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AlzDiagnostics: A Mobile Alzheimer's Diagnosis Solution

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Abstract

Alzheimer's disease (AD) is a neurodegenerative disorder that progressively affects cognitive function and which is the leading cause of dementia. Early diagnosis of AD is critical as it allows for timely intervention, and improves the individual's quality of life, having the potential to reduce the burden of the disease on individuals, families, and society. This study presents AlzDiagnostics, a mobile application whose primary goal is to offer a user-friendly tool for the early diagnosis of AD, integrating established clinical tools, state-of-the-art machine learning techniques, and multiple diagnostic approaches. Furthermore, the application seeks to assess the effectiveness and accuracy of the Mini-Mental State Examination (MMSE) test, machine learning models trained on MRI images, as well as ones trained on clinical data, evaluating their contributions to enhance early diagnosis. Choosing the best classification models for the diagnosis module involved the conduct of numerous classification experiments on an extensive MRI dataset obtained from Kaggle, which consisted of 6400 MRI images from different sources including websites, hospitals, and public repositories. These experiments encompassed the exploration of various parameter configurations, leading to the identification of a top-performing model that exhibited an accuracy rate of 98%. Additionally, extensive experiments were conducted on clinical data retrieved from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which comprised entries from 2425 patients. By incorporating features such as gender, marital status, education, race, and MMSE scores, a second machine learning model was developed, yielding an accuracy level of 76%.

Keywords: Alzheimer's Disease Diagnosis; Mild Cognitive Impairment; Mobile Application; Machine Learning; Cognitive Assessment; Neuroimaging

1. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a gradual decline in cognitive function, particularly affecting memory, thinking, and behavior. It is the leading cause of dementia, accounting for an estimated

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60% to 80% of the cases [4]. The lifespan of individuals suffering from this condition can fluctuate widely, depending on a range of factors including the age of onset, overall health, and the progression of the disease. Those with AD can survive for a period of more than 20 years after diagnosis [5]. The prolonged duration of AD contributes significantly to the financial and social costs of the illness because much of the time is spent in a state of significant disability and dependence. Taking these into account, early diagnosis of AD represents a subject of great scientific interest, as it allows for timely initiations of treatments that can improve the individual's quality of life. Mobile applications developed for diagnosing AD provide a convenient and accessible means of early diagnosis, allowing for timely intervention, with the potential of improving cost-effectiveness. In particular, AlzDiagnostics is designed with the objective of offering a user-friendly tool for the early diagnosis of AD. The application utilizes a comprehensive approach to diagnosis, incorporating the MMSE test, as well as machine learning-based methods that leverage either MRI images or clinical data. However, it is important to note that any results should be followed up with professional health support.

1.1. Related Work

Zorluoglu et al. [37] proposed a mobile application designed for the cognitive screening of dementia, by employing several cognitive tests, including MMSE and the Clock Drawing Test (CDT) [26]. As opposed to this solution, AlzDiagnostics provides support for diagnosis based also on neuroimaging, by employing artificial intelligence approaches, which can contribute to the more accurate and reliable diagnosis of AD. The authors report promising results in testing the application on a sample of eight elderly individuals. The MMSE app [43] is a digital version of the MMSE test, which was released on the Google Play store in 2016. On completion of the questionnaire, the user is assigned a score of up to 30 points, based on the provided answers. The main aim of the application is to assist users in evaluating their cognitive health and to advise them to seek additional medical assistance and support if needed.

Nirjon et al. [28] describe the development and testing of MOBI-COG, a mobile application that aims to provide complete automation of the dementia screening test called the Mini-Cog test [7]. The application stores the history of the test results, so they can be shared with the caregivers for a better understanding of the patient's condition. Another mobile application that allows users to share the test results with a healthcare professional, rather than generating a score itself is BrainCheck [14]. This is supposed to be completed both by the evaluated subject and by a close informant of the person being assessed. It involves a CDT and seven questions derived from the 7-item version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [8]. According to [14], it proved to have a sensitivity of 97.4% and specificity of 81.6% in identifying cases of dementia and MCI.

CogniDecline [47] is another mobile application, which aims to provide early detection of dementia, but based on changes in mobile phone usage patterns. The authors suggest that changes in mobile phone usage could represent a useful indicator of cognitive decline. However, this study has two main limitations. The first one is that the application was tested on a small group of only 13 participants, which implies the need for further testing with larger populations. The second limitation is represented by the ethical considerations involved in collecting and analyzing personal data.

2. Proposed Solution: AlzDiagnostics

AlzDiagnostics has a mission to raise awareness about the crucial importance of early detection of Alzheimer's disease. It strives to guide users through the process of conducting cognitive tests to assess whether they are experiencing mild cognitive impairment (MCI) or AD symptoms. Furthermore, AlzDiagnostics attempts to identify anomalies in MRI images collected from users by employing a machine learning model. These anomalies can be strong indicators of the onset and evolution of MCI, respectively AD, therefore contributing to the early detection of this condition. Early diagnosis enables patients, according to [36], to access timely and appropriate treatment and support services, which can help them effectively manage their symptoms and enhance their overall quality of life. In a study conducted by Rasmussen et al. [13], a US claims database was analyzed to investigate the outcomes of treatment for individuals aged 65 to 100 who were newly diagnosed with Alzheimer's disease. The results showed that those who received treatment had higher rates of survival and a 20% reduced likelihood of institutionalization, even after adjusting for other medical conditions.

The proposed solution enables users to monitor their health status continuously using the following methods: (1) *Firstly*, they can conduct an MMSE test. This test was first proposed by Marshal F. Folstein in 1975 [17] as a brief screening measure for cognitive impairment. If the results indicate a possible cognitive decline, a notification is displayed on the patient's screen. Moreover, the results of the tests are saved and can be accessed as a historical record to monitor progress over time. (2) *Secondly*, the mobile application provides users with the ability to submit their own MRI scans for evaluation. The evaluation process involves utilizing a machine learning model, which has been trained on a larger dataset incorporating both AD and cognitively normal (CN) patients. (3) *Lastly*, the mobile application employs an additional machine learning model, which has the capability to generate a potential diagnosis, by utilizing both the MMSE test score, along with patient-specific information, such as age, marital status, and ethnicity. Upon receiving an AD diagnosis from any of the diagnosis modules, the application generates a notification with a displayed disclaimer, explicitly stating that the results obtained should not be regarded as a definitive medical diagnosis. The purpose of this measure is to highlight the importance of seeking a comprehensive evaluation from a qualified healthcare professional to ensure an accurate assessment.

2.1. Architecture

AlzDiagnostics is designed to offer users an intuitive and user-friendly experience in the diagnosis of Alzheimer's disease. The application's *back-end component* assumes responsibility for rendering essential services, including data persistence, web services, and data analysis through artificial intelligence models. As a critical element, this component plays a vital role in the product's overall functionality, allowing for the delivery of precise and dependable information pertaining to the cognitive health of users. *The front-end component* of the mobile application represents the primary interface with which users engage. It encompasses a straightforward and user-friendly design that enables individuals of all technical backgrounds to access the solution's functionalities with ease and efficiency, as depicted in Figure 1.

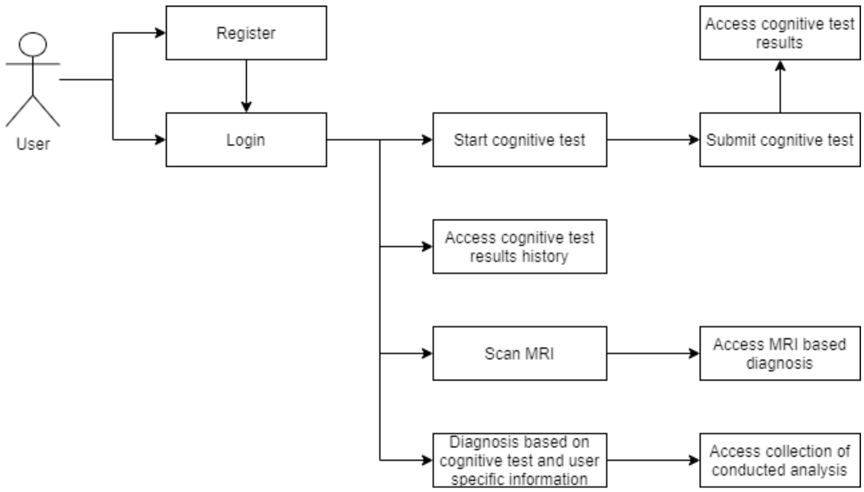

Fig. 1. Main Use Cases of the Application

2.1.1. Authentication Module

The application includes an authentication module. Therefore, any patient can create a user account and log in to view their personal data in the application. It is important to note that when creating the account, the user must provide, in addition to username/email address and password, personal information such as gender, marital status, education, and race. All fields are mandatory to be completed because the corresponding information is further fed to the machine learning model, along with the cognitive test result, in order to provide an accurate diagnosis.

2.1.2. Cognitive Test Evaluation Module

An important diagnosis component is the MMSE cognitive test. The user receives a set of questions to which they must provide answers, as depicted in Figure 2. Further elaboration on this topic is expounded upon in 2.4.1.

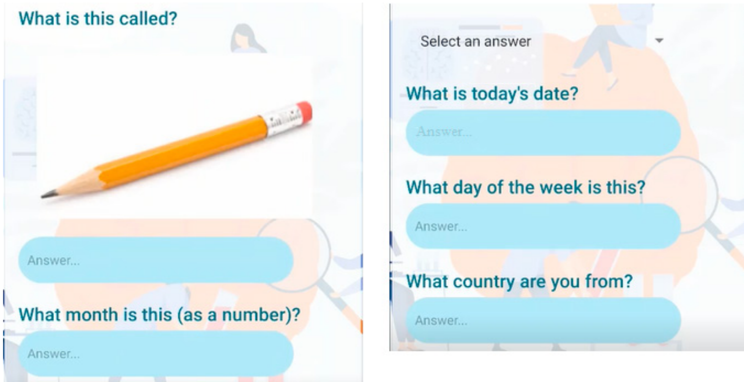

Fig. 2. Examples of Questions from the MMSE Cognitive Test

The user's performance in the MMSE cognitive test is assessed based on the number of correct answers provided, resulting in a score of up to 30 points, which is then recorded in their personal profile. Additionally, patients have the ability to access a record of their previous test results in order to monitor any cognitive decline.

2.1.3. MRI Evaluation Module

This diagnosis component offers the capability to perform scanning and analysis of MRI through the utilization of a pre-trained machine learning model. To initiate analysis, the user is required to scan the medical image (MRI) using their phone camera and transmit it via the application to the server. Once the medical image is evaluated by the model, the outcome is returned to the user, as depicted in Figure 3. Similar to the cognitive test results, the output of the MRI evaluation is also saved in the database, to be retrievable as a historical record.

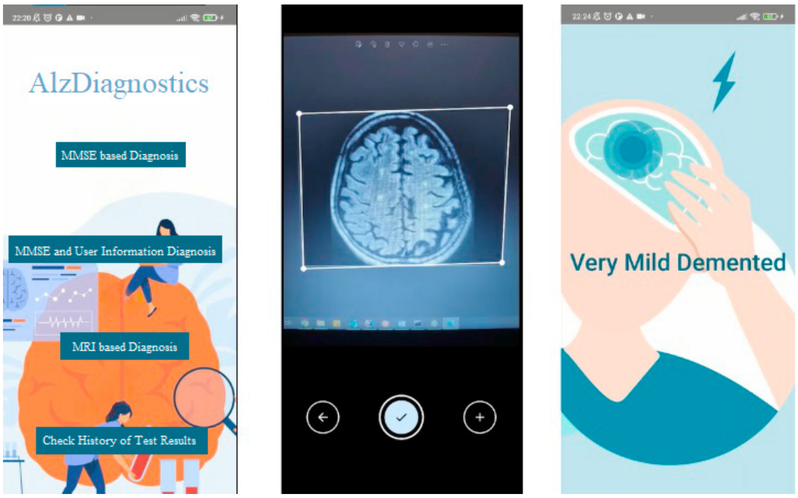

Fig. 3. User Experience for the Flow of Submitting and Analyzing an MRI

2.1.4. Aggregated Data Evaluation Module

The diagnosis of a user can be ascertained by utilizing aggregated data, which includes two data points, i.e., the outcome of the MMSE cognitive test, and personalized user information such as gender, marital status, education, and race, which were originally provided during the account creation process. This data is subsequently fed into a machine learning model, which was trained on a larger set of data containing the aforementioned features.

2.2. Application Design

The subsequent section outlines the key components of the mobile application, from the application design point of view, namely the front-end and the back-end modules.

2.2.1. Front-End Component

The user interface is the component of the mobile application that displays the data and the functionalities described in 2.1 to the user, enabling user interactions. This component only sends requests to the back-end component, which receives the requests and is responsible for processing the tasks, performing data processing, storage, and retrieval.

2.2.2. Back-End Component

Specifically, the main API of the application performs the following functionalities: (1) It features an authentication module that facilitates the creation of user accounts and validates user authentication. (2) It generates an MMSE test and automatically evaluates users' responses. This evaluation is based on the standardized scoring system of the MMSE. (3) It receives user-specific information, including data provided during account creation and potential MRI scans uploaded by the user.

To enhance scalability and system maintenance, two additional web services have been used within the back-end component: (1) The first one serves the function of receiving MRI data from the main API, subsequently providing relevant results to the user with the help of a machine-learning model. This service operates as a mediator between the user and the main API, allowing for data exchange and enhancing the overall efficiency of the application. (2) The second service is tasked with aggregating and processing user data, including personal information and results from cognitive tests. Based on this data and by leveraging another machine learning model, the application provides insights into the cognitive functions of the user.

Finally, the user-specific data, the MMSE test results, as well as the MRI evaluation results are stored in a database to ensure data persistence. The database provides access to user data only to the microservices, while also maintaining security by hashing passwords and avoiding transmission of user-specific data to the external client (front-end mobile application). A clearer illustration of how the components interact with one another is presented in Figure 4.

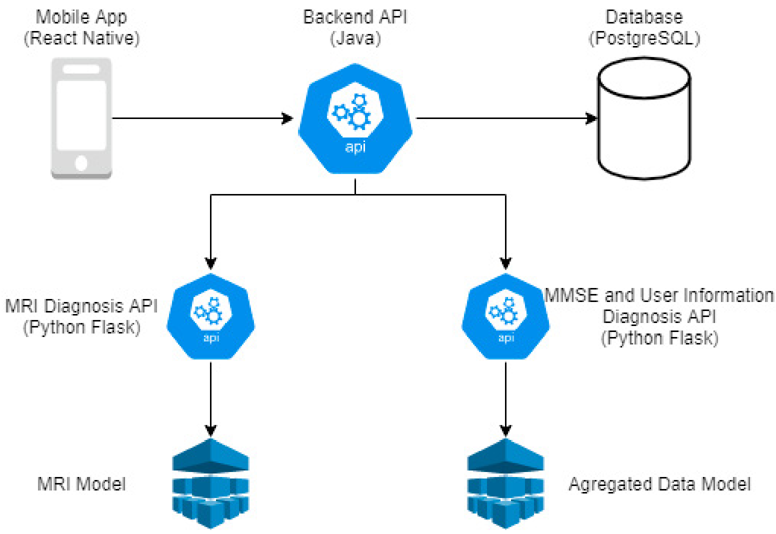

Fig. 4. AlzDiagnostics Back-End Design

2.3. Implementation Details

The *front-end component* of the mobile application was developed using standard web application technologies, including HTML, CSS, and JS. In addition to these, the most important utilized technology was React Native [27], which is a framework for developing mobile applications for both Android and iOS. It was used to build the user interface and handle JavaScript code, which makes calls to the main API.

The *back-end* consists of several components, with the central component being a Java-based API developed using Java Enterprise [32] technologies. This API allows the front-end to access different endpoints as needed via a web service. In order to develop a highly scalable application that can adapt to changing requirements, a dependency injection design was employed. Additionally, the application needs to be secure, which is why several security components from Java EE were used. Among these, it is worth mentioning the use of JSON Web Tokens (JWT) [20]. A JWT is a compact, URL-safe means of securely transmitting data as a JSON object, used for authentication and authorization purposes. It typically contains a digitally signed payload that can be verified and trusted. Additionally, for faster code development, Lombok [25] was used, which is a library that provides annotations to automatically generate boilerplate code, such as getters, setters, and constructors, making the code shorter and more concise. Also, Log4J [3] was used to provide logs through which the system status can be monitored. This library is a logging utility that allows developers to easily log messages from their applications to various output targets, such as files, databases, or the console, to facilitate troubleshooting and debugging.

For storing the data, a *relational database*, Postgres [35], was used. It interacts only with the aforementioned main API using Java Persistence API (JPA) [31]. This is a specification that provides an Object-Relational Mapping (ORM) framework for mapping objects to relational database tables, allowing developers to interact with databases using Java code in a seamless and convenient manner. Thus, by using an ORM, there is no need to write SQL code, while also providing a more straightforward approach to entity and data management.

To aid in the diagnosis, the application leveraged *two ML models* that were developed using Python programming language. Additionally, for the development of these models, there were used Pandas [33] and Numpy [29] for the data filtering part and libraries such as TensorFlow [44] and Keras [22] for the training part. Finally, the Flask [16] web framework was used to expose them as web services that can be used by the main API.

To ensure the proper functionality of the main API, *functional tests* were developed and executed, resulting in a Java code coverage of at least 80%. In addition to functional testing, non-functional testing was employed, specifically, load testing and stress testing. This was done using Jmeter [2], which is an open-source software tool used for load testing, performance testing, and functional testing of web applications. It allows developers to simulate and measure the performance of their applications under different conditions. This tool was used for verifying that the system can support a high number of users and can withstand periods of high usage and traffic.

In addition to these, other tools were used in the development process, such as: (1) SonarQube [40], which ensured that the tested code is clean, bug-free, and properly tested, (2) pgAdmin4 [34], which was used for managing information in the database, (3) Android Studio [12], which was used to simulate the mobile application environment, (4) IntelliJ [9], PyCharm [10] and Visual Studio Code [42], which facilitated fast and organized code development.

2.4. AD Diagnosis Module

MMSE based Diagnosis - One of the primary features of the application is the MMSE diagnosis module that allows the users to conduct regularly a MMSE test. The application maintains a history of test results to enable continuous monitoring of the patient's progress. *MRI-based Diagnosis* - The categorization process of medical images is conducted through the utilization of a machine learning model that has been trained on a vast collection of medical images. The selection of this model was based on a series of experiments that are comprehensively expounded upon in 2.4.2. *MMSE and User Information Diagnosis* - The third diagnosis solution provided by the application consists in employing data from two data sources, specifically the result of the cognitive tests and the personal user information: gender, marital status, education, and race. This data is further used as input for the machine learning model, which provides the diagnostic result.

2.4.1. Evaluated Biomarkers

In order to provide a diagnosis through each of the aforementioned methods, the following biomarkers were considered: cognitive tests (MMSE), neuroimaging biomarkers (MRI images), and personal background variables of the participant (such as gender, marital status, education, and race). Stoleru et al. [41] conducted a comprehensive analysis of these biomarkers, which have been employed in state-of-the-art research to construct highly accurate diagnostic models for AD, highlighting their respective advantages and limitations. Each of the aforementioned biomarkers is further detailed.

Neuropsychological Tests - The neuropsychological assessment employed the use of the MMSE test. This is a widely used tool for assessing cognitive functions, including memory, attention, language, and orientation. The user receives a set of either personal or common questions to which they must provide answers, such as *What year is this?*, *What is today's date?*, *What country are you from?*, *What city are you from?*. The test further comprises a series of basic tasks, the responses to which are evaluated through the mobile application. The following are some examples of such tasks: *Recognition of a pencil from an image*, *Spelling the word "world"*, *Naming three presented objects in their given order*, *Recognition of a given phrase*. The score, which can range up to 30 points, is determined based on the number of correct answers provided.

The diagnostic module of the application which utilizes the MMSE test delivers a response aligned with the thresholds outlined in [13]. According to these established criteria, a score of 25 or above is generally indicative of cognitive functioning within the normal range. If the score is below 24, the result is usually considered to be abnormal, indicating possible cognitive impairment. The MMSE test confers several advantages, including its ease to conduct, short completion time, lack of requirement for specialized personnel, cost-effectiveness, non-invasiveness and widespread availability. The accuracy, sensitivity, and specificity of this test may vary depending on factors such as the characteristics of the population being tested and the chosen cutoff score. Multiple studies have explored its utility as a screening tool for the diagnosis of cognitive decline. According to Kahle-Wrobleski et al. [21], the MMSE demonstrated high diagnostic accuracy in identifying dementia among individuals aged 90 and above, encompassing various age and education groups. The study reported AUC (Area Under the Curve) values ranging from 0.82, the lowest observed in the 97 and older age group with a high school education or less, to 0.98, the highest observed in the 90 to 93 age group with vocational or some college education.

Neuroimaging Biomarkers - MRI is a medical imaging technique that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body. According to [46], the MRI technique is the most used in AD diagnosis due to its high spatial resolution, which allows the difference between two arbitrarily similar but not identical tissues and multiparametric acquisitions to be distinguished. MRI does not involve X-rays or the use of ionizing radiation, it is non-invasive and has no significant adverse health effects.

2.4.2. Methods

Data Collection - Two different datasets were used for training the machine learning models: (1) An Alzheimer MRI Preprocessed Dataset obtained from Kaggle [23] employed for the task of classifying MRI images. It was reportedly compiled from multiple sources, including various websites, hospitals, and public repositories. The dataset consists of 6,400 images and has four classes, respectively: Mild Demented, Moderate Demented, Non-Demented, and Very Mild Demented. (2) Clinical Data obtained from the ADNI dataset [1], which is a subset of data comprised of entries from ADNI1, ADNI2, ADNI3, and ADNIGO. It consists of 16,202 entries collected from 2,425 patients, yielding three primary outcomes: Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), and Normal Cognitive (CN). This dataset contains a wide range of information related to participants in the study, including cognitive assessments (results of cognitive tests such as MMSE) and demographic information, such as age, sex, race, education, and marital status.

Data Preprocessing - (1) Neuroimaging Data - The images were resized into 48×48 pixels. (2) Clinical Data - During the preprocessing step, columns that did not contain personal user data (e.g., the id of the entry, the initial dataset to which the entry belongs), as well as ones containing results of cognitive tests other than MMSE were removed. This resulted in a selection of variables including age, marital status, MMSE score, education level, and gender. The aforementioned variables were used in the training step of the model and are requested from the user upon account creation to provide a more accurate diagnosis.

Machine Learning Models - (1) MRI - An MRI scan is categorized into one of four classes, which comprise three stages of dementia and one class for the absence of dementia. To assess the efficacy of the model, the dataset was partitioned into two distinct subsets, consisting of an 80% training set and a 20% test set, respectively. The MRI classification model utilized in this study was a Convolutional Neural Network (CNN) architecture. The model consists of a rescaling layer, followed by three convolutional layers, with each convolutional layer accompanied by a max pooling layer. Finally, a flattened layer is added, followed by two dense layers. To optimize the model, it was compiled with the Adam optimizer. (2) MMSE and User Information Diagnosis - In order to diagnose user information, a set of demographic variables including gender, marital status, education, race, and the MMSE score are employed. To accomplish this task, a suite of machine learning algorithms, specifically Naive Bayes, Random Forest, and XGBoost, are utilized. These models have been trained to accurately classify input data into three categories, CN, MCI, and AD.

Data Statistics - The dataset comprised of clinical data, which was used for the training of the machine learning model, is presented below, stratified by patients' age, gender, marital status, and level of education. Figure 5 indicates the age range of patients in the dataset, spanning from 55 to 100 years old, with a majority falling between the ages of

70 and 80 years. Advanced age is one of the strongest risk factors for developing AD. While it can occur at any age, the likelihood of developing this condition increases as a person gets older [6, 15, 24, 39].

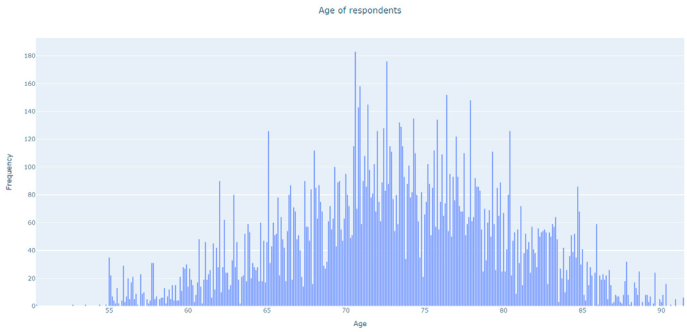

Fig. 5. Distribution of Subjects by Age

Regarding the distribution of patients by gender, there is a slight majority of male subjects in the dataset (the difference is under 9%). Regarding an individual's marital status, there exist five distinct categories, namely married, widowed, divorced, never married, and unknown. The distribution of patients by their marital status is illustrated in Figure 6. It has been observed that this factor can impact one's susceptibility to AD, with a higher risk being observed amongst those who have never been married [18, 19, 38].

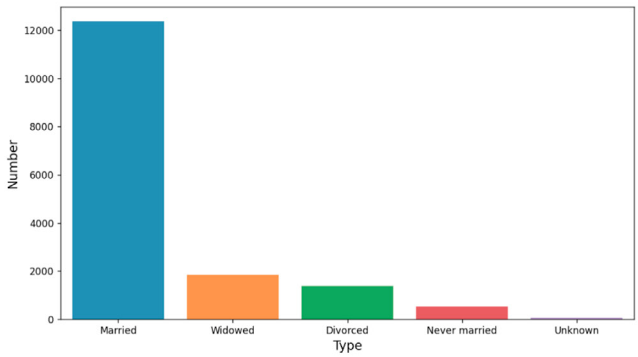

Fig. 6. Distribution of subjects by marital status

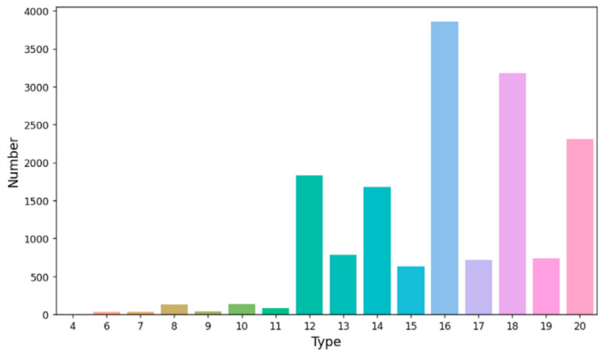

Fig. 7. Distribution of subjects by education

Several studies have established a correlation between lower educational attainment and a heightened susceptibility to dementia. According to Figure 7, a majority number of patients in the dataset have acquired a higher level of education [11, 37, 45].

2.5. Results

For the MRI model, the dataset was split into two subsets, consisting of an 80% training set and a 20% test set. Experiments were conducted by testing different parameter settings such as varying the number of epochs and using multiple optimizers. The model achieved its highest accuracy of 98% after 20 epochs while utilizing the Adam optimizer. Considering its superior performance within the specified configurations, it was selected as the MRI model to integrate within the diagnosis module.

For the clinical data, in order to determine the best machine learning model which would be integrated into the diagnosis module, several experiments have been conducted, employing the following machine learning models: *Naive*

Bayes, Random Forest, and *XGBoost*. These experiments involved multiclass classification, where the machine learning model was trained to classify input data into three categories, namely CN, MCI, and AD. The chosen features for these experiments included gender, marital status, education, race, as well as the MMSE score.

In the case of *Naive Bayes* classification, there were performed experiments with different parameter settings. However, no improvement was achieved beyond a validation accuracy of 61%. Conversely, the *Random Forest* classifier led to a validation accuracy of 72% when providing a diagnosis. The best results were obtained using the *XGBoost* algorithm for the entire set of aforementioned features, i.e. a validation accuracy equal to 76%. The parameters employed for the XGBoost model were determined via a grid search across a predefined parameter space. This search yielded a gamma value of 0, a learning rate of 0.1, and a maximum tree depth of 3. The model was further assessed on OASIS (Open Access Series Of Imaging Studies) [30], an independent dataset, where it exhibited a test accuracy equal to 76%. Consequently, the XGBoost model, trained on the complete set of aforementioned features (gender, marital status, education, race, and MMSE score), was selected as the second model to integrate into the diagnosis module.

3. Conclusion and Future Work

AlzDiagnostics provides a convenient and accessible way for users to evaluate their neurological health and detect Alzheimer's disease using cognitive tests, MRI images, and machine learning approaches. The application has the potential to enhance the early detection of Alzheimer's disease by incorporating a diagnosis module encompassing multiple classification approaches. These approaches include utilizing the MMSE score for diagnosis, employing a machine learning model trained on MRI images, which demonstrated a high validation accuracy of 98% on a Kaggle dataset, and utilizing a separate machine learning model trained on clinical data, achieving a validation accuracy of 76% when evaluated on both the ADNI dataset and an independent test dataset. An early diagnosis can improve patient outcomes, as it allows for the prompt initiation of appropriate medical interventions and treatments, slowing cognitive decline and therefore, reducing the burden on the healthcare system. AlzDiagnostics allows users to conduct cognitive tests anytime, anywhere, and at the same time, as opposed to other diagnostic tools, it provides support for diagnosing AD based on MRI images. This is done by employing a machine learning model with 98% validation accuracy. However, these results should be further communicated to qualified healthcare professionals.

There are several areas for future work on this application, including improving the machine learning algorithms, integrating it with other data sources, enhancing the user experience, and expanding it to new platforms. By addressing these areas, the solution has the potential to become an even more powerful tool for detecting AD.

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