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Deep learning-based classification of multi-categorical Alzheimer's disease data

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Abstract

It is urgent to find the appropriate technology for the early detection of Alzheimer's disease (AD) due to the unknown AD etiopathologies that bring about serious social problems. Early detection of mild cognitive impairment (MCI) has pivotal importance in delaying or preventing the AD onset. Herein, we utilize deep learning (DL) techniques for the purpose of multiclass classification between normal control, MCI, and AD subjects. We used multi-categorical data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) including brain imaging measurements, cognitive test results, cerebrospinal fluid measures, ApoE4 status, and age. We achieved an overall accuracy of 87.197% for our artificial neural network classifier and a similar overall accuracy of 88.275% for our 1D convolutional neural network classifier. We conclude that DL-based techniques are powerful tools in analyzing ADNI data although further method refinements are needed.

Keywords

Alzheimer's Disease (AD); Mild Cognitive Impairment (MCI); Deep Learning (DL); Artificial Neural Networks (ANNs); Convolutional Neural Networks (CNNs); Alzheimer's Disease Neuroimaging Initiative (ADNI)

Introduction

Alzheimer's disease (AD), also known as senile dementia, is the most common cause of dementia in the elderly. Although there is no current cure, research is ongoing for the development of new treatments. AD has pathologically and clinically unique characteristics. Post-mortem studies of AD have shown four typical lesions in AD brains: intraneuronal neurofibrillary tangles (NFTs), extracellular deposits of Aβ amyloid plaques, glial

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Author Contributions Statement

DC conceived and conducted the analysis, KC assisted in the analysis, JJ assisted in writing the manuscript, XH initiated the research, edited the final draft of the manuscript, and guided the project throughout the process.

Conflict of Interest Statement

The authors declare that they have no competing interests.

responses, and neuronal loss with synaptic loss [1,2]. As life expectancy increases, so does the risk for AD. In the United States alone, projections show the prevalence in individuals aged 65 years or older nearly tripling from 4.7 million in 2010 to 13.8 million in 2050 [3]. In both developed or developing countries, the morbidity and mortality rates of dementia are both quickly growing. In China, for example, projections show prevalence quadrupling from 6 million in 2011 to 28 million in 2050 [4]. The disease causes increasingly serious economic burdens and social issues [5], making it one of humanity's great challenges in the 21st century.

Methods have been proposed in the literature for providing an automatic tool that guides clinicians in diagnosing AD [6–14]. In order to distinguish AD or mild cognitive impairment (MCI) subjects from normal control (NC) subjects, machine learning techniques have received some attention [15–17]. Deep learning (DL) is categorized under machine learning. It processes data in a fashion inspired by biological nervous systems and contains deep layers that are often hidden [18]. It is an exciting frontier of machine learning for learning data representations and is rapidly evolving as technology becomes increasingly capable of accommodating big data. DL has versatility of application across different contexts and types of data, including the utilization of AD data for diagnosis classification [19,20]. Artificial neural networks (ANNs), a DL model, process data in a fashion similar to the connections of neurons in the brain [21]. They have been applied in uniquely different classification tasks that have been useful for AD research [22–24]. ANNs utilize neuronal weights between nodes and make use of back-propagation and gradient descent over a series of training epochs. They are often applied on tables of data, of which the contents can be multi-categorical [22]. Different varieties of activation functions, which define the output of nodes within a neural network, include both sigmoidal and ReLU [25]. Convolutional neural networks (CNNs) are a subset of ANNs that are characterized by their convolution, which are often used for image recognition but can be used across a variety of different contexts as well [26–28].

In this manuscript, we propose a method of multiclass classification between NC, MCI, and AD patients using multi-categorical data using deep learning. We utilize both an ANN and a 1D CNN for this purpose. Our aim is to demonstrate the effectiveness of our multi-categorical data in classification as well as to compare ANNs with CNNs in this type of task.

Materials and Methods

Experimental data

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). The ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and both clinical and neuropsychological assessment can be combined to measure the progression of MCI and AD.

ADNI initially planned to recruit 800 adults, ages 55–90, to participate in the research. Out of these 800 individuals, approximately 200 cognitively normal older individuals were to be followed for three years, 400 people with MCI were to be followed for three years, and 200 people with early AD were to be followed for two years [29]. Later on, these time periods were extended and more subjects were added [30].

Procedure

ADNI data from a multi-categorical set was used to generate an ANN and 1D CNN capable of diagnosis. Table 1 includes data trained and tested against diagnosis (NC, MCI, and AD) data. Figure 1 contains a diagram of the brain regions included in our data set [31,32], all of which are located within the temporal lobe. Cerebrospinal fluid measures associated with AD were included [33,34] as well as cognitive tests results [35], ApoE4 status [36, 37], and age. Figure 2 contains MRI of an NC, MCI, and AD patient from the ADNI trials, demonstrating that the naked eye can have some difficulty differentiating between them.

R was used to extract the data the ADNI dataset and clean it for use in the neural network as well as for interpretation of the results. Brain region measurements were averaged between the left and right structures. Incomplete instances of subject data were not utilized. 19 total values per subject, as shown in Table 1, were used and 3706 entries total were utilized. 1299 were NC (599 male, 630 female) patients, 1683 were MCI (1002 male, 681 female) patients, and 794 were AD (407 male, 387 female) patients. These entries represent different sessions in which none of the features were missing, meaning that some patients had their data used multiple times but from different dates. There were 1093 unique subjects utilized, of which 352 had been NC, 531 had been MCI, and 334 had been AD. Some of these subjects had transitioned from one diagnosis to another between sessions. The neural networks were built in Python using Theano, TensorFlow, and Keras libraries. The ANN was composed of an input and hidden layer with ReLU activation, followed by a second hidden layer with ReLU activation, followed by an output layer with Softmax [38] activation. The CNN was composed of a 1D convolutional layer with ReLU activation, followed by a max pooling layer [39], followed by a flatten layer, followed by an output layer with Softmax activation. Both the ANN and CNN included 100 epochs, or training iterations. Internal validation occurred with 80% of entries being used for training and 20% being used for testing. We used R to interpret results. The framework of the method is shown in Figure 3.

Results

We achieved an overall accuracy of 87.197% for our ANN classifier, as demonstrated in Table 2, and a similar overall accuracy of 88.275% for our 1D CNN classifier, as demonstrated in Table 3. Each table lists the recall and precision for each class. These 3×3 confusion matrices are provided with precision and recall for each category of classification due to our multiclass classification, as opposed to binary disease classification, which can be represented by precision and recall for the disease class alone. This is effectively illustrative of the classification as a whole.

AD and NC weren’t misclassified as each other, which is a positive indication of the ability of the classifiers. Misclassifications occur at the level of NC with MCI and MCI with AD.

This is understandable because these are states that are far more similar to each other and are likely to have overlap. There is a transition that occurs from NC to MCI to AD and a patient transitioning to MCI from NC, for example, may resemble an MCI patient to the classifier. This may also be indicative of a combination of characteristics that a clinician may not be aware of but an algorithm could interpret from the data. Figure 4 contains the accuracy and loss reported by Keras over each epoch during runs of the ANN and CNN. Both networks exhibit a similar drastic curve in the early epochs for gains in accuracy and reductions in loss, and then slowly become less and less drastic over the 100 epochs. This represents the adaptations of the networks in their ability to classify throughout the epochs.

Discussion

We have demonstrated a successful multiclass classifier between NC, MCI, and AD subjects using multi-categorical data. Classification between all three diagnoses simultaneously using different types of data demonstrates the power of what deep learning is able to achieve.

The 1D CNN achieved similar results as the ANN. This may be because of the nature of the data. CNNs typically excel in image recognition, which is why they are so useful in classification using 3D brain images [40,41]. 1D CNNs are useful in certain pattern recognition tasks [42] but may not be as useful in general datasets like the one we have implemented in this study. It performed well but didn't excel far beyond our ANN. Variations on this experiment could include the utilization of different combinations of ADNI collected data. Limited data from imaging was used. As shown in table 1, a few measurements from a few regions of interest were utilized in our dataset. Perhaps some type of expansion on this section of our data could boost results significantly. If the whole 3D brain image was somehow incorporated with our other data, or simply more measurements from more brain regions, the results could potentially be better. Another interesting addition to the dataset could include different genetic data from ApoE4 status.

Classification of a disease is often thought about from the perspective of utilizing a single category of data, such as imaging or genetics. Since AD is a polygenic, multifactorial complex disease, utilizing multiple categories may be necessary for optimal diagnosis. This may also be necessary in understanding AD before it develops. Developing classifiers like ours are important in better understanding the multipronged nature of the disease. We are hoping that experiments will continue of this nature thanks to ADNI's collection of different forms of data from its patients. Resources like ADNI make data analysis using different methods on different variations of data from the same database possible. This study is also important in understanding the ways newer technologies such as DL can be useful for understanding AD. As software and hardware breakthroughs have provided increasingly efficient data processing, the scientific community's ability to classify at higher accuracies has become more obtainable. This is all crucial in improving prevention and treatment of AD, as it becomes a growing concern in our society due to increasing life spans.

Conclusions

In conclusion, we have presented a classifier capable of efficient three-way classification using carefully selected data that was predicted to yield the best results in the context of MCI and AD prediction. Our dataset included different categories of data including cognitive test results, brain imaging measurements, cerebrospinal fluid measures, ApoE4 status, and age. Our ANN and CNN performed very similarly. Our results show that a well-selected set of data can yield powerful results using DL-based algorithms.

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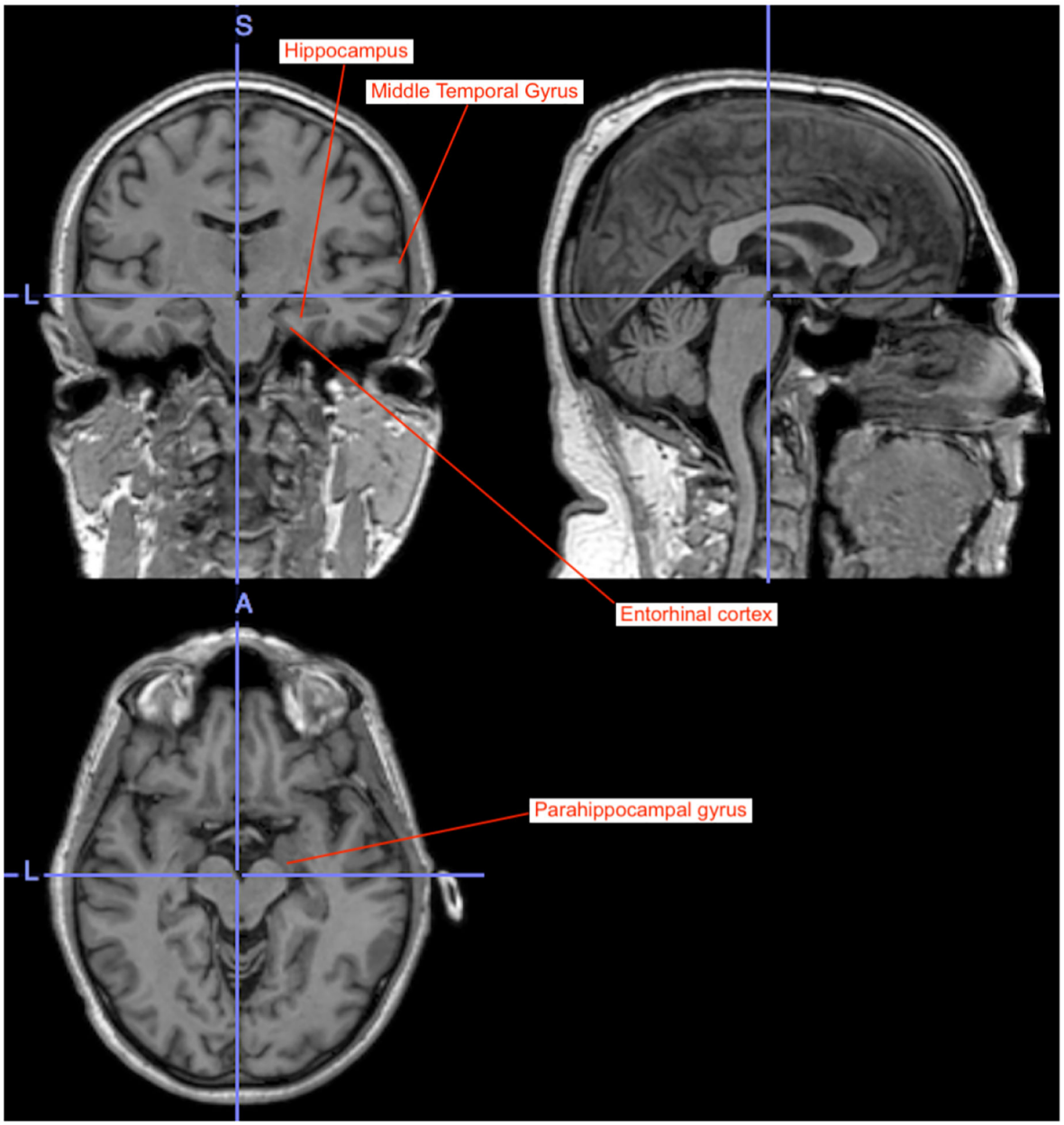

Figure 1: Brain regions included in our dataset.

This diagram utilizes MRI of a NC patient from the ADNI study. L, left; A, anterior; S, superior. The images are oriented in coronal, sagittal, and axial view.

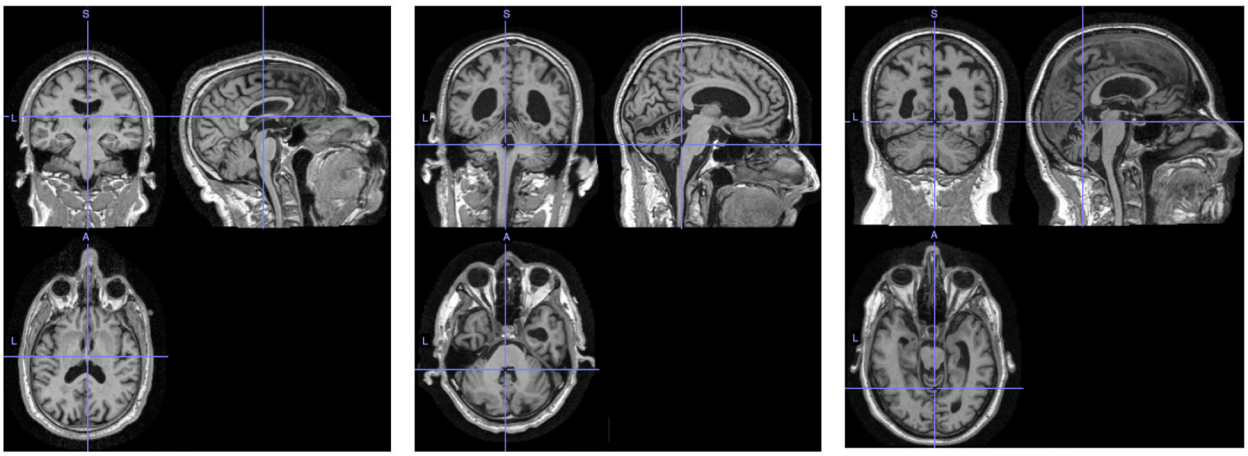

Figure 2: MRI of an NC, MCI, an AD patient.

These are images of MRI scans from ADNI patients. L, left; A, anterior; S, superior. The images are oriented in coronal, sagittal, and axial view.

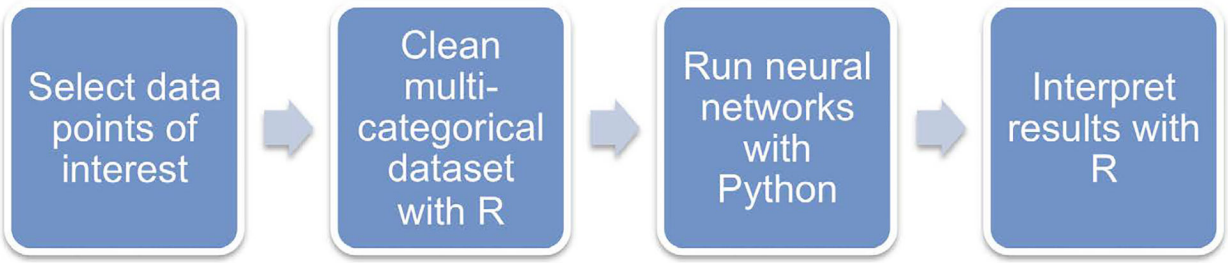

Figure 3: The steps of our process.

We utilized data associated with AD, used R to generate a usable dataset, ran neural networks with Python on that dataset, then used R to interpret the results.

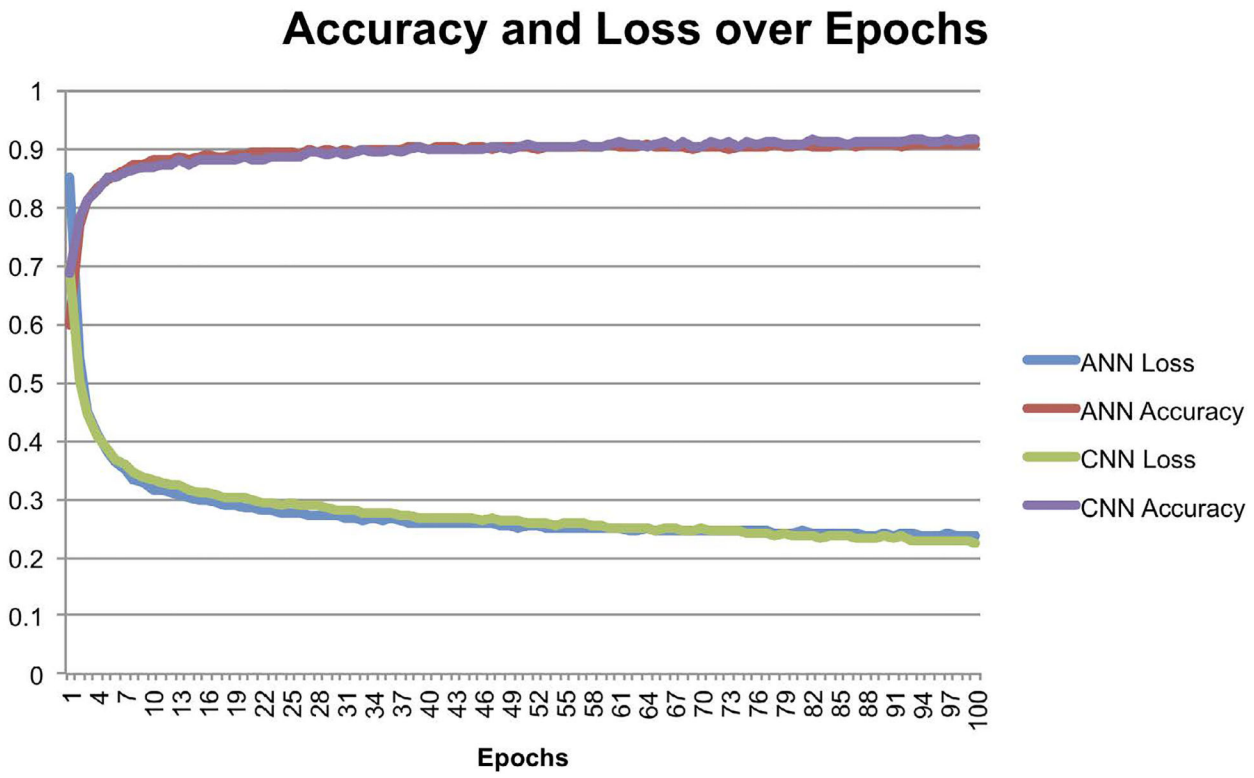

Figure 4: Accuracy and Loss.

Accuracy and loss over 100 epochs of our ANN and CNN as reported by Keras.

Table 1:

Multi-categorical dataset.

Cognitive test results			
CDR-SB	ADAS 11	MMSE	RAVLT (5 sum)
MRI volume, surface area, cortical thickness average, and cortical thickness standard deviation measurements			
Parahippocampal gyrus	Hippocampus (Just Volume)	Entorhinal cortex	Middle temporal gyrus
Cerebrospinal fluid Measures			
Amyloid-beta level in CSF	Tau level	Phosphorylated tau level	
Risk Factors Associated with AD			
ApoE4	Age		

Table 2:

ANN results.

	Truth Data				
		NC	MCI	AD	Classification Overall	Producer Accuracy (Precision)
Classifier Results	NC	243	18	0	261	93.103%
	MCI	25	288	37	350	82.286%
	AD	0	15	116	131	88.550%
	Truth Overall	268	321	153	742	
	User Accuracy (Recall)	90.672%	89.720%	75.817%		

Overall Accuracy: 87.197%, Kappa: 0.798

Table 3:

CNN results.

	Truth Data				
		NC	MCI	AD	Classification Overall	Producer Accuracy (Precision)
Classifier Results	**NC**	253	26	0	279	90.681%
	MCI	15	272	23	310	87.742%
	AD	0	23	130	153	84.967%
	Truth Overall	268	321	153	742	
	User Accuracy (Recall)	94.403%	84.735%	84.967%		

Overall Accuracy: 88.275%, Kappa: 0.817