

Prediction of Cognitive Impairment Using a Deep Learning Autoencoder Algorithm

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Abstract— Dementia is a decline in cognitive function and typically diagnosed when acquired cognitive impairment has become severe enough to compromise social and/or occupational functioning. From no cognitive impairment (NCI) to dementia, there are many states intermediate. Prediction of cognitive impairment will be helpful to start treatment to avoid possible further brain damage. Some deep learning based approaches have been proposed for the classification of Magnetic Resonance Imaging (MRI) to diagnose Alzheimer disease (AD) or dementia. The diagnosis of the cognitive impairment was made based on the Magnetic Resonance Imaging (MRI) data, and also based on other associated factors. Therefore, in this study, we aim to predict cognitive impairment based on both the neuroimaging markers and other associated factors of the subjects using a deep learning Autoencoder algorithm. We propose a new way to apply Autoencoders to a multi-class classification task and also provide the feature importance too. The Autoencoder model performance was compared with two widely used machine learning classification algorithms, namely, the multinomial logistic regression (MLG) and the Extreme Gradient Boosting (XGBoost). The results of Autoencoder algorithm show good performance and outperform the machine learning methods.

Keywords— Cognitive Impairment, Dementia, Supervised Classification, Deep Learning, Autoencoder, Neuroimaging Markers, XGBoost, MRI

I. INTRODUCTION

Dementia and cognitive impairment pose a significant public health problem globally [17]. As reported at the Alzheimers Association International Conference (AAIC) 2021, each year, an estimated 10 in every 100,000 individuals develop dementia with early onset (prior to age 65). This corresponds to 350,000 new cases of early onset dementia per year, globally. Based on the top 10 causes of death reported by World Health Organization, in 2019, AD and other forms of dementia ranked as the 7th leading cause of death [1]. Early detection and accurate prognosis of this devastating disease involve complex and heterogeneous mechanisms.

Recently, deep-learning-based approaches have started permeating into health-care and also been proposed for the classification of neuroimaging data related to AD and other forms of dementia. Convolutional Neural Network (CNN) first rose to prominence in 2012 when they demonstrated state-of-the-art performance on the ImageNet Large-Scale Visual Recognition Challenge (ILSVRC) [16], and then is the most widely used technique for MRI datasets. A deep residual neural network combined with other transfer learning techniques was trained in [20] for AD classification into different categories. [8] proposed and trained CNN from

scratch for early detection of AD. [15] proposed an unsupervised convolutional Autoencoder network which was used for the classification of AD and normal control. [7] proposed a method to classify or discriminate AD using support vector machine with feature selection technique. [14] used a machine learning model together with artificial neural network (ANN) algorithm to predict cognitive impairment based on the neuropsychological test data. [2] used a combined methodology of machine learning and semi-parametric survival analysis to estimate the relative importance of 52 predictors in forecasting cognitive impairment and dementia in a large, population-representative sample of older adults. Deep neural networks have shown same or better performance than clinicians in many tasks owing to the rapid increase in the available data and computational power. In this paper, we would like to develop deep learning algorithms for classifying cognitive impairment which have the same process as diagnoses given by clinicians. A diagnosis of cognitive impairment or dementia by clinicians was made not only according to the MRI, but also considering the other associated risk factors such as demographic information and cardiovascular risk factors. Therefore, in this study, we aim to classify cognitive impairment based on both the neuroimaging markers of the subjects and the associated risk factors. To the best of our knowledge, this is new in the area of classification of cognitive impairment.

The main deep learning algorithm used in this study is Autoencoder which has been first introduced in [12]. Autoencoder is an unsupervised ANN which attempts to produce output identical to its input. Its architecture can be simplified into two main parts: the encoder and decoder. The encoder portion receives the input data and compress it into a smaller dimension which we call it latent space. Then the encoded data goes into the decoder. Ideally, the output of the decoder, that is, the reconstructed data would be identical to the input data. The difference between the input data and reconstructed data is called reconstruction error. The smaller the reconstruction error is, the more the reconstructed data is similar to the input data. Therefore, it is usually used for anomaly detection and has been shown that Autoencoder-based algorithms perform well for anomaly detection in brain MRI (see more details at [4]). For anomaly detection, the Autoencoder model will be trained on normal data only. For a new observation, if its reconstruction error is higher or above a threshold, then it will be considered to be anomaly. However, deciding the threshold of reconstruction error is very difficult and objective. To overcome this problem, in this study, we propose a new way to use Autoencoder for

classification problem which does not require to determine the threshold. The classification results demonstrate that this method works well for multi-class classification problems.

The rest of the paper is organized as follows. Section 2 gives a brief overview of the dataset used in this study. Section 3 introduces how to use the deep learning Autoencoder algorithm in the multi-class classification problems and get the feature importance. The exploratory data analysis and classification results are given in Section 4 and the conclusions and future work are presented in Section 5.

II. MATERIALS

This study conducted the dataset from Epidemiology of Dementia in Singapore (EDIS) study. EDIS Study participants, aged 60-90 years, were drawn from the Singapore Epidemiology of Eye Disease (SEED) study, a population-based study among Chinese (Singapore Chinese Eye Study [SCES], [10]), Malays (Singapore Malay Eye Study [SiMES-2], [11]), and Indians (Singapore Indian Eye Study [SINDI-2], [23]). The dataset contains $n = 864$ subjects with $p = 67$ variables which include subject ID, diagnosis of subject, some demographic information, some risk factors, some neuroimaging markers as well as some scores which were used for cognitive impairment and dementia assessment. Cognitive impairment no dementia (CIND) was defined as impairment in at least one domain of neuropsychological test battery (NTB). The battery assesses seven domains which include five non-memory domains and two memory domains. CIND mild was diagnosed when ≤ 2 domains were impaired and CIND moderate as impairment of > 2 domains. See more details at [10] and [24]. Hence these subjects can be divided into four classes based on the diagnosis of cognitive impairment and dementia, namely, NCI, CIND mild, CIND moderate, and Dementia. Since the test scores were used for diagnosis of cognitive impairment, they should not be included in the prediction model. Therefore, in this study, we first manually select 25 variables. Then, we removed those observations with missing values, and the potential outliers. For each class, we treat the values outside three standard deviations from the mean as outliers and then remove all observations entirely with outliers. As a result, 78 observations have been removed from the dataset. Hence, there are 786 observations in the cleaned dataset which include 238 had NCI, 258 had CIND mild, 263 had CIND moderate, and 27 had dementia. Since the number of dementia cases is very low, CIND moderate and dementia were grouped together for classification analyses. We call this group CIND moderate/Dementia.

The variables for the modelling was grouped into three clusters, namely, basic demographic information, risk factors, and neuroimaging markers.

A. Basic Demographic Information

The basic demographic information of subjects we considered in this subsection are age, race, gender, and education level. Note that the prevalence of any cognitive impairment equals to $(n_2 + n_3 + n_4)/n$. Where $n_2 =$ CIND mild sample size, $n_3 =$ CIND moderate sample size, $n_4 =$ Dementia sample size and $n =$ the total sample size for the study. For the feature age, we grouped the continuous ages into three categories, namely, 60-69 years, 70-79 years, and > 80 years. The prevalence is displayed in Table 1 below.

Table 1: Demographic Information

Feature	Category	NCI ($n_1 = 238$)	CIND mild ($n_2 = 258$)	CIND moderate ($n_3 = 263$)	Dementia ($n_4 = 27$)	Total ($n = 786$)	Prevalence of any cognitive impairment (%)
Age	60 – 69 years	172	1	78	2	396	56.57
	70 – 79 years	64	4	139	1	315	79.68
	> 80 years	2	4	46	5	75	97.33
	> 80 years		9		1		
Race	Chinese	113	75	72	4	264	57.20
	Indian	77	98	79	4	264	70.16
	Malay	48	85	112	19	258	81.82
Gender	Female	99	126	172	22	419	76.37
	Male	139	132	91	5	367	62.13
Education Level	Nil	14	35	92	15	156	91.03
	Primary	93	124	111	10	338	72.49
	Secondary	82	75	51	2	210	60.95
	Tertiary	49	24	9	0	82	40.24

From Table 1, we see that adults over 80 years of age have the highest cognitive impairment prevalence (97.33%), whereas adults between 70-79 years of age have a prevalence of 79.68% compared to adults between 60-69 years of age, a cognitive impairment prevalence of 56.57%. The Chinese have the lowest prevalence for all three cognitive impairment categories. Females have a higher cognitive impairment prevalence (76.37%) compared to males (62.13%). Tertiary level adults have the lowest prevalence for cognitive impairment (40.24%) while adults with ‘Nil’ education have a prevalence of 91.03%.

B. Risk Factors

The risk factors we studied in this subsection are Body Mass Index (BMI), smoking history, stroke, and whether the adults were diagnosed with diabetes, hyperlipidemia or hypertension. We grouped the continuous BMI values into four categories, namely, underweight (below 18.5), normal (18.5 24.9), overweight (25.0 29.9), and obese (30.0 and above). The prevalence of the different risk factors is shown in Table 2 below.

Table 2: Risk Factor Prevalence for Cognitive Impairment

Feature	Category	NCI ($n_1 = 238$)	CIND mild ($n_2 = 258$)	CIND moderate ($n_3 = 263$)	Dementia ($n_4 = 27$)	Total ($n = 786$)	Prevalence of any cognitive impairment (%)
BMI	Underweight	3	8	14	3	28	89.29
	Normal	120	118	110	11	359	66.57
	Overweight	89	100	92	9	290	69.31
	Obese	26	32	47	4	109	76.15
Smoking History	Ever	64	73	66	3	206	68.93
	Never	174	185	197	24	580	70.00
Stroke History	Yes	6	12	18	4	40	85.00
	No	232	246	245	23	746	68.90
Diabetes	Yes	75	97	109	12	293	74.40
	No	163	161	154	15	493	66.94
Hyperlipidemia	Yes	163	194	214	19	590	72.37
	No	75	64	49	8	196	61.73
Hypertension	Yes	174	203	229	26	632	72.47
	No	64	55	34	1	154	58.44

Adults who are underweight have the highest prevalence of cognitive impairment (89.29%), while adults who are obese have the second highest prevalence of cognitive impairment (76.15%). The prevalence of cognitive impairment for non-smokers is 70% which is slightly higher than that of smokers (68.93%). Adults who have any of stroke history, diabetes,

hyperlipidemia, or hypertension have a higher prevalence of cognitive impairment than those adults who do not have these medical histories.

C. Neuroimage Markers

We first considered the volumes (in mm) of total intracranial (ICV), total grey and white matter (GWM), total grey matter (GM), total white matter (WM), total white matter lesions (WML), left hippocampus (LH), and right hippocampus (RH) which was determined from the MRI scans and measured by the radiologists on the EDNIS study. Since GWM, GM, and WM are highly correlated, and LH and RH are highly correlated, we only present the results of GWM and LH. The boxplots of these neuroimaging markers in different classes are plotted in Fig. 2 below.

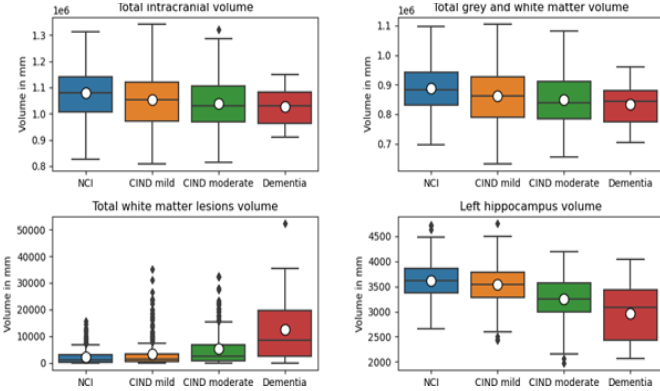


Fig. 2: Boxplots of the volumes (in mm) of ICV, GWM, WML and LH

The white dot in each boxplot indicates the mean value. It is seen that except for WML, the mean values for the neuroimaging markers decrease from NCI to CIND mild to CIND moderate to dementia. Adults who had dementia have much larger volume of WML than the other groups.

Besides the volumes, this dataset also includes other neuroimaging markers such as number of lacunes, cortical cerebral microinfarcts (CMI) numbers, central atrophy rate, number of cortical infarcts and number of stenosed artery. The analysis results are displayed in Table 3 below.

Table 3: Lacunes, CMI numbers, Central atrophy rate, Number of Cortical Infarcts and Number of Stenosed Artery

Feature	Category	NCI ($n_1 = 238$)	CIND mild ($n_2 = 258$)	CIND moderate ($n_3 = 263$)	Dementia ($n_4 = 27$)	Total ($n = 786$)	Prevalence of any cognitive impairment (%)
No. of lacunes	0	223	216	200	13	652	65.80
	> 0	15	42	63	14	134	88.81
CMI numbers	0	232	247	243	20	742	68.73
	> 0	6	11	20	7	44	86.36
Central atrophy rate	None	24	37	10	0	71	66.20
	Mild	169	164	148	8	489	65.44
	Moderate	42	51	90	15	189	78.39
	Severe	2	6	15	4	27	92.59
No. of cortical infarcts	0	235	250	255	26	766	69.32
	> 0	3	8	8	1	20	85.00
No. of stenosed artery	0	216	226	221	18	681	68.28
	> 0	22	32	42	9	105	79.05

The adults who have any of lacunes, CMI, or stenosed artery have a higher prevalence of cognitive impairment than those who do not have. Further, adults who have severe central

atrophy rates have the highest prevalence of cognitive impairment. Adults who have cortical infarcts have a higher prevalence of cognitive impairment.

III METHOD AND EXPERIMENTS

Autoencoder is an unsupervised ANN which attempts to produce output identical to its input. Its architecture has been introduced in Section 1. As mentioned before, when Autoencoder is used for anomaly detection, a threshold is always needed to detect whether the reconstruction error is large. However, deciding on the threshold for the reconstruction error is difficult and objective. Therefore, to overcome this problem, for the multi-class classification problem in this study, instead of training the Autoencoder model on normal observations only, we trained k Autoencoder models for k classes separately. For example, we have three classes in this study, that is, (1) No Cognitive Impairment (NCI), (2) Cognitively Impaired, No Dementia (CIND) mild, and (3) CIND moderate/Dementia. We therefore train three Autoencoder models for the three classes based on NCI subjects, CIND mild subjects, and CIND moderate/Dementia subjects, respectively. For a new coming observation, we obtain three construction errors by inputting it into the three trained Autoencoder models, respectively. This new observation will be assigned to the class with the smallest reconstruction error.

The categorical variables were represented using one-hot encoding and then the whole dataset was normalized into range $[-1, 1]$ by using min-max normalization. The architectures of the Autoencoder models in this study is described as follows. The encoder and decoder are two fully-connected networks. Specially, we use one fully-connected hidden layers in both encoder and decoder and we also use batch-normalization [13]. The activation function of the last layer of decoder is Tanh function and the activation functions of the hidden layers are LeakyReLU function [18]. To overcome overfitting, on each hidden layer, we also use dropout [21]. Mean Square Error (MSE) is used as the reconstruction error. The Autoencoder was coded using a Python deep learning library, PyTorch [19]. It is also important to understand the feature importance by analysing the latent space in the trained Autoencoder model. Hence, in this study, after the model is trained, we input an identity matrix I_p where p is the number of neurons on the input layer into the trained encoder again and get the encoded data. The value of this encoded data can be treated as the feature importance. For example, if we input the vector $[1, 0, \dots, 0]$ into the trained encoder, then the mean absolute value of the encoded data can be treated as the importance of the first feature.

An overview of the research framework for our study is shown in Fig. 1 below.

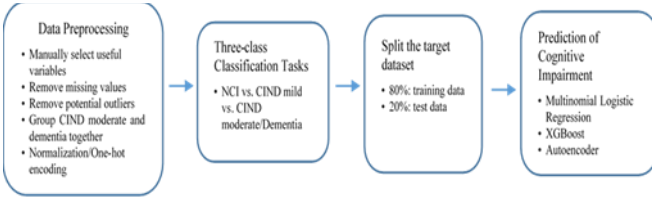


Fig. 1: Framework of the study

The sample sizes of these three groups was 238, 258, and 290, respectively. The cleaned dataset was split into two parts, 80% of the dataset were used as training dataset, and the rest 20% were used as test dataset. The experiment was performed on Windows 10 Pro using Python (version 3.9.6) with a 2.3 GHz, 4 cores, intel core i7, 16 GB RAM of memory running the classification algorithms.

IV RESULTS

The results of the three-class classification problem by using the proposed Autoencoder algorithm together with MLG [5] and XGBoost [6] are presented in this subsection. In the test dataset with 158 observations, 45 come from NCI class, 50 come from CIND mild class, and 63 come from CIND moderate/Dementia class. We use 4 measures to compare the performance of the methods we used, namely, overall accuracy, precision, recall, and f1-score. Except overall accuracy, the other three metrics are used for binary classification and the equations below indicates how to calculate them for each class:

$$\text{Precision} = \frac{TP}{TP + FP}, \text{Recall} = \frac{TP}{TP + FN}, \text{and F1-score} = \frac{2 \times TP}{2 \times TP + FP + FN}, \quad (1)$$

where FP, FN, TP, TN are given as false positives, false negatives, true positives, and true negatives, respectively. The classification results are presented in Table 4 below.

Table 4: Classification results given by MLG, XGBoost and Autoencoder

MLG			XGBoost			Autoencoder		
Precision	Recall	F1-score	Precision	Recall	F1-score	Precision	Recall	F1-score
NCI	0.49	0.62	0.55	0.51	0.6	0.55	0.7	0.66
CIND milc	0.46	0.32	0.38	0.43	0.24	0.31	0.49	0.74
CIND mod	0.65	0.68	0.67	0.6	0.73	0.66	0.79	0.52
Overall Accuracy	0.5506		0.538				0.6203	

It can be seen that the Autoencoder outperforms the other two machine learning methods in terms of overall accuracy and precision. In particular, our proposed Autoencoder classifier performs much better than the other two machine learning methods on classifying the observations from CIND mild group. For MLG and XGBoost, they correctly classified more observations from CIND moderate/Dementia group rather than those from CIND mild group since CIND moderate/Dementia is quite different from CIND mild and NCI. However, our proposed Autoencoder classifier also distinguishes the difference between CIND mild and NCI since the trained models learned from each class

independently. That is very helpful for the classification of cognitive impairment at the different levels. In addition, based on the feature importance given by these three classifiers, we found that the basic demographic information and neuroimaging markers were more important than the risk factors.

V CONCLUSION AND FUTURE WORK

In this study, we apply a deep learning Autoencoder algorithm together with two machine learning classifiers, namely, MLG and XGBoost to predict cognitive impairment based on dataset from a Singaporean study. We proposed a new method to apply Autoencoder to multi-class classification problems. It is not necessary to detect the threshold of reconstruction errors by using our method, and the classification results show that Autoencoder performs best among these three classifiers. In addition, we also introduced a new method to get feature importance given by Autoencoder classifier. The feature importance given by our method is consistent with those given by MLG and XGBoost. Based on the results, we found that basic demographic information and neuroimaging markers are more important than risk factors.

Our method is simple and the features required are easy to collect. However, due to the limitation of the dataset in this study, the classification accuracy is not high and the study of prediction of cognitive impairment using neuroimaging markers is not comprehensive. This dataset only includes the total volumes of ICV, GWM, WML, GM, WM, LH, RH, and cerebrospinal fluid volume. Many of these variables are highly correlated. Hence, these variables may not be able to represent all information of the brain MRI. Image segmentation to get volumes of all the regions in brain MRI is needed, and we can select which regions are important to predict cognitive impairment using some machine learning and deep learning methods. Further study in this direction is interested and warranted.

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