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Unlocking Neurological Mysteries: Machine Learning Approaches to Early Detection of Alzheimer's Disease

Nörolojik Gizemleri Aydınlatmak: Alzheimer Hastalığının Erken Tespitinde Yapay Öğrenme Yaklaşımları

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UNLOCKING NEUROLOGICAL MYSTERIES: MACHINE LEARNING APPROACHES TO EARLY DETECTION OF ALZHEIMER'S DISEASE

Abstract

Dementia is a clinical illness that becomes more common as people get older. It is defined by a decline in cognitive abilities across several domains and eventually impacts everyday functioning. Consequently, this leads to a decline in autonomy, impairment, dependence on assistance even criminal tendencies/insecure behaviors and ultimately, the disease frequently results in mortality. Particularly with regard to neurodegenerative disorders, various forms of dementia are correlated with criminal activity. According to research, criminal and socially inappropriate behavior is prevalent among dementia patients and is sometimes the initial symptom of the disease. Alzheimer's Disease (AD) is responsible for 60-80% of all occurrences of dementia, and its occurrence increases double every five years beyond the age of 65. Given the availability of health data and the decrease in data processing costs, it is now feasible to detect Alzheimer's disease at an early stage. The objective of this study is to classify individuals as either Alzheimer's sufferers or healthy individuals by employing various machine learning techniques. The "OASIS-2 dataset", which consists of "longitudinal MRI data" from both nondemented and demented older adults, was utilized for this study. Given its potential for early detection of Alzheimer's dementia, the study is anticipated to enhance clinical decision support systems pertaining to modifiable risk factors

Keywords: Machine Learning, Dementia, Alzheimer, Clinical Decision Support Systems, Augmented Intelligence.

NÖROLOJİK GİZEMLERİ AYDINLATMAK: ALZHEİMER HASTALIĞININ ERKEN TESPİTİNDE YAPAY ÖĞRENME YAKLAŞIMLARI

Öz

Yaşla birlikte prevalansı artan demans, birden fazla kognitif alanda bozulma ile seyreden ve sonunda günlük yaşamı etkileyen bir klinik sendromdur. Buna bağlı olarak da bireylerde bağımsızlık kaybı, engellilik, bakıma ihtiyaç duyma hatta suça meyil/güvenlik dışı davranışlar ortaya çıkmakta ve nihayetinde hastalık sıklıkla ölümle sonuçlanmaktadır. Özellikle nörodejeneratif hastalıklar bağlamında, suça meyilli davranışlar farklı demans türleriyle ilişkilendirilmektedir. Araştırmalar, demans hastalarında suç teşkil eden ve sosyal açıdan uygunsuz davranışlara rastlanıldığını hatta bunların bazen demans hastalığının ilk belirtisi olduğunu ortaya koymaktadır. Tüm demans vakalarının %60-80'ini Alzheimer (Alzaymur) Hastalığı (AH) oluşturmakta, 65 yaşından sonra olguların görülme sıklığı her beş yılda bir ikiye katlanmaktadır. Bu kapsamda Alzheimer hastalığının erken tespiti sağlık verilerinin erişilebilirliği ve veri işleme maliyetlerinin azalmasıyla artık mümkün hâle gelmektedir. Çalışmanın amacı, farklı yapay öğrenme yöntemleri kullanarak bireyleri Alzheimer ve sağlıklı olarak sınıflandırmaktır. Bu amaçla "OASIS-2: Longitudinal MRI Data" veri seti kullanılmıştır. Çalışmanın Alzheimer demansını erken tespit etme potansiyeli taşıdığı düşünüldüğünden değiştirilebilir risk faktörleri üzerinde klinik karar destek sistemlerine katkıda bulunması beklenmektedir.

Anahtar Kelimeler: Yapay Öğrenme, Demans, Alzheimer, Klinik Karar Destek Sistemleri, Artırılmış Zekâ.

INTRODUCTION

Currently, Alzheimer's disease (AD) represents a significant share of progressive illnesses. The prevalence of AD is progressively rising in accordance with the demographic phenomenon of population aging. Based on data released by the Turkish Statistical Institute (2023), the population of individuals aged 65 and over, categorized as the elderly population, experienced a 22.6% growth over the past five years, rising from 6,895,385 individuals in 2017 to 8,451,669 individuals in 2022. From 2017 to 2022, the proportion of the geriatric population relative to the total population increased from 8.5% to 9.9%. The survey's death and cause of death results reveal that the mortality rate due to AD among the elderly was 13,642 in 2017 and 12,239 in 2021. The mortality rate attributed to AD among the elderly decreased from 4.6% in 2017 to 3.0% in 2021. The World Health Organization (2023) reports that there are already over 55 million individuals globally who are afflicted with dementia, and roughly 10 million new cases emerge every year. AD is the predominant kind of dementia, comprising around 60-80% of all cases.

Neurocognitive disorders like AD can be the subject of forensic psychiatry due to their potential to impair a person's functionality and the problems caused by judgment errors (Petersen, 2007, p.15). In other words, AD is a severe disorder that impacts cognitive function and might result in criminal behavior in certain cases. Studies indicate that patients/cases diagnosed with frontotemporal dementia (FTD) and AD may display criminal conduct, with as many as 57% of FTD patients having engaged in illegal activities (Darby et al., 2017, p. 601). Criminal behavior includes minor offenses like stealing or traffic violations, as well as serious crimes like physical abuse, sexual offenses, or murder. When evaluating elderly first-time offenders for criminal behavior, it is crucial to consider the potential presence of neurodegenerative illnesses during the commission of the crime (Prent et al., 2023, p. 181). In this context, early detection of the Alzheimer's disease is of critical importance both in the forensic and clinical aspects.

It is observed that especially Alzheimer's risk factors are identified and solutions are developed for the early diagnosis of the AD progress by leveraging classification models in the literature (Yiğit & Işık, 2018; Buyrukoğlu, 2021;

Sertkaya & Ergen, 2022). The aim of this study is to provide a basis for machine learning-based clinical decision support systems that can classify patients as Alzheimer's or healthy based on the data obtained from the OASIS-2 dataset. For this purpose, algorithms such as Logistic Regression, Naive Bayes, LightGBM and Random Forest, which have proven to be successful especially in classification problems in health datasets, were used. The results are evaluated according to different performance metrics. Remarkable outcomes in the classification of AD were observed with the models utilized in the study. As the study suggests, an approach for automatic detection of Alzheimer's type dementia with machine learning-based methods can contribute to the literature when the diagnosis, treatment and cost of AD are taken into account.

The study consists of four main sections. The first section reviews the relevant literature. The second section covers the machine learning process from the acquisition of the dataset to the presentation of the results. The third section reports the findings and the last section includes conclusions and recommendations.

1. RELATED WORK

The application of machine learning methods for diagnosing AD has been evolving in parallel with advancements in image processing technology, as evidenced in the literature. Furthermore, it has been noted that conventional and traditional machine learning techniques yield efficient responses for challenges related to the classification of AD. Table 1 provides a concise overview of the part of the existing research on this subject.

Table-1. Related Literature

Data Type	Data	Models	Best Model	Reference
Audio	Carolina Conversations Collection (Pope & Davis, 2011). 21 patients	Logistic Regression (LR), Naive Bayes (NB), C4.5, AdaBoost, SVM, Random Forest (RF)	AdaBoost: 86.5% 81.1% (overall accuracy)	Luz et al. (2018)
Image + Clinic	OASIS dataset & demographic and clinical information from 416 right-handed people aged 18 to 96 years	ANN, LR, k-Nearest Neighbor (k-NN), Decision Tree (DT)	ANN: 0.832 (AUC)	Yiğit & Işık (2018)
Image (rs-fMRI)	138 data with 4 classes (ADNI)	ResNet-18	97.92% (accuracy)	Ramzan et al. (2019)
Text	Pitt Corpus from DementiaBank dataset- 98 AD & 98 healthy controls	SVM, RF, k-NN,	SVM: 81.1% (acc)	Guerrero-Cristancho et al. (2019)
Audio	222 healthy controls - 255 AD patients (DementiaBank)	LR, SVM, ANN, CNN, RNN	84.73% (acc)	Pan et al.(2020)
Clinic	61 aMCI, 60 AD & 60 healthy controls	ANN, LR	ANN: 0.814 (AUC)	Hemrungronjn et al. (2021)
Clinic	229 healthy controls, 402 Mild Cognitive Impairment (MCI) &188 AD	RF, ANN, SVM, NB	RF: 91% (acc)	Buyrukoğlu (2021)

Image (MR)	6400 data with 4 classes	VGG-16, VGG-19, ResNet-18, ResNet-34, ResNet-50, ResNet101	ResNet-101: 99,70% (acc)	Subramoniam et al. (2022)
Image (MR)	6400 data	CNN, SVM	100% (acc)	Karabay& Çavaş (2022)
Image(MR)	464 AD & 863 healthy controls (ADNI)	YOLOv4	66% (F1 score)	Aydın et al. (2022)
Image + Clinic	190 healthy, 146 AD, 37 initially healthy then dementia group	DT, GBM, XGBoost, LGBost, CatBoost, RF	GBM: 91.55% (Overall acc)	Sertkaya & Ergen (2022)
Image(MR)	2561 AD, 906 Parkinson's and 3010 healthy controls	ResNet-18, VGG-16, ConvNext	ConvNext: 99.7% (acc)	Yüzgeç & Talo (2023)

As can be seen in Table 1, the utilization of machine learning techniques for detecting AD has gained significant prominence in the literature. The growing availability of datasets accessible to researchers, such as ADNI (Alzheimer's Disease Neuroimaging Initiative), OASIS (Open Access Series of Imaging Studies), COBRE, and FBIRNX, makes a substantial contribution to the body of literature. The influence of real and patient-derived datasets on the outcomes of studies in certain domains like AD is currently of utmost importance.

2. MATERIAL and METHOD

2.1. Dataset

The study utilized the OASIS dataset, a publicly available dataset frequently used in Alzheimer's disease research (Marcus et al., 2010). "Longitudinal MRI data" which is part of the OASIS dataset were used. The dataset can also be obtained from the Kaggle platform¹. This dataset has a longitudinal sample of 150 participants, ranging in age from 60 to 96. For a total of 373 imaging sessions, each individual underwent two or more scans spaced at least a year apart.

There are three or four separate T1-weighted MRI scans for each person, acquired during a single scan session. Men and women are among the subjects; they are all right-handed. A total of 72 participants were classified as 'Nondemented' for the whole duration of the study. In the dataset, 64 individuals were classified as 'Demented' on their initial visits and maintained this classification throughout the whole study. At the time of their first visit, 14 participants were classified as 'Nondemented', but later, on a subsequent visit, they were identified as 'Demented'. These items belong to the 'Converted' classification. The dataset's features are displayed in Table 2.

Table-2. Features of the Dataset

Feature	Description
M/F	Gender (Female=0, Male=1)
Age	Patients' Age
EDUC	Education Years
SES	Status (Socioeconomic)
MMSE	Mini Mental State Examination Test Scores
CDR	Clinical Dementia Rating
eTIV	Total Intracranial Volume (Estimated)
nWBV	Normalize Whole Brain Volume
ASF	Atlas Scaling Factor
Group (Target Variable)	Nondemented = 0, Demented =1

Following acquiring the data presented in Table 2, the exploratory data analysis (EDA) step was proceeded. During this phase, many visualization techniques were employed on the dataset to facilitate data interpretation prior to analysis. The following part delves into the phase of exploratory data analysis.

¹ <https://www.kaggle.com/datasets/sabikunmonisha/oasis-longitudinal>

2.2. Exploratory Data Analysis (EDA)

During the exploratory data analysis phase, the status of individuals with AD was initially categorized based on their gender. In other words, the figures representing the “Demented” and “Nondemented” individuals were depicted in relation to their gender.

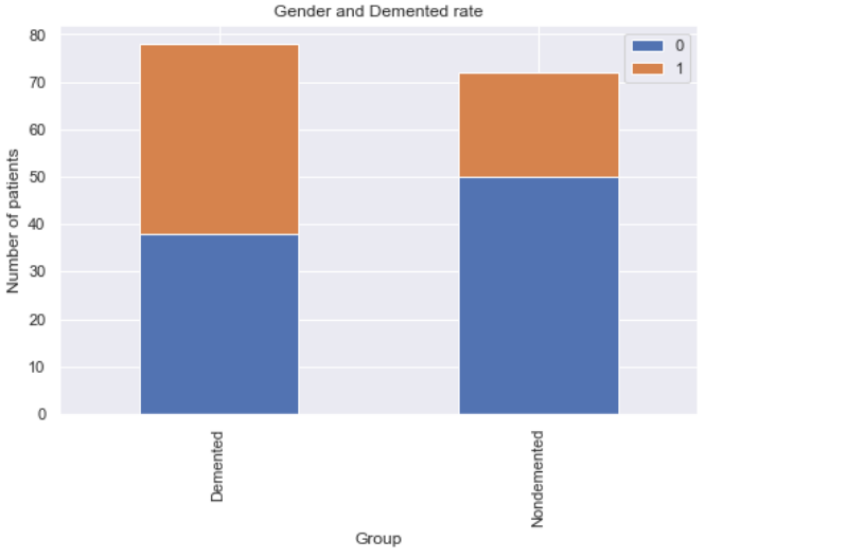


Figure-1. Number of patients in terms of Gender

Figure-1. illustrates a higher prevalence of dementia among men compared to women.

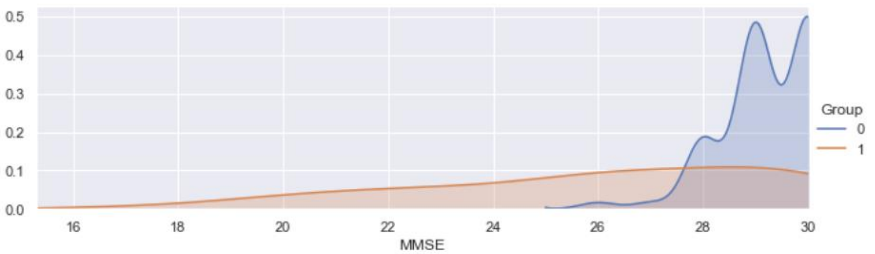


Figure-2. MMSE Scores for Each Group

Figure-2 illustrates MMSE (A widely used 30-point screening test utilized for the identification of dementia, delirium, and other cognitive problems) scores

categorized by group. The graphic also illustrates that the Nondemented group obtained significantly higher MMSE scores compared to the Demented group.

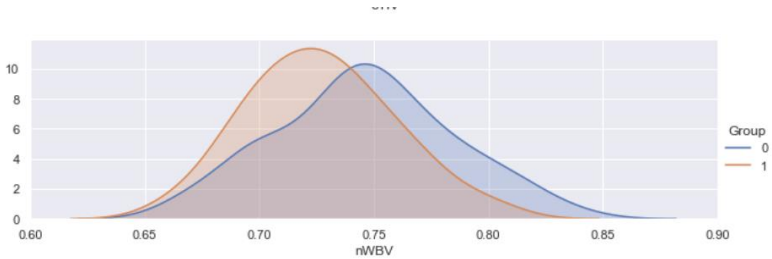


Figure-3. Normalize Whole Brain Volume for Each Group

When each group is examined in relation to the Normalize Whole Brain Volume as seen Figure-3, data suggests that the Nondemented group exhibits a higher brain volume ratio in comparison to the Demented group. It is evident that these disorders lead to a reduction in brain tissue.

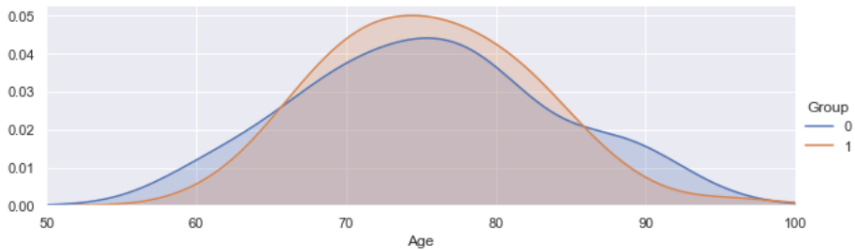


Figure-4. Age for Each Group

Based on the analysis of Figure 4, it is evident that the Demented patient group has a greater proportion of individuals aged 70-80 years compared to the nondemented patients.

In summary, during the exploratory data analysis phase, an initial examination of the dataset was conducted with the aim of comprehending its contents. This established the groundwork for the preprocessing and analysis stage. The following stage focuses on the steps involved in the data preprocessing phase.

2.3. Data Preprocessing

In “Data Preprocessing” phase, various feature engineering techniques were applied. Initially, an evaluation was conducted to identify any missing values in each feature. Subsequently, a decision was made regarding the appropriate technique to address these missing values.

Subsequently, the dataset performed scaling and normalization to account for the varying ranges of its features. A training set including 70% of the data, and a test set comprising 30%. 5-fold cross-validation was utilized for models that necessitated hyperparameter tuning.

2.4. Modeling

During the Modeling phase, the preferred classification models for health datasets were Logistic Regression, Naive Bayes, Random Forest and LightGBM. These models are known for their great performance in classification tasks. The machine learning models used are described in Table-3.

Table-3. Model Descriptions

Model	Description
Logistic Regression (LR)	Logistic regression is employed to analyze the association between categorical variables. Logistic regression is primarily characterized by the fact that the dependent variable is binary or categorical, setting it apart from linear regression. It has a widespread use in the domain of health (Bircan, 2010: p. 187).
Naive Bayes (NB)	The Naive Bayes method is a supervised machine learning technique that relies on conditional probability and applies Bayes' theorem (Vangara et al., 2020). By presuming that the attributes of the input data are conditionally independent with respect to the class, this methodology empowers the algorithm to generate predictions that are both lightning-fast and accurate.
Random Forest (RF)	As an instance of ensemble learning classifier, a random forest (RF) classifier generates a number of decision trees from a subset of training samples and variables that are selected at random. The Random Forest classifier employs a collection of Classification and Regression Trees (CARTs) to generate predictions (Breiman, 2001). Trees are created by randomly selecting a portion of the training samples using the bagging approach, which allows for replacement. This indicates that certain samples may be chosen multiple times, while others may not be chosen at all (Belgiu and Drȧgut, 2016: 25).

LightGBM	First proposed LightGBM in 2017 by Ke, the algorithm has provided a basis of various researches. LightGBM is based on adaptive gradient boosting model, which is a kind of gradient boosting trees. To enhance the model's computational power and prediction accuracy, LightGBM uses various algorithms. The logic behind LightGBM is to begin by decomposing the continuous feature values into M integers, followed by the construction of an M-width histogram.
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Hyperparameter optimization was also performed for LightGBM, Logistic Regression and Random Forest models. As a result of its robustness and exhaustive search capabilities, GridSearchCV method is applied for hyperparameter optimization. Table 4 shows the hyperparameters applied for these models. The best performing parameters was implemented (ie, **bolded** in Table 4).

Table-4. Hyperparameters for LightGBM, LR and RF

Model	Hyperparameters
LightGBM	"n_estimators":[100,500,1000,2000], "subsample":[0.6,0.8,1.0], "max_depth":[3,4,5,6], "learning_rate":[0.1,0.01,0.02,0.05], "min_child_samples":[5,10,20]
LR	for c in [0.001, 0.1, 1, 10, 100]
RF	for M in range(2, 15, 2): # combines M trees: 2 for d in range (1, 9): # maximum number of features considered at each split : 5 for m in range(1, 9): # maximum depth of the tree : 7

3. FINDINGS

Regarding the performance of the classification models, the “accuracy” metric is initially evaluated. However, accuracy disregards the specific types of errors made by the model due to its construction. The main emphasis is on achieving correctness in a comprehensive manner. In order to assess the model's performance in accurately recognizing and predicting True Positives, it is more appropriate to quantify precision that is defined as “a metric that quantifies the accuracy of a model by calculating the proportion of true predictions it makes”, recall is defined as “proportion of data samples properly classified by a machine learning model as belonging to a specific/positive class” and F1 Score (harmonic mean of precision and recall). In addition, the confusion matrix providing a concise presentation of how well a machine learning model performs on test data was considered. The models are listed in Table 5 based on their accuracy.

Table-5. Performance Metrics of the Models (Accuracy)

Model	Accuracy
LightGBM	0.755
LR	0.763
NB	0.755
RF	0.868

Precision and Recall metrics for each class are listed in Table 6 (Nondemented = 0, Demented =1)

Table-6. Performance Metrics of the Models (Precision/Recall/F1 Score)

Model	Class	Precision	Recall	F1 Score
LightGBM	0	0.69	0.91	0.78
	1	0.88	0.61	0.72
LR	0	0.67	0.73	0.70
	1	0.71	0.65	0.68
NB	0	0.69	0.91	0.78
	1	0.88	0.61	0.72
RF	0	0.75	0.82	0.78
	1	0.81	0.74	0.77

The confusion matrix is a frequently-used tool for evaluating the effectiveness of classification algorithms that seek to predict a categorical class for each input sample. The matrix shows the different results generated by the model when applied to the test data, including true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). Table 7 displays the confusion matrix that arises from all the models.

Table-7. Confusion matrix

Model	Confusion Matrix									
LightGBM	<table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td>0</td> <td>20</td> <td>2</td> </tr> <tr> <td>1</td> <td>9</td> <td>14</td> </tr> <tr> <td></td> <td>0</td> <td>1</td> </tr> </table>	0	20	2	1	9	14		0	1
0	20	2								
1	9	14								
	0	1								
LR	<table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td>0</td> <td>16</td> <td>6</td> </tr> <tr> <td>1</td> <td>8</td> <td>15</td> </tr> <tr> <td></td> <td>0</td> <td>1</td> </tr> </table>	0	16	6	1	8	15		0	1
0	16	6								
1	8	15								
	0	1								
NB	<table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td>0</td> <td>20</td> <td>2</td> </tr> <tr> <td>1</td> <td>9</td> <td>14</td> </tr> <tr> <td></td> <td>0</td> <td>1</td> </tr> </table>	0	20	2	1	9	14		0	1
0	20	2								
1	9	14								
	0	1								
RF	<table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td>0</td> <td>18</td> <td>4</td> </tr> <tr> <td>1</td> <td>6</td> <td>17</td> </tr> <tr> <td></td> <td>0</td> <td>1</td> </tr> </table>	0	18	4	1	6	17		0	1
0	18	4								
1	6	17								
	0	1								

Upon analyzing the applied models in terms of performance measures, it becomes evident that different models outperform in different metrics. For instance, although the Random Forest model exhibits good accuracy, it can be stated that both the LightGBM and Random Forest models provide reasonably high performance when considering the Recall metric. Given the high cost of false negatives in Alzheimer's dementia detection, particularly in terms of patient care and preventive measures in dementia research, it is appropriate to prioritize the recall metric.

CONCLUSION

The healthcare ecosystem encompasses a wide range of stakeholders, including patients and their families, clinical care teams, public health program directors, hospital executives, and researchers. Patients are a vital component of this ecosystem. Patients consistently produce data and transmit it to various applications. The field of medicine is making significant strides in providing personalized care, which is informed by an evidence-based approach to decision-making. In order to make treatment decisions that are based on the evidence at hand, it is crucial for both patients and healthcare professionals to have access to all the clinical data that is accessible.

The application of machine learning techniques for the early detection of neurodegenerative disorders, which advance quickly and pose a comparable threat to cancer, is currently capturing the interest of academics and healthcare professionals working in this field of study. Alzheimer's disease (AD) is the predominant form of dementia globally and in our country. It is characterized by a gradual and mild onset, progressive symptoms, and ultimately requires full-time care (Işık, 2009: p. 90). Within the context of the research, classification-based machine learning techniques were used to determine the patient's status as either healthy or having Alzheimer's disease. This was performed using the Longitudinal MRI data from the OASIS-2 dataset. After conducting an experiment using Logistic Regression, Naive Bayes, LightGBM, and Random Forest algorithms, it was found that the Random Forest model achieved the highest accuracy rate, while the LightGBM model achieved the highest recall rate.

The results obtained within the scope of the study should not be considered completely independent of healthcare professionals. As Sadiku and Musa (2021) suggest, combining human intelligence and artificial intelligence as "Augmented Intelligence" focuses on the supporting or auxiliary role for algorithms and emphasizes that these technologies are designed to enrich human brain data processing, cognition, perception and decision-making mechanism rather than replace humans. In further studies, it is planned to repeat the analysis and compare the results after increasing both the number and variety of data. In addition, applying machine learning methods in crime prevention studies that

emphasize the social dimension of AD in further studies will shed light on different dimensions of neurodegenerative diseases.

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