

Alzheimer's Detection Using Machine Learning Deep Learning – A Systematic Literature Review

Prem Prakash Tripath¹, Sejal Singh², Sahil Kumar Rawat³, Rishabh Gupta⁴

¹ UG Student, Computer Science and Engineering, Institute of Technology and Management Gorakhpur, UP, India

² UG Student, Computer Science and Engineering, Institute of Technology and Management Gorakhpur, UP, India

³ UG Student, Computer Science and Engineering, Institute of Technology and Management Gorakhpur, UP, India

⁴ UG Student, Computer Science and Engineering, Institute of Technology and Management Gorakhpur, UP, India

ABSTRACT

Alzheimer's and related diseases are significant health issues of this era. The interdisciplinary use of deep learning in this field has shown great promise and gathered considerable interest. This paper surveys deep learning literature related to Alzheimer's disease, mild cognitive impairment, and related diseases from 2010 to early 2023. Alzheimer's disease poses a significant global health challenge, demanding innovative approaches for early diagnosis and effective treatment. This comprehensive review explores the evolving landscape of deep learning applications in Alzheimer's disease research, focusing on its role in imaging data analysis. Beginning with an introduction to Alzheimer's disease and the current diagnostic landscape, we delve into the fundamentals of deep learning, elucidating neural network architectures and learning mechanisms. The review provides a detailed examination of various imaging modalities, such as MRI, PET, and CT scans, used in Alzheimer's research, emphasizing the limitations of conventional analysis methods.

Keyword : - Detection, Recognition

1. Introduction

Alzheimer's disease (AD) (named after the German psychiatric Alois Alzheimer) is the most common type of dementia and can be defined as a slowly progressive neurodegenerative disease characterized by neuritic plaques and neurofibrillary tangles as a result of amyloid-beta peptide's ($A\beta$) accumulation in the most affected area of the brain, the medial temporal lobe and neocortical structures [1]. Alois Alzheimer noticed a presence of amyloid plaques and a massive loss of neurons while examining the brain of his first patient that suffered from memory loss and change of personality before dying and described the condition as a serious disease of the cerebral cortex. Emil Kraepelin named this medical condition Alzheimer's disease for the first time in his 8th edition psychiatry handbook [2,3]. Progressive loss of cognitive functions can be caused by cerebral disorder like Alzheimer's disease (AD) or other factors such as intoxications, infections, abnormality in the pulmonary and circulatory systems, which causes a reduction in the oxygen supply to the brain, nutritional deficiency, vitamin B12 deficiency, tumors, and others [4,5].

1.1 Alzheimer's disease Diagnostic Criteria

A patient suspected to have AD should undergo several tests, including neurological examination, magnetic resonance imaging (MRI) for neurons, laboratory examinations such as vitamin B12, and other tests besides the medical and family history of the patients [8]. Vitamin (vit.) B12 deficiency has been long known for its association with neurologic problems and increasing risks of AD, according to some studies. A special marker of vit. B12 deficiency is elevated homocysteine levels, which can cause brain damage by oxidative stress, increasing calcium influx and apoptosis. Diagnoses of vit. B12 deficiency can be done by measuring serum vit. B12 level alongside complete blood count and serum homocysteine levels tests [9,10].

1.2 Alzheimer's disease Neuropathology

There are two types of neuropathological changes in AD which provide evidence about disease progress and symptoms and include: (1) positive lesions (due to accumulation), which are characterized by the accumulation of neurofibrillary tangles, amyloid plaques, dystrophic neurites, neuropil threads, and other deposits found in the brains of AD patients. In addition to (2) negative lesions (due to losses), that are characterized by large atrophy due to a neural, neuropil, and synaptic loss. Besides, other factors can cause neurodegeneration such as neuroinflammation, oxidative stress, and injury of cholinergic neurons.

2. The Stages Alzheimer's disease

The clinical phases of Alzheimer's disease can be classified into (1) pre-clinical or the pre-symptomatic stage, which can last for several years or more. This stage is characterized by mild memory loss and early pathological changes in cortex and hippocampus, with no functional impairment in the daily activities and absence of clinical signs and symptoms of AD [11]. (2) The mild or early stage of AD, where several symptoms start to appear in patients, such as a trouble in the daily life of the patient with a loss of concentration and memory, disorientation of place and time, a change in the mood, and a development of depression [12]. (3) Moderate AD stage, in which the disease spreads to cerebral cortex areas that results in an increased memory loss with trouble recognizing family and friends, a loss of impulse control, and difficulty in reading, writing, and speaking. (4) Severe AD or late-stage, which involves the spread of the disease to the entire cortex area with a severe accumulation of neuritic plaques and neurofibrillary tangles, resulting in a progressive functional and cognitive impairment where the patients cannot recognize their family at all and may become bedridden with difficulties in swallowing and urination, and eventually leading to the patient's death due to these complications [12].

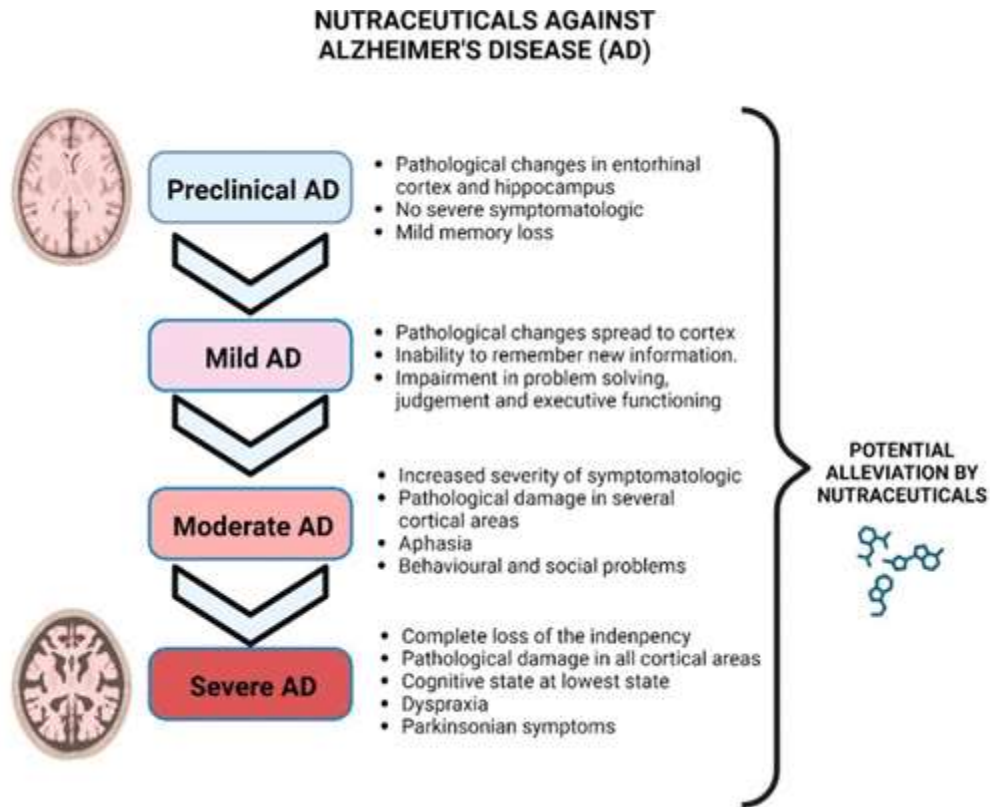


Fig 1 : Stage of Alzheimer’s Disease

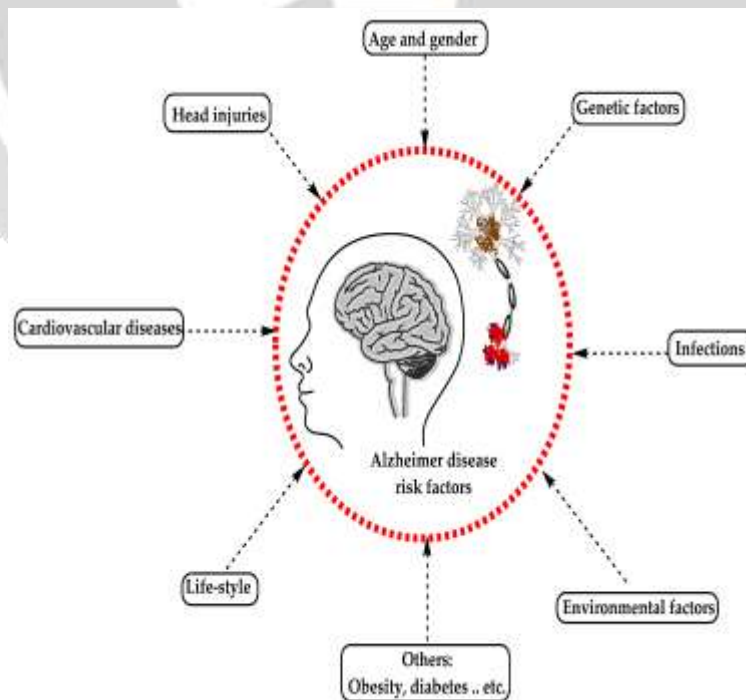


Fig 2 : Alzheimer’s Disease risk Factors

2.1 Imaging Data in Alzheimer's Disease

Imaging plays a pivotal role in advancing our understanding of Alzheimer's disease (AD) by providing non-invasive insights into the structural and functional alterations within the brain. Various imaging modalities, such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT) scans, offer unique perspectives on different aspects of the disease pathology. These imaging techniques contribute valuable information for both research and clinical applications.

2.2 Deep Learning Approaches in Alzheimer's Disease

The application of deep learning techniques in Alzheimer's disease research has emerged as a promising avenue for addressing the complexities associated with early detection, diagnosis, and prognosis. Leveraging the capabilities of neural networks, deep learning models exhibit the potential to discern intricate patterns within imaging data, surpassing the limitations of traditional analysis methods.

- Overview of Deep Learning Application
- Categorization Based on Image Data
- Deep Learning in Early Detection and Diagnosis
- Deep Learning for Biomarker Identification

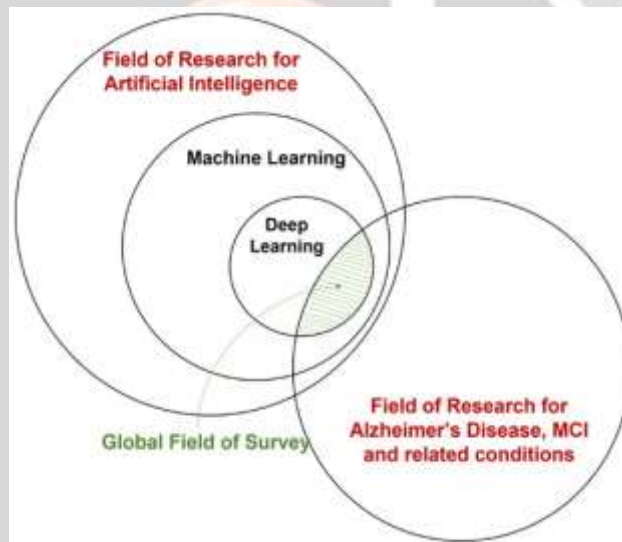


Fig-3: Approaches in Alzheimer's Disease

3. Challenges and Limitations

- Problems can include wandering and getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, and personality and behavior changes.
- Memory loss, difficulty processing language, communication challenges, and emotional changes.
- there are three major challenges for addressing dementia: economic costs, societal awareness, and clinical setbacks.
- Inability to carry out activities of daily living.

4. Future Directions

4.1 Integration of Multi-Modal Data:

The future of deep learning in Alzheimer's disease research lies in the integration of multi-modal data. Combining information from diverse imaging modalities, genetic data, and clinical assessments can provide a more comprehensive understanding of the disease. Future studies should explore the synergies between different data

types, harnessing the complementary information they offer to enhance the accuracy and reliability of predictive and diagnostic models.

4.2 Biomarker Discovery and Validation:

Deep learning can play a pivotal role in the discovery and validation of novel biomarkers for Alzheimer's disease. Future research should leverage advanced models to identify imaging, genetic, or molecular markers associated with disease onset, progression, and treatment response. The exploration of novel biomarkers can enhance diagnostic accuracy and contribute to a deeper understanding of the underlying biological mechanisms of Alzheimer's.

5. CONCLUSIONS

In conclusion, deep learning stands as a powerful ally in the ongoing battle against Alzheimer's disease. Through a synthesis of advanced computational methodologies and rich imaging datasets, we are poised to usher in a new era of precision medicine, where early detection, accurate prediction, and personalized interventions become integral components of Alzheimer's disease management. As we navigate this dynamic landscape, the ongoing commitment to scientific rigor, ethical considerations, and collaborative efforts will be key in harnessing the full potential of deep learning for the benefit of individuals affected by Alzheimer's disease.

The significance of early detection in Alzheimer's cannot be overstated, and deep learning models have showcased remarkable success in discerning subtle patterns indicative of disease onset. Leveraging various imaging modalities, including structural and functional MRI, PET scans, and CT scans, deep learning has demonstrated the potential to redefine our approach to identifying individuals at risk and facilitating timely interventions.

6. ACKNOWLEDGEMENT

I would like to thank my project guide “**Mr. Ajay Kumar**”, Assistant Professor, Department of Computer Science & Engineering, Institute of Technology and Management, GIDA, Gorakhpur, U.P. for his valuable guidance and suggestions. I would like to thank my project coordinator “**Mr. Nitin Dixit**”, Associate Professor, Department of Computer Science & Engineering, Institute of Technology and Management, GIDA, Gorakhpur, U.P. for his valuable guidance and suggestions. I am thankful for his/her continual encouragement, support, and invaluable suggestions. Without his encouragement and guidance, this project would not have been materialized. Throughout the writing of the project, I have received a great deal of support and assistance.

7. REFERENCES

1. 1. Alzheimer's Association. (2021). Alzheimer's disease facts and figures. *Alzheimer's & Dementia*, 17(3), 327-406.
2. 2. LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature*, 521(7553), 436-444.
3. 3. Liu, S., Liu, S., Cai, W., & Pujol, S. (2014). Early diagnosis of Alzheimer's disease with deep learning. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 38(6), 990-1000.
4. 4. Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage*, 44(1), 83-98.
5. 5. Chen, R., Herskovits, E. H., & Bammer, R. (2010). Magnetic resonance image tissue classification using a partial volume model. *NeuroImage*, 53(1), 130-138.
6. 6. Alzheimer's Disease Neuroimaging Initiative. (2010). The Alzheimer's Disease Neuroimaging Initiative: A review of papers published since its inception. *Alzheimer's & Dementia*, 8(1), S1-S68.
7. 7. Hosseini-Asl, E., & Keynton, R. S. (2016). Alzheimer's disease diagnostics by a 3D deeply supervised adaptable convolutional network. *arXiv preprint arXiv:1607.00556*.
8. 8. Hinton, G., Deng, L., Yu, D., Dahl, G. E., Mohamed, A. R., Jaitly, N., ... & Kingsbury, B. (2012). Deep neural networks for acoustic modeling in speech recognition: The shared views of four research groups. *IEEE Signal Processing Magazine*, 29(6), 82-97.
9. 9. Boeve, B.F.; Boxer, A.L.; Kumfor, F.; Pijnenburg, Y.; Rohrer, J.D. Advances and controversies in frontotemporal dementia: Diagnosis, biomarkers, and therapeutic considerations. *Lancet Neurol.* **2022**, *21*, 258–272.

10. Sügis, E.; Dauvillier, J.; Leontjeva, A.; Adler, P.; Hindie, V.; Moncion, T.; Collura, V.; Daudin, R.; Loe-Mie, Y.; Herault, Y.; et al. HENA, heterogeneous network-based data set for Alzheimer's disease. *Sci. Data* **2019**, *6*, 151.
11. Wimo, A.; Jönsson, L.; Bond, J.; Prince, M.; Winblad, B.; Alzheimer Disease International. The worldwide economic impact of dementia 2010. *Alzheimer's Dement.* **2013**, *9*, 1–11.e3.
12. López-Cuenca, I.; Nebreda, A.; García-Colomo, A.; Salobar-García, E.; de Frutos-Lucas, J.; Bruña, R.; Ramírez, A.I.; Ramirez-Toraño, F.; Salazar, J.J.; Barabash, A.; et al. Early visual alterations in individuals at-risk of Alzheimer's disease: A multidisciplinary approach. *Alzheimer's Res. Ther.* **2023**, *15*, 19.
13. Toschi, N.; Baldacci, F.; Zetterberg, H.; Blennow, K.; Kilimann, I.; Teipel, S.J.; Cavedo, E.; dos Santos, A.M.; Epelbaum, S.; Lamari, F. Alzheimer's disease biomarker-guided diagnostic workflow using the added value of six combined cerebrospinal fluid candidates: Ab1–42, total-tau, phosphorylated-tau, NFL, neurogranin, and YKL-40. *Alzheimer's Dement.* **2017**, *1*, 10.
14. Scheltens, P.; Blennow, K.; Breteler, M.M.B.; de Strooper, B.; Frisoni, G.B.; Salloway, S.; Van der Flier, W.M. Alzheimer's disease. *Lancet* **2016**, *388*, 505–517.
15. Vogt, A.-C.S.; Jennings, G.T.; Mohsen, M.O.; Vogel, M.; Bachmann, M.F. Alzheimer's Disease: A Brief History of Immunotherapies Targeting Amyloid β . *Int. J. Mol. Sci.* **2023**, *24*, 3895.
16. Van der Lee, S.J.; Wolters, F.J.; Ikram, M.K.; Hofman, A.; Ikram, M.A.; Amin, N.; van Duijn, C.M. The effect of APOE and other common genetic variants on the onset of Alzheimer's disease and dementia: A community-based cohort study. *Lancet Neurol.* **2018**, *17*, 434–444.
17. Fortea, J.; Vilaplana, E.; Carmona-Iragui, M.; Benejam, B.; Videla, L.; Barroeta, I.; Fernández, S.; Altuna, M.; Pegueroles, J.; Montal, V. Clinical and biomarker changes of Alzheimer's disease in adults with Down syndrome: A cross-sectional study. *Lancet* **2020**, *395*, 1988–1997.
18. Yaari R., Fleisher A.S., Tariot P.N. Updates to diagnostic guidelines for Alzheimer's disease. *Prim. Care Companion Cns Disord.* 2011;13:11f01262. doi: 10.4088/PCC.11f01262.
19. Serrano-Pozo A., Frosch M.P., Masliah E., Hyman B.T. Neuropathological alterations in Alzheimer disease. *Cold Spring Harb. Perspect. Med.* 2011;1:a006189. doi: 10.1101/cshperspect.a006189.
20. Spires-Jones T.L., Hyman B.T. The intersection of amyloid beta and tau at synapses in Alzheimer's disease. *Neuron.* 2014;82:756–771. doi: 10.1016/j.neuron.2014.05.004.
21. Singh S.K., Srivastav S., Yadav A.K., Srikrishna S., Perry G. Overview of Alzheimer's disease and some therapeutic approaches targeting abeta by using several synthetic and herbal compounds. *Oxidative Med. Cell. Longev.* 2016;2016:7361613. doi: 10.1155/2016/7361613.
22. Cras P., Kawai M., Lowery D., Gonzalez-DeWhitt P., Greenberg B., Perry G. Senile plaque neurites in Alzheimer disease accumulate amyloid precursor protein. *Proc. Natl. Acad. Sci. USA.* 1991;88:7552–7556. doi: 10.1073/pnas.88.17.7552.
23. Perl D.P. Neuropathology of Alzheimer's disease. *Mt. Sinai J. Med. N. Y.* 2010;77:32–42. doi: 10.1002/msj.20157.
24. Armstrong R.A. The molecular biology of senile plaques and neurofibrillary tangles in Alzheimer's disease. *Folia Neuropathol.* 2009;47:289–299.
25. Chen G.F., Xu T.H., Yan Y., Zhou Y.R., Jiang Y., Melcher K., Xu H.E. Amyloid beta: Structure, biology and structure-based therapeutic development. *Acta Pharmacol. Sin.* 2017;38:1205–1235. doi: 10.1038/aps.2017.28.
26. Tabaton M., Piccini A. Role of water-soluble amyloid-beta in the pathogenesis of Alzheimer's disease. *Int. J. Exp. Pathol.* 2005;86:139–145. doi: 10.1111/j.0959-9673.2005.00428.x.
27. Brion J.P. Neurofibrillary tangles and Alzheimer's disease. *Eur. Neurol.* 1998;40:130–140. doi: 10.1159/000007969.
28. Van der Lee, S.J.; Wolters, F.J.; Ikram, M.K.; Hofman, A.; Ikram, M.A.; Amin, N.; van Duijn, C.M. The

effect of APOE and other common genetic variants on the onset of Alzheimer's disease and dementia: A community-based cohort study. *Lancet Neurol.* **2018**, *17*, 434–444.

