, García Vázquez MS, Acosta AÁR. Visual vs internal attention mechanisms in deep neural networks for image classification and object detection. Pattern Recognition, 2022 Mar 1; 123: 108411.
19. Computational modelling of visual attention | Nature Reviews Neuroscience [Internet]. [cited 2025 May 8]. Available from: https://www.nature.com/articles/35058500.
20. Guo MH, Xu TX, Liu JJ, Liu ZN, Jiang PT, Mu TJ, et al. Attention mechanisms in computer vision: A survey. Comp Visual Media, 2022 Sep 1; 8(3): 331–68.
21. Du C, Xu G, Guo Y, Wang Z, Yu W. A Novel Seed Generation Approach for Vulnerability Mining Based on Generative Adversarial Networks and Attention Mechanisms. Mathematics, 2024 Jan; 12(5): 745.
22. Bank D, Koenigstein N, Giryes R. Autoencoders. In: Rokach L, Maimon O, Shmueli E, editors. Machine Learning for Data Science Handbook: Data Mining and Knowledge Discovery Handbook [Internet]. Cham: Springer International Publishing; 2023 [cited 2025 May 20]. p. 353–74. Available from: https://doi.org/10.1007/978-3-031-24628-9_16.
23. Medical Image Analysis using Convolutional Neural Networks: A Review | Journal of Medical Systems [Internet]. [cited 2025 May 20]. Available from: https://link.springer.com/article/10.1007/s10916-018-1088-1.

24. Bhatkoti P, Paul M. Early diagnosis of Alzheimer's disease: A multi-class deep learning framework with modified k-sparse autoencoder classification. In: 2016 International Conference on Image and Vision Computing New Zealand (IVCNZ) [Internet]. 2016 [cited 2025 Jun 3]. p. 1–5. Available from: https://ieeexplore.ieee.org/abstract/document/7804459.
25. Martinez-Murcia FJ, Ortiz A, Gorriz JM, Ramirez J, Castillo-Barnes D. Studying the Manifold Structure of Alzheimer's Disease: A Deep Learning Approach Using Convolutional Autoencoders. IEEE Journal of Biomedical and Health Informatics, 2020 Jan; 24(1): 17–26.
26. Martinez-Murcia FJ, Ortiz A, Gorriz JM, Ramirez J, Castillo-Barnes D. Studying the Manifold Structure of Alzheimer's Disease: A Deep Learning Approach Using Convolutional Autoencoders. IEEE Journal of Biomedical and Health Informatics, 2020 Jan; 24(1): 17–26.
27. Yagis E, de Herrera AGS, Citi L. Convolutional Autoencoder based Deep Learning Approach for Alzheimer's Disease Diagnosis using Brain MRI. In: 2021 IEEE 34th International Symposium on Computer-Based Medical Systems (CBMS) [Internet]. 2021 [cited 2025 May 20]. p. 486–91. Available from: https://ieeexplore.ieee.org/abstract/document/9474695.
28. Hinton GE, Salakhutdinov RR. Reducing the Dimensionality of Data with Neural Networks. Science, 2006 Jul 28; 313(5786): 504–7.
29. A new deep belief network-based multi-task learning for diagnosis of Alzheimer's disease | Neural Computing and Applications [Internet]. [cited 2025 Jun 3]. Available from: https://link.springer.com/article/10.1007/s00521-021-06149-6.
30. Faturrahman Moh, Wasito I, Hanifah N, Mufidah R. Structural MRI classification for Alzheimer's disease detection using deep belief network. In: 2017 11th International Conference on Information & Communication Technology and System (ICTS) [Internet]. 2017 [cited 2025 May 20]. p. 37–42. Available from: https://ieeexplore.ieee.org/abstract/document/8265643.
31. Purwono P, Wulandari ANE, Ma'arif A, Salah WA. Understanding Generative Adversarial Networks (GANs): A Review. Control Systems and Optimization Letters, 2025 Feb 7; 3(1): 36–45.
32. Isola P, Zhu JY, Zhou T, Efros AA. Image-To-Image Translation With Conditional Adversarial Networks. In 2017 [cited 2025 Jul 15]. p. 1125–34. Available from:

https://openaccess.thecvf.com/content_cvpr_2017/html/Isola_Image-To-Image_Translation_With_CVPR_2017_paper.html.

33. Yi X, Walia E, Babyn P. Generative adversarial network in medical imaging: A review. Medical Image Analysis, 2019 Dec 1; 58: 101552.
34. Warren SL, Moustafa AA. Functional magnetic resonance imaging, deep learning, and Alzheimer's disease: A systematic review. J Neuroimaging, 2023; 33(1): 5–18.
35. Jiang H, Cao P, Xu M, Yang J, Zaiane O. Hi-GCN: A hierarchical graph convolution network for graph embedding learning of brain network and brain disorders prediction. Computers in Biology and Medicine, 2020 Dec 1; 127: 104096.
36. Song X, Zhou F, Frangi AF, Cao J, Xiao X, Lei Y, et al. Graph convolution network with similarity awareness and adaptive calibration for disease-induced deterioration prediction. Medical Image Analysis, 2021 Apr 1; 69: 101947.
37. Wang M, Lian C, Yao D, Zhang D, Liu M, Shen D. Spatial-Temporal Dependency Modeling and Network Hub Detection for Functional MRI Analysis via Convolutional-Recurrent Network. IEEE Transactions on Biomedical Engineering, 2020 Aug; 67(8): 2241–52.
38. Li W, Lin X, Chen X. Detecting Alzheimer's disease based on 4D fMRI: an exploration under deep learning framework. Neurocomput, 2020; 388: 280-7.
39. Bi X, Sun Q, Zhao J, et al. Non-linear ICA analysis of resting-State fMRI in mild cognitive impairment. Front Neurosci, 2018; 12: 413.
40. Qureshi MNI, Ryu S, Song J, et al. Evaluation of functional decline in Alzheimer's dementia using 3D Deep learning and group ICA for rs-fMRI measurements. Front Aging Neurosci, 2019; 11: 8.
41. Zeng N, Li H, Peng Y. A new deep belief network-based multi-task learning for diagnosis of Alzheimer's disease. Neural Comput & Applic, 2023 Jun 1; 35(16): 11599–610.
42. Zhou N, Zhang C, Lv H, Hao C, Li T, Zhu J, et al. Concordance Study Between IBM Watson for Oncology and Clinical Practice for Patients with Cancer in China. Oncologist, 2019 Jun; 24(6): 812–9.
43. How to Appropriate Value from General-Purpose Technology by Applying Open Innovation | Request PDF [Internet]. [cited 2025 Jul 2]. Available from: https://www.researchgate.net/publication/354292501_How_to_Appropriate_Value_from_General-Purpose_Technology_by_Applying_Open_Innovation.

44. Strickland E. IBM Watson, heal thyself: How IBM overpromised and underdelivered on AI health care. *IEEE Spectrum*, 2019 Apr; 56(4): 24–31.
45. Ahmed MN, Toor AS, O'Neil K, Friedland D. Cognitive Computing and the Future of Health Care Cognitive Computing and the Future of Healthcare: The Cognitive Power of IBM Watson Has the Potential to Transform Global Personalized Medicine. IEEE Pulse, 2017 May; 8(3): 4–9.