

Artificial Intelligence's Aid in Diagnosing Alzheimer's Disease

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ABSTRACT

Alzheimer's disease (AD) is a brain disorder that gradually destroys memory and thinking skills and is the most common cause of dementia among older adults. AD results from the progressive degeneration of brain cells and can affect the ability of people to carry out simple tasks. AD is extremely hard for clinicians to detect and understand because an accurate diagnosis of the disease is possible only through an autopsy after the death of an affected patient. Artificial Intelligence, referring to the ability of a computer to simulate human tasks, shows great potential in helping clinicians better understand a patient's brain condition and spot and analyze brain deformity. This paper explores how Artificial Intelligence can revolutionize Alzheimer's disease diagnosis and proposes a diagnosis roadmap for doctors to use when assessing a patient's brain health.

Introduction

Alzheimer's disease (AD) is a complex, progressive neurological disorder that sparks brain atrophy and affects the memory, thinking, and behavior of those infected. Currently, more than 18 million people globally are affected by this disease and the rate of those infected is on the rise (Kohyama & Matsumoto, 2015). Of this number, approximately 4.5 million people in the United States are affected by AD (Farlow et al., 2008, p. 408). AD is part of a greater classification of mental conditions characterized by the impairment of certain brain functions known as *dementia*. According to experts from the Department of Pharmacological and Biomolecular Sciences in Milan, Italy, AD accounts for about half of dementia cases (Marcello et al., 2015, p. 795). This makes AD a widespread issue and one that not only affects the well-being of millions with mental illnesses but also puts a tremendous strain on the medical system and facilities, families, and the federal budget of many countries. AD mostly affects people of ages sixty-five years and older and could make them completely dependent on others even for their everyday tasks; AD is the leading cause of death for this age group.

AD diagnosis with absolute certainty is impossible because the presence of plaques, tumors, tangles, and inflammation that are characteristic of AD can be established only during autopsy examination of an affected patient. However, doctors can *predict* the likelihood of a patient having AD, or another form of dementia, by assessing a patient's symptoms, cognitive skills, and behavioral changes. Common early symptoms of AD include memory impairment, concentration or problem-solving issues, sudden mood swings, misidentification of items or misinterpretation of distances, confusion with location or passage of time, and poor judgment in decisions. Cognitive tests to test memory and concentration can help doctors obtain a clear idea of a patient's brain health. An example of such a test is the Mini-Mental State Exam (MMSE), an 11-question measure used to test five areas of cognitive function: orientation, registration, attention and calculation, recall, and language (Kurlowicz and Wallace, 1999, p. 2). Behavioral changes that doctors could study to detect AD include impaired daily life functioning, such as excessive sleeping, and personality changes, such as extreme depression. Since 100% accurate AD diagnosis is impossible, it becomes critical

for clinicians to be able to predict the onset of AD with reasonable confidence by assessing a patient’s cognitive functions and abilities in a systematic, structured, and detailed manner.

McKhann et al. describe how clinical criteria for AD diagnosis can be categorized into three categories: 1) *probable*, 2) *possible*, 3) *definite* (McKhann et al., 1984, p. 940). A clinical diagnosis of *probable* AD can be established if a patient matches criteria such as deficits in two or more areas of cognition, the absence of systemic or brain disorders that could explain a patient's advancing memory and other cognitive deficits, dementia established by clinical examination and the results of exams like the MMSE. A clinical diagnosis of *possible* AD can be made if the patient meets criteria such as having dementia syndrome, a second systemic or brain disorder sufficient to produce dementia, or a single severe cognitive deficit that can be attributed to invoking dementia in the absence of other identifiable causes. A clinical diagnosis of *definite* AD can be made on the basis of histopathological confirmation, evidence of AD from brain tissue, from a biopsy or autopsy, etc. Thus, doctors are certain of an AD case in a patient only after they have died due to it, so AD diagnoses can rarely be made with full confidence. However, as described in this paper, Artificial Intelligence (AI) can serve as a powerful tool for doctors in diagnosing and treating AD patients with better efficacy, accuracy, and confidence compared to conventional methods.

Artificial Intelligence in the Medical Field

AI is a computer science discipline that refers to the simulation of human intelligence in machines to perform tasks the way humans do. The use of AI has been steadily increasing in today’s “app-centric” world; for example, today’s smartphone agents such as Siri and Alexa leverage AI in assisting smartphone users in performing simple tasks such as setting alarms. Fueled by significant growth in computing power and by the development of advanced algorithms and software engineering tools, AI has been making its headway in the medical field as well. Figure 1 shows the evolution of the market size of AI as applicable for the Healthcare industry for this decade.

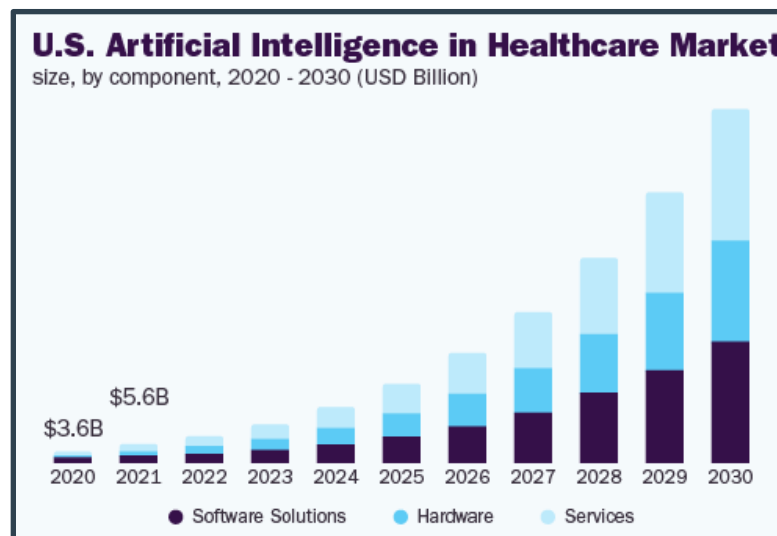


Figure 1. The projected increasing utilization of AI in American healthcare facilities based on current trends

One subdiscipline of AI that has proven to be useful in the medical field is Machine Learning (ML), which refers to how computers can be “trained” to identify data patterns and synthesize them into a database that can be used for future decision-making. Some of the key capabilities of ML tools that can be leveraged in the medical field include

support for storing, comparing, classifying, and analyzing vast and diverse sets of information, ranging from high-quality diagnosis images and videos to detailed patient symptoms and treatment outcomes. For example, ML tools can help study, in a structured and detailed manner, patients' diagnosis images and videos from a sufficient population of patients and disease conditions and establish correlation mapping between trends in these diagnosis images and the likely disease conditions they indicate. These ML tools can then accumulate the correlation findings from these studies into a large database that can later be used to predict the disease condition of a new patient by comparing information from that patient's diagnosis with that in the database.

Two key areas in which AI and ML tools can be leveraged by AD clinicians are imaging and data classification. The ability of these tools to detect and diagnose abnormalities and make accurate disease and to sort, compare, analyze, and classify large amounts of data enables clinicians to both understand patient's conditions in a detailed manner prior to treatment as well as optimize treatment outcomes.

This paper provides an overview of the various ways in which AI could aid in prediction-making and infection detection, specifically in imaging and data classification techniques, in relation to AD diagnosis and proposes a roadmap for AD clinicians to use in diagnosing and treating their patients.

AI-Assisted Advanced Imaging

Medical imaging, including both photos and videos, is extremely important in assessing a patient's brain health as doctors are able to see a clear picture of what's happening in a patient's brain, allowing them to better understand a patient's condition and health. This imaging will help them treat the patient more accurately by easily identifying abnormalities and signs of AD.

One of the common first symptoms of Alzheimer's disease is mild cognitive impairment (MCI), which refers to an early stage of memory, thinking, judgment, and cognitive ability loss. MCI is the earliest clinically identifiable sign of a possible development of Alzheimer's disease or other dementias. Figure 2 shows the transitional period between the usual cognitive decline associated with aging and the more severe decline associated with AD. As can be noted in the figure, the cognitive continuum overlaps in the boundary between normal aging and MCI and AD, showing that the distinction between the three is rather subtle.

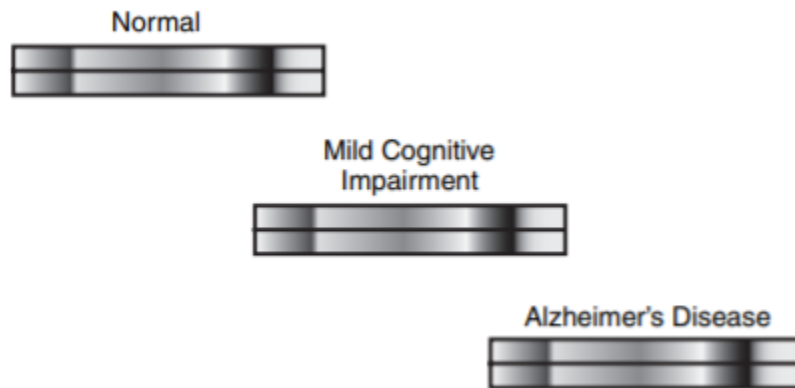


Figure 2. Cognitive continuum portraying the different mental stages ranging from normal aging to AD.

Although the earliest stages of MCI often have little clear symptoms, *neuroimaging* can detect many cases. Neuroimaging is a subdivision of medical imaging commonly used for diagnosing disease and assessing brain health,

while also studying the brain's activities and structure and the function of the central nervous system¹ (CNS). Neuroimaging processes are able to identify brain differences in those who may have brain disorders, like MCI, making them useful in diagnosing AD.

MCI can either revert to normal cognition, stabilize, or develop into other forms of dementia so early detection of MCI is imperative to ensure lasting health of those infected. For instance, a study conducted at the Mayo Alzheimer's Disease Research Center, a group of about 220 individuals of a mean age of 79 years has been followed for 3-6 years using the following criteria: a) memory complaint, b) objective memory impairment for age, c) relatively preserved general cognition for age, d) essentially intact activities of daily living, and e) not demented (Petersen, 2004, p.185). Based on these criteria, the participants in this study progressed to dementia at a rate of 12% per year, and if they are followed for up to six years, about 80% of them will have converted to dementia, making this group a population at great risk (Petersen, 2004, p.185). Hence, it is important to treat MCI as early as possible to avoid MCI patients progressing to AD. By employing ML to analyze spatial patterns of brain atrophy in MCI and AD, professionals can gain valuable insights on how to establish more personalized and efficacious treatment plans for those with cognitive disorders. A promising method to improve the identification and understanding of MCI and AD symptoms is to integrate AI and ML tools into Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT) scans, as discussed below.

AI-Assisted Magnetic Resonance Imaging (AI-MRI)

Magnetic Resonance Imaging (MRI) is an imaging technology that provides high-resolution images and exceptional soft-tissue contrast. A brain MRI involves a) enclosing the patient's head in a magnetic chamber with a powerful magnetic field that is strong enough to pull the protons in the body to align with the field, b) emitting a radiofrequency current that is pulsed through the patient, stimulating the protons and forcing them out of equilibrium, and c) turning the current off and using sensors to detect the energy released as the protons return back to their original positions. Medical specialists can understand the condition and state of the brain by analyzing the protons' response to the magnetic field, such as the time the protons take to realign with the magnetic field, the extent to which the protons distort from equilibrium, and the amount of energy released from the process. *Structural MRI* (sMRI), a specialized MRI technique, is primarily employed to assess the size, shape, and integrity of brain regions, and other static anatomical information. By detecting the direction of the rotational axis of protons in water at different locations throughout the brain, sMRI is able to create a detailed anatomical picture of the brain that allows clinicians to differentiate between different kinds of tissue and brain structures to clearly understand brain activity. *Functional MRI* (fMRI), another specialized MRI technique, is used for measuring and mapping brain activity and time-varying changes in brain metabolism. By detecting changes in blood oxygenation and blood flow that happen in response to neural activity, fMRI provides dynamic physiological information about the brain's metabolic function. Together, these neuroimaging techniques "help understand and evaluate the anatomical changes of sensitive regions related to AD" (Yang and Emad, 2020, p. 1). MRI, with its ability to produce excellent soft-tissue contrast and to distinguish between fat, water, muscle, and tissues, thus, is a leading image modality tool in assessing brain activity and determining whether or not a patient shows signs of having AD.

However, MRI has limitations with respect to image acquisition time and image resolution. Due to the high sampling rate requirements, MRI data acquisition is intrinsically slow, which leads to patient discomfort due to the long procedure duration, low patient throughput, artifacts from patient motion, and high examination costs (Johnson et al., p. 1, 2020).

¹ system consisting of brain and spinal cord that controls most functions of the body and mind, including movements, sensations, awareness, thoughts, memory, and cognitive ability

These shortcomings of MRI have prompted the use of AI to realize accelerated MRI technologies, which employ techniques such as Deep Learning (DL) and ML representation learning. These techniques imitate the way humans gain knowledge by exploiting several layers of non-linear information processing for supervised or unsupervised feature extraction and for pattern analysis and categorization. DL employs a special class of algorithms and multi-layered computing systems known as Artificial Neural Networks (ANNs), which mimic the operation of neurons in the human brain processing data sets and spotting complex or numerous patterns in them. With ANNs, “input data is processed at several levels of abstraction” (Boyle et al., 2021, p. 2). Convolutional Neural Networks (CNNs) are specialized ANNs that are specifically designed to process pixel input and are utilized in image recognition and processing. A CNN learns by using linear algebra principles to locate patterns in images by comparing the output of the network with the target output, and then having the weights in the model updated to minimize the difference between the output and the target. In a CNN, learned elements of the network are grouped into “convolution kernels” that extract specific features of an input image (Boyle et al., 2021, p. 2). CNN image processing takes an input image, passes it through a series of convolution layers with filters (kernels), analyzes it, and categorizes it into the data type it is looking for. It is thus useful because it is convenient, given its record high accuracy in image prediction and the fact that there is no need for feature extraction. CNNs, with their high accuracy image prediction capability, can thus be leveraged in MRI scans to better locate and highlight brain abnormalities that could be signs of cognitive impairment.

Another tool within DL that can be used in MRI is a variational network (VN), which is a proven image-based method for accelerated image reconstruction and acquisition. VNs solve the image reconstruction problem that many MRI scanners face by enforcing consistency and using a CNN to learn the prior information and estimate the fully sampled image. Methods for image construction involving VNs are both better in quality than other MRI reconstruction methods like U-net and PI-CS methods and also have the benefit of very fast reconstruction times (Boyle et al., 2021, p. 4).

AI can also improve the resolution of imaging produced by MRI. For example, a three-dimensional CNN called Deep Resolve produces high-resolution images from low-resolution input using intelligent denoising². Deep Resolve can also increase the image matrix size by a factor of up to two along both in-plane axes, resulting in significantly enhanced image sharpness. This method of generating high-quality images outperforms conventional imaging processes that do not employ DL, such as tricubic interpolation, sparse coding super-resolution, and Fourier interpolation. Figure 3 shows the differences in image clarity and sharpness between the conventional methods and the Deep Resolve based methods.



² process used to remove noise from images, while also preserving important features

Figure 3. Example of brain scan made without DL methods (on left) and with Deep Resolve method on the right, showing that Deep Resolve substantially improves image clarity and sharpness and provides more image details.

Thus, the use of AI in MRI is extremely valuable in AD detection as it enables clinicians to study and assess the brain's architecture, shrinkage, vascular abnormalities, and other anatomical alterations that could cause cognitive problems with higher clarity, precision, and speed compared to conventional methods. The several machine learning algorithms and statistical models that have been developed to date in the area of MRI have shown great promise in helping clinicians in understanding the health conditions of patients. With an eye to building a better healthcare environment, it is thus imperative that clinicians and AI specialists work together to continually improve these algorithms and models so as to further improve diagnostic accuracy and precision and the streamlining of the MRI workflows.

AI-Assisted Computer Tomography (AI-CT) Scan

Computerized Tomography (CT) scan is a valuable medical diagnostic tool that makes internal anatomy more apparent and allows radiologists and physicians to locate internal organ structures and examine their shape, texture, size, and density. Some of the shortcomings of conventional CT scans include proneness to image noise, representing unwanted changes in pixel values in images that hurt the quality and contrast of the images, thereby decreasing the diagnostic utility of CT scans.

AI methods based on DL algorithms can be used in CT imaging to provide data analysis results at a faster speed and with lower reconstruction errors compared to methods that do not use AI. The use of AI in CT scans has been shown to significantly reduce image noise across a broad range of image types and to enable fast image reconstruction.

The AI-based diagnosis methods used in CT, MRI, and Positron Emission Tomography (PET) scans employ what is known as a deep convolutional auto-encoder (DCAE), which is an unsupervised model for representation learning that maps input data into a new representation space that allows one to obtain useful features through the encoding procedure (Alqahtani et al., 2018, p. 1). A DCAE is essentially a CNN with 13 convolutional layers that take in scan data (from a CT, MRI, or PET scan) and reduce its resolution, followed by another set of 13 convolutional layers that reconstruct images until a scan of original resolution is produced. In one particular exploratory study, a DCAE was trained to identify air, bone, and soft tissue using 30 MRI co-registered to CT imaging and to produce synthetic CT data (Boyle et al., 2021, p. 2). The algorithm was evaluated in ten patients by comparing the synthesized CT to the obtained CT scan, and the synthesized CT scans were utilized to perform attenuation correction (AC), a mechanism that removes soft tissue artifacts from images, for additional PET scans in five healthy subjects. Results showed that the PET reconstruction error was significantly lower using the DCAE method than using conventional MR-based approaches without using AI.

The integration of AI in CT scans helps reduce both reconstruction errors, thereby providing a more accurate scan for doctors to study a patient's condition, as well as the time required to generate accurate scans. In an example study, CT scans were generated using a group of patients with brain tumors to train a CNN model to map the input pictures to their corresponding CT scans (Han, 2017, p. 2). This method outperformed more time-consuming atlas-based approaches that do not use AI by a factor of 100 and also eliminated the possibility of inter- and intra-rater variations in the clinical data. This allowed experts to better filter out important data in a timely and efficient manner.

ML methods in CT scans are also helpful in identifying infected areas of the brain. A study was conducted to detect the hyperdense middle cerebral artery (MCA) dot sign, the earliest visible sign of MCA infarct³, on CT using ML methods (Byun et al., 2017, p. 281). To accomplish this, the Sylvian fissure region of the brain, an area separating

³ an area of dead tissue deprived of its blood supply

the frontal and parietal lobes on the lateral surface of the human brain, was studied on 109 CT images. This method achieved a sensitivity of 97.5% for detection of the MCA dot sign on the cerebral hemisphere suspected of acute stroke (Byun et al., 2017, p. 281). The great accuracy with which this ML algorithm was able to identify problematic areas shows how AI-based identification methods can help clinicians better assess a patient's brain condition and whether infected areas are clear signs of AD.

Thus, the advanced image processing, pattern analysis, and reconstruction capabilities of AI-assisted CT, MRI, and other scans greatly improve clinical accuracy and confidence in diagnosis and radiologists' report turnaround time.

AI-Assisted Data Classification

Neurologists have to analyze large volumes and diverse types of data and draw conclusions from them when assessing a patient's cognitive state. Another key related task for these professionals is to index health information and organize different kinds of data using special data classification systems. Since humans can analyze these vast, complex datasets with only a limited level of rigor, the specificity and accuracy of conclusions from analyses based on these systems may be compromised. AI's ability to compile, correlate, process, interpret, categorize, and establish connections among large and complex datasets enables clinicians to accurately assess the brain condition of patients and their predicted response to treatments and to build more effective data classification systems.

For AD diagnosis specifically, AI's help in information classification helps systematically organize the data samples collected from each patient regarding their cognitive abilities and brain conditions so that the data could be more systematically analyzed and an accurate diagnosis could be made.

Support Vector Machines (SVMs)

Support vector machines (SVMs) are supervised machine learning models that use classification methods for two-group classification and regression models. SVMs have been proved to provide high classification accuracy and are widely used classification ML algorithms in the brain MRI classification literature (Fan et al., 2008, p. 31). SVM algorithms are constructed by first plotting each data item as a point in a z-dimensional space (with z as the number of variables involved) and then classifying the points by finding a hyperplane that differentiates the two classes. It is able to, given a set of training examples, build a model that assigns examples of one category or the other. Figure 2 provides an example of a hyper-plane with support vectors.

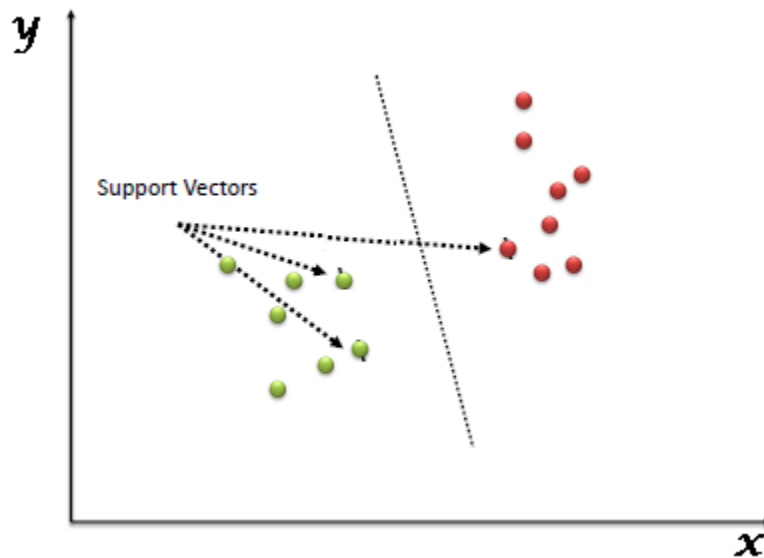


Figure 4. An example of an SVM classifier with a line that acts like a frontier separating two distinct classes.

Standard SVMs, however, fall short in performance when trying to sort labeled data. A modified SVM learning procedure that addresses this issue is a proposed *cutting plane semi-supervised support vector machine (CutS3VM)*, an algorithm that involves mediating issues associated with the *semi-supervised support vector machine (S3VM)*, the latter being an algorithm that attempts to learn a decision boundary that goes through low data density regions and treats the unknown data labels as additional optimization variables in the standard SVM problem (Zhao et al., 2008, p. 1). S3VMs are useful in many real-life situations dealing with sets of unlabeled training data and taking advantage of it to boost learning performance. They maximize the margin over labeled and unlabeled data to learn a decision boundary that traverses through low data density regions while respecting labels in the input space. Specifically, CutS3VMs propose “a nested sequence of successively tighter relaxations” (Zhao et al., 2008, p. 1). When building a hyperplane to classify all data into classes, CutS3VM converges faster and with greater accuracy than other S3VM models. It is able to iteratively select the data points that most stray from other values and add them to a working constraint set until no other violation of the constraint is discovered. This means that the algorithm can effectively group data records with the longest margin hyperplane as possible, which is optimal because maximizing the margin allows for little low certainty classification decisions since more data points near the decision surface represent undetermined decisions.

A model developed by Roman Filipovych and Christos Davatzikos is a classification approach that incorporates CutS3VMs to help differentiate MCI cases with 3 main steps: 1) an input consisting of base-line images of normal subjects and AD subjects, 2) a leave one-out (LOO) scheme for classifying MCI subjects into AD-like and normal-like classes that involves a) removing one subject from the population (AD or normal) at every run of the procedure, b) employing a Support Vector Machine-Recursive Feature Elimination (SVM-RFE) technique to rank computed features according to their effect on the leave-one-out error bound, c) extracting features at the detected regions from the images of normal, AD, and MCI subjects to obtain feature-vector representation of original images, and d) have the aforementioned images serve as the input to a linear semi-supervised SVM algorithm using the procedure discussed in (Zhao et al., 2008, p. 3), and 3) assigning a final label which indicates whether the subject’s brain has AD-like or normal-like structure for a given subject to be the one that corresponds to the majority of labels obtained for a subject during all runs of LOO procedure (Filipovych & Davatzikos, 2011, p. 4). This model proves successful because it is able to obtain a proper indicator of AD-like brain patterns that has the power to predict conversion from MCI to AD. Unlike other algorithms, it is able to study the heterogeneity of MCI and is able to more precisely separate

“normal” cases of MCI from cases that could potentially turn into AD or other forms of dementia through analysis of volumetric differences of AD-like and normal-like MCI. For example, according to results from Fan et al.’s study, the SVM classification techniques that were applied separately to each data group 1) AD vs. CN, 2) MCI vs. CN, and 3) AD vs. MCI, and the classification accuracy was found to be 94.3%, 81.8%, and 74.3% respectively (Fan et al. 6). This highly accurate method of separation and classifying cases is possible by studying, through neuroimaging, the different gray matter⁴ (GM) volumes in different brain regions.

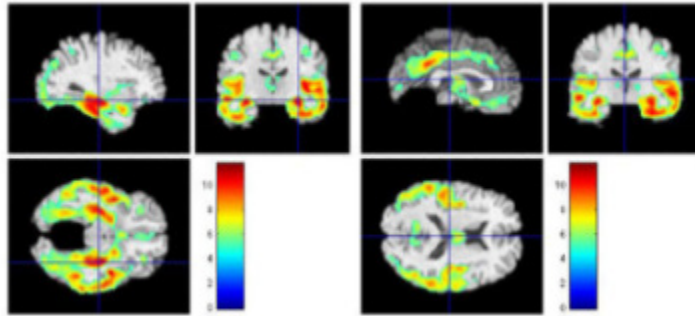


Figure 5. Representative sections with areas of relatively reduced GM in AD-like MCI compared to other regions of MCI.

Thus, SVMs prove useful in accurately classifying different patients’ cognitive states, which makes it easier for clinicians to classify patient data, spot outliers, and ultimately arrive at a more confident conclusion about whether or not a patient shows symptoms of AD. By efficiently handling non-linear data, having regularization capabilities, and being relatively stable, SVMs have great classification abilities and are able to assess patterns among data sets to better comprehend patients’ brain health.

Deep Neural Networks (DNNs)

In addition to SVMs, deep learning models for neuroimaging data can also help clinicians categorize different brain conditions to better understand AD progression and patients’ brain health. Deep neural networks (DNNs) are ANNs with several layers between the input and output layers. DNNs aim to learn feature levels by improving abstraction, by starting from the networks’ initial input and processing each additional hidden layer of the network to add on to the values in preceding layers, with as little human input as possible. In comparison to other kinds of networks, DNNs, with their multiple-layer systems, can learn, interpret, and classify more complex data. This benefit is helpful in determining whether patients show signs of AD since DNNs can help doctors better understand possible pathological mechanisms and get a more comprehensive idea of a patient’s condition.

Li et al., for instance, proposed a robust DL framework to categorize different progression phases of AD patients using PET and MRI scans. The study involved using public Alzheimer’s Disease Neuroimaging Initiative (ADNI) data sets consisting of data from MRI and PET images from 51 AD patients, 99 MCI patients (43 of whom converted to AD), and 52 healthy normal controls (Li et al. pg. 3, 2015). An image processing procedure involving skull-stripping, cerebellum removal, and spatial normalization was utilized and 93 region-of-interest (ROI) based volumetric features from the images were extracted. These features, combined with three cerebrospinal fluid⁵ (CSF)

⁴ Tissue is primarily made of neuronal cell bodies that serve as a key component of the central nervous system by processing signals generated in the sensory organs to enable individuals to move, think, and feel.

⁵ clear liquid in the tissue that surrounds the human brain and spinal cord

biomarkers of A β 42, t-tau, and p-tau, measures useful as supplementary information to diagnostic investigations, add to 198 total features for each subject. The proposed framework included PCA, stability selection, dropout, and multi-task learning (MTL) (Li et al. pg. 9, 2015). To analyze these features, a principal component analysis (PCA) DL tool, is a linear orthogonal transformation used for reducing the dimensionality of large datasets by converting large sets of features into linearly uncorrelated variables, where each variable is a linear combination of all original features (Jolliffe 1986). A PCA is useful as it can display the data points' relative positions in fewer dimensions while maintaining as much information as possible, making it easy to examine correlations between dependent variables. This technique was applied first to obtain principal components (PCs), the components that can explain the largest variance in the patient data set, as new features. Then, stability selection, a data analysis method based on subsampling with high-dimensional selection algorithms, was utilized to extract the most effective features. This method was useful as it worked in a high-dimensional setting and provided control in the finite sample setting. The dropout technique was then incorporated during the fine-tuning phase to improve the model's generalization capability. The clinical scores of Minimum Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog) were also assigned to each patient, in addition to the AD, MCI, or Healthy labels (Li et al. pg. 2, 2015). The DL program was structured using an MTL framework, a system where related tasks are learned simultaneously by extracting appropriate information that the tasks share in common to improve performance. In the framework, the researchers treated the learning of class labels, MMSE, and ADAS-Cog as related tasks to improve the prediction of class labels. This method was effective because it outperformed other methods like adding regularization on weights or using a committee machine for increasing the generalization capability of a model. The dropout procedure was able to do both tasks in an efficient way by doing them simultaneously. It was also able to achieve 91.4%, 77.4%, and 70.1% accuracy for AD vs Healthy Condition (HC), MCI vs HC, and AD vs MCI classifications, respectively (Li et al. pg. 10, 2015). Thus, this DL method showed promising aid in effectively classifying data which is imperative to AD diagnosis as it makes interpreting and analyzing the data much easier.

In summary, AI, with its ability to process, sort, classify, and analyze patient cognitive data, shows excellent potential for use in AD diagnosis and treatment.

Proposed Diagnosis Roadmap

Figure 6 shows a roadmap that outlines a specific process clinicians could use when assessing a patient's brain condition and deciding whether or not to diagnose them with AD.

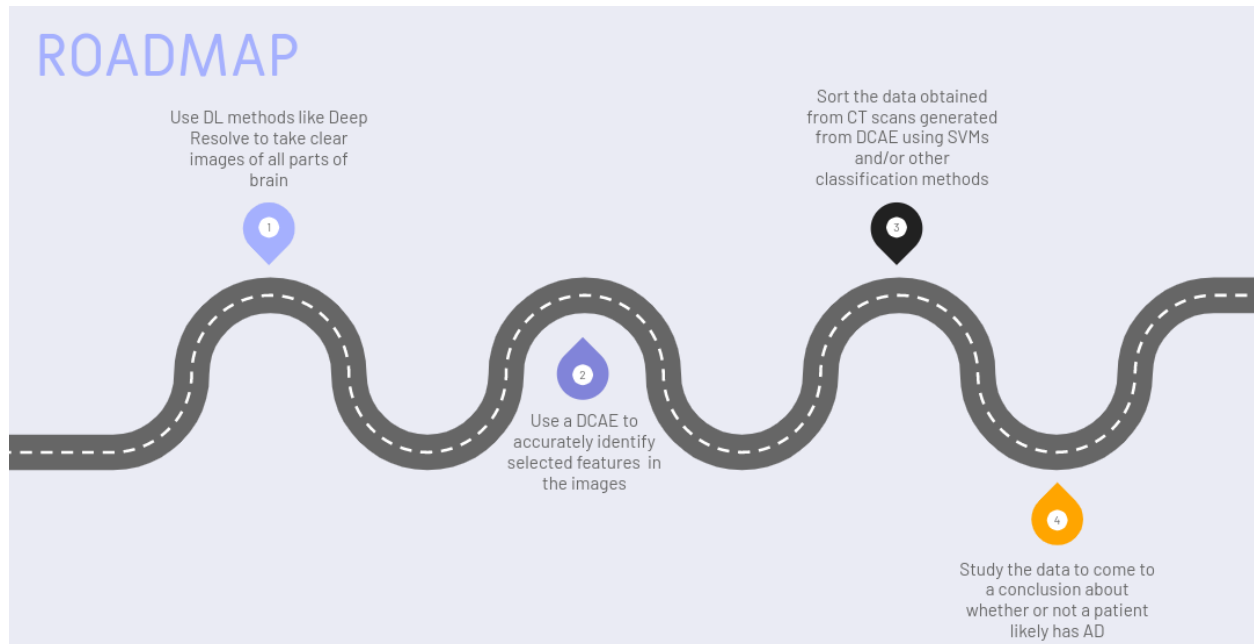


Figure 6. *Alzheimer's Disease Diagnosis With Artificial Intelligence Roadmap* by Author

The step-by-step method outlined in the roadmap is intended to help medical experts improve their diagnosis accuracy by leveraging high-quality imaging and fast, effective, and accurate analysis. The assessment would start by employing DL methods like Deep Resolve to MRI processes to take clear, sharp images of the brain so doctors could get a clear idea of the patient's brain condition; as described in the AI-MRI section above in the paper, even if the input image itself was of low quality, high-resolution images could be generated using Deep Resolve. Use of these DL methods significantly reduces image noise and improves the precision and accuracy of image reconstruction.

Clinicians could then feed the images produced by the DL methods in the MRI process to a DCAE to learn semantic feature representation in a process similar to the one depicted in Fig 6.

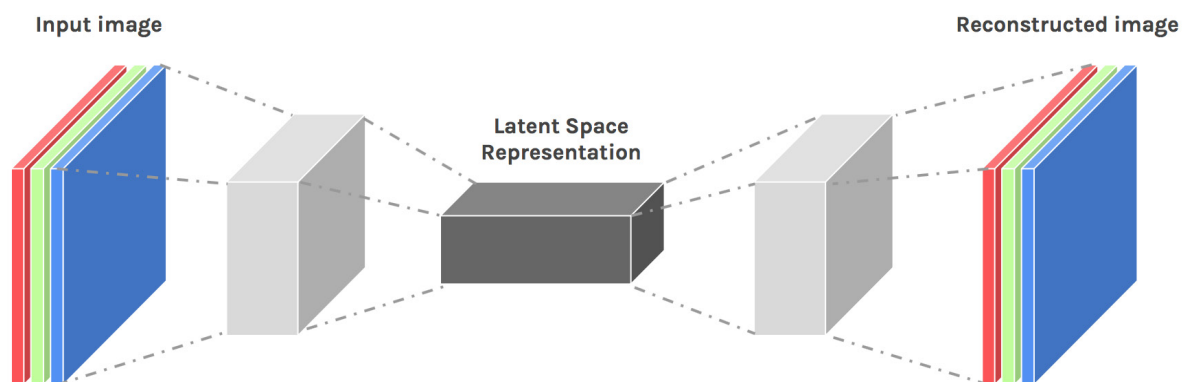


Figure 7. The process by which the proposed DCAE will receive and process information to produce a useful reconstructed image.

A DCAE would be able to learn nonlinear, discriminant, and invariant features from the unlabeled data it is given and identify changes in neural activity or tumors and plaques. Doctors would then be able to study these elected features and see if they could be signs of serious brain impairment. The multimodal neuroimaging data can then be sorted using DL methods in SVMs to find the best hyperplane that separates groups of similar data points and the data points

that show signs of AD from those that do not. This categorization will assign weights to diagnostically relative symptoms and thus allow doctors to holistically and accurately assess a patient's condition and decide whether or not to diagnose them with AD. AI's utilization in these diagnosis processes produces more robust results in a timely and efficient manner and improves the accuracy of AD diagnosis.

Conclusion

In conclusion, AI can help revolutionize the AD diagnosis process by providing medical experts with more accurate data of a patient's brain condition and by allowing them to extract the information they need for diagnosis faster and organize it in order to compare the markers for AD and arrive at a conclusion on whether they resemble signs of AD. Although AD is nearly impossible to diagnose with certainty, AI's help in evaluating a patient's brain health can greatly improve the diagnosis accuracy as to whether or not a patient has AD. Use of AI in brain MRI and CT scans enables detection of cognitive decline with a faster speed, higher quality, better convenience, and lower cost compared to conventional scans. In addition, the high quality data from AI-assisted brain MRI and CT scans can be fed into SVMs, DNNs, and other AI-based classification methods for analysis and interpretation across multiple variables to arrive at accurate, timely, and life-saving diagnosis conclusions. Thus, AI is poised to revolutionize AD diagnosis, and the medical field in general, and greatly improve patient's quality of life and life expectancy.

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References

- Alqahtani, A., Deng, J., & Jones, M. W. (2018). A DEEP CONVOLUTIONAL AUTO-ENCODER WITH EMBEDDED CLUSTERING. 1–5. https://cs.swan.ac.uk/~csmark/PDFS/2018_DeepCAE.pdf
- Artificial Intelligence In Healthcare Market Report, 2022–2030*. (2022). Artificial Intelligence In Healthcare Market Size (2022 - 2030). <https://www.grandviewresearch.com/industry-analysis/artificial-intelligence-ai-healthcare-market>
- Boyle, A. J., Gaudet, V. C., Black, S. E., Vasdev, N., Rosa-Neto, P., & Zukotynski, K. A. (2021). Artificial intelligence for molecular neuroimaging. *Annals of Translational Medicine*, 9(9), 822. <https://doi.org/10.21037/atm-20-6220>
- Byun, M.S., Yi, D., Lee, J., Choe, Y.M., Sohn, B.K., Lee, J., Choi, H.J., Baek, H., Kim, Y., Lee, Y., Sohn, C., Mook-Jung, I., Choi, M., Lee, Y.J., Lee, D.W., Ryu, S., Kim, S.G., Kim, J.W., Woo, J.I., & Lee, D.Y. (2017). Korean Brain Aging Study for the Early Diagnosis and Prediction of Alzheimer's Disease: Methodology and Baseline Sample Characteristics. *Psychiatry Investigation*, 14, 851 - 863.
- Cummings, J. L., Tong, G., & Ballard, C. (2019). Treatment Combinations for Alzheimer's Disease: Current and Future Pharmacotherapy Options. *Journal of Alzheimer's Disease*, 67(3), 779–794. <https://doi.org/10.3233/jad-180766>

- Fan, Y., Batmanghelich, N., Clark, C.M., Davatzikos, C., & Initiative, A.D. (2008). Spatial patterns of brain atrophy in MCI patients, identified via high-dimensional pattern classification, predict subsequent cognitive decline. *NeuroImage*, *39*, 1731-1743.
- Farlow, M. R., Miller, M. L., & Pejovic, V. (2008). Treatment Options in Alzheimer's Disease: Maximizing Benefit, Managing Expectations. *Dementia and Geriatric Cognitive Disorders*, *25*(5), 408-422.
<https://doi.org/10.1159/000122962>
- Filipovych, R., & Davatzikos, C. (2011). Semi-supervised pattern classification of medical images: Application to mild cognitive impairment (MCI). *NeuroImage*, *55*, 1109-1119.
- Han, X. (2017). Automatic Liver Lesion Segmentation Using A Deep Convolutional Neural Network Method. *ISBI 2017 LiTS Challenge ISIC 2017*, 1-4. <https://arxiv.org/pdf/1704.07239.pdf>
- Johnson, P. M., Recht, M. P., & Knoll, F. (2020). Improving the Speed of MRI with Artificial Intelligence. *Seminars in Musculoskeletal Radiology*, *24*(01), 012-020. <https://doi.org/10.1055/s-0039-3400265>
- Jolliffe, I.T. (1986). Principal Component Analysis for Special Types of Data.
- Kurlowicz, L., & Wallace, M. (1999). The Mini Mental State Examination (MMSE). *The Hartford Institute for Geriatric Nursing*, *3*. <https://cgatoolkit.ca/Uploads/ContentDocuments/MMSE.pdf>
- Li, F., Tran, L.Q., Thung, K., Ji, S., Shen, D., & Li, J. (2015). A Robust Deep Model for Improved Classification of AD/MCI Patients. *IEEE Journal of Biomedical and Health Informatics*, *19*, 1610-1616.
- Marcello, E., Gardoni, F., & di Luca, M. (2015). Alzheimer's disease and modern lifestyle: what is the role of stress? *Journal of Neurochemistry*, *134*(5), 795-798. <https://doi.org/10.1111/jnc.13210>
- Matsumoto, Y., & Kohyama, K. (2015). Alzheimer's disease and immunotherapy: what is wrong with clinical trials? *ImmunoTargets and Therapy*, *27*. <https://doi.org/10.2147/itt.s49923>
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (2011). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS--ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, *77*(4), 333.
<https://doi.org/10.1212/01.wnl.0000400650.92875.cf>
- Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine*, *256*(3), 183-194. <https://doi.org/10.1111/j.1365-2796.2004.01388.x>
- Petersen, R.C., Smith, G.E., Waring, S.C., Ivnik, R.J., Tangalos, E.G., & Kokmen, E. (1999). Mild cognitive impairment: clinical characterization and outcome. *Archives of neurology*, *56* 3, 303-8 .
- Ray, S. (2021, August 26). SVM | Supporting Vector Machine Algorithm in Machine Learning. Analytics Vidhya. <https://www.analyticsvidhya.com/blog/2017/09/understaing-support-vector-machine-example-code/>

Sankari, Z., & Adeli, H. (2011). Probabilistic neural networks for diagnosis of Alzheimer's disease using conventional and wavelet coherence. *Journal of Neuroscience Methods*, 197, 165-170.

Serengil, S. (2020, May 4). Convolutional Autoencoder: Clustering Images with Neural Networks. Sefik Ilkin Serengil. <https://sefiks.com/2018/03/23/convolutional-autoencoder-clustering-images-with-neural-networks/>

Yang, K., & Mohammed, E. (2020). A Review of Artificial Intelligence Technologies for Early Prediction of Alzheimer's Disease. *A Review of Artificial Intelligence Technologies for Early Prediction of Alzheimer's Disease*, 1-9. <https://arxiv.org/pdf/2101.01781.pdf>

Zhao, B., Wang, F., & Zhang, C. (2008). Cuts3vm: a fast semi-supervised svm algorithm. *KDD*.

Zhao, Y., Raichle, M.E., Wen, J., Benzinger, T.L., Fagan, A.M., Hassenstab, J., Vlassenko, A.G., Luo, J., Cairns, N.J., Christensen, J.J., Morris, J.C., & Yablonskiy, D.A. (2017). In vivo detection of microstructural correlates of brain pathology in preclinical and early Alzheimer Disease with magnetic resonance imaging. *NeuroImage*, 148, 296-304.