Exploring Classification in Open and Closed Eyes EEG Data for People with Cognitive Disorders

Ioanna Chouvarda[1][a], Lampros Mpaltadoros[1][b], Ioanna Boutziona[1], George Nikolaos Tsakonas[1], Magda Tsolaki[2][c] and Konstantinos Diamantaras[3][d]

[1]*Lab of Computing Medical Informatics and Biomedical Imaging Technologies, School of Medicine, Aristotle University of Thessaloniki, Greece*

[2]*Greek Alzheimer Association, Thessaloniki, Macedonia, Greece*

[3]*Department of Information and Electronic Engineering, International Hellenic University, Thessaloniki, Greece*

Keywords: Alzheimer's Disease, Mild Cognitive Impairment, EEG, Signal Processing, Machine Learning.

Abstract: Cognitive disorders, including Alzheimer's Disease (AD), are health issues concerning all society. The evolution of technology and Artificial Intelligence (AI)/ Machine Learning (ML) in the health domain promises an earlier and more accurate diagnosis for Alzheimer's disease and Dementia. In this study, we examine Healthy patients and patients with AD and Mild Cognitive Impairment (MCI), often a prior step of AD. With the use of EEG, we collect data from their brain activity. After a basic processing step, kernel PCA is applied as a dimensionality reduction method using segments of the multichannel signal, and the transformation output is employed as input for the predictive model. Machine learning functions are used to classify data correctly into Healthy, AD, MCI classes, and a postprocessing step allows for classification at the patient level. The results show that the algorithm can predict with an accuracy of 90 percent and more in total, AD or MCI patients vs. Healthy patients.

1 INTRODUCTION

The aging population is increasing at an alarming rate. The prevalence of diseases more frequent in older adults like Dementia is therefore increasing. Because of the heterogeneity of clinical presentation and complexity of disease neuropathology, dementia classification remains controversial (Raz et al., 2016).

Current research also focused on investigating patients with mild cognitive impairment that will evolve to Alzheimer's disease (Dallora et al., 2017). An early characterisation of MCI, especially progressing MCI, may help timely interventions and slow disease progression.

There are many studies concerning Dementia and AD. AD is the most common type of Dementia. The difference between Dementia and AD is that AD has a higher severity of EEG abnormalities (Kulkarni & Bairagi, 2014). MCI on the other hand, is also characterized from memory loss but is an early stage of Dementia and AD with no apparent symptoms. Some MCI patients may return to the normal stage, but a small percentage of them proceed to AD (Amezquita-Sanchez et al., 2019).

Numerous approaches have been proposed towards the classification of dementia patients, based on EEG, MRI images, biomarkers, daily life tests (Buegler M, 2020). With respect to EEG for AD and MCI characterisation, either evoked potentials, or rest EEG, can be of use.

EEG is a medical modality used for brain disorders, including AD and Dementia recognition. In most Dementia types, slow brain activity is common, so EEG is used for diagnostic evaluation. EEG signals are categorized based on the frequency (delta, theta, alpha, beta and gamma) from 0.1 Hz to almost 100 Hz (Kumar & Bhuvaneswari, 2012). There are many pieces of research concerning the detection of Dementia, AD, and MCI. Regarding rest EEG analysis, several approaches include feature

[a] https://orcid.org/0000-0001-8915-6658
[b] https://orcid.org/0000-0001-8652-7628
[c] https://orcid.org/0000-0002-2072-8010
[d] https://orcid.org/0000-0003-1373-4022

Chouvarda, I., Mpaltadoros, L., Boutziona, I., Tsakonas, G., Tsolaki, M. and Diamantaras, K.
Exploring Classification in Open and Closed Eyes EEG Data for People with Cognitive Disorders.
DOI: 10.5220/0011010100003123
In *Proceedings of the 15th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2022) - Volume 4: BIOSIGNALS*, pages 298-305
ISBN: 978-989-758-552-4; ISSN: 2184-4305

extraction, in terms of spectral, wavelet, entropy features in specific channels, or network analysis and connectivity features among channels, combined with machine learning for classification. Newer studies incorporate deep learning approaches.

In the research on early stages of AD, some researchers used Deep Neural Networks (DNN) for classification with Relative Power (RP) to re-combine features from the system's learning method, which improved diagnosis results compared to another NN, which contained RP features as domain knowledge (Kim & Kim, 2018). In newer studies, though, Multiple Signal Classification and Empirical Wavelet Transform (MUSIC-EWT) was used to reconstruct signals into proper EEG frequencies, analyze them with non-linear indices to discriminate AD from MCI patients, evaluate features with ANOVA for feature selection and use Epoch Neural Network (EPNN) for classification (Amezquita-Sanchez et al., 2019). Usually, preprocessing filters are applied to EEG signals, while Independent Component Analysis (ICA) or Blind Source Separation (BSS) are considered for signal improvement, Fast Fourier Transform (FFT) or Wavelet Transform (WT) for feature extraction and Linear Discriminant Analysis (LDA) or Support Vector Machine (SVM) for the classification. In addition to FFT for feature extraction, Continuous Wavelet Transform (CWT) can also be applied, and for data classification, K-Nearest Neighbor (KNN) has been used successfully (Durongbhan et al., 2019).

The current study aims to use the information hidden in all EEG channels without selecting the most informative ones. It is explored whether open or closed eyes recordings, are more informative. Also, to identify the most informative frequency zones, high-pass and low-pass filtered versions of the signal are used. This study explores the value of a classification method based on Kernel PCA and Random Forest classifier in classifying Healthy, MCI and AD patients on the preprocessed EEG data, in the above-mentioned schemes. Classification follows two steps, classification of EEG segments as a first step, and classification of patients via segment majority voting as a second step.

2 METHODS

As a starting point, the EEG data stored in European Data Format (EDF), which included both open and closed eyes parts, was serialized via Python object serialization (pickle) for more efficient data handling of the open-eye closed-eye segments separately. During the preprocessing of the data, the data were segmented into multiple parts for every patient and for every status (open eyes, closed eyes). After this process, major artifacts were rejected via standard deviation thresholding, and two types of filters were used (delta-theta, and alpha-beta bands, respectively).

ML algorithms were used to study the accuracy of different classifiers when classifying patients as MCI patients, AD patients, or Healthy, with different schemes, e.g., eyes closed and low-pass filtered. The algorithms used were based on the Random Forest (RF) Classifier as a first step classifying patient segments and a majority voting scheme as a second step.

These methodological steps are described in more detail in the following subsections.

2.1 EEG Data

In this paper EEG data were collected through a set of 21 electrodes following the 10-20 international reference system (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1 and O2) at 500Hz.

For EEG signal collection an Nihon274Kohden Neurofax J921A system was used. Input impedance was set to Z<10kω, and the signals were digitized with the Neurofax EEG-12200 Ver. 01-93, and a sampling frequency of 500Hz. The protocol used for data acquisition of the EEG signals refers to the resting stage that lasts for 10 minutes, from which 5 minutes the patient's eyes are closed, and the other 5 are opened, while being seated in an upright position.

For the experiment, we used 27 AD, 22 Healthy και 24 MCI. The data were provided from the Greek Association of Alzheimer's Disease and Related Disorders, with ethical approval for use, and based on the patient data privacy legislation, the data were anonymized.

The EEG data collected are saved in raw EEG EDF files. Every EDF consists of 19 EEG signal channels. Each file contains annotations about signal phases such as open eyes, calibration, closed eyes, A1+A2 electrode ON. Those annotations were used to distinguish segments into open and closed eyes and remove irrelevant ones. Then the data were processed and stored in pickle format for storage capacity reasons.

Following, a preprocessing pipeline is used, including segmentation, filtering and transformation.

2.2 Preprocessing

Data preprocessing includes filtering and segmentation of data before data analysis. Filtering is used to refine data and remove noise and artifacts.

Segmentation is a technique used in this case with the prospect of separating data depending on the annotations of EEG signals for the machine learning algorithm, so that there is sufficient data to be properly trained. The data transformation via KPCA is applied for dimensionality reduction to provide the classifier with a reasonable number of features representing the information of the multichannel EEG segments.

2.2.1 Segmentation

In this study, the recordings were segmented into smaller chunks, allowing us to train the machine learning algorithm with smaller data chunks and facilitating training as our dataset was quite limited. All open-eye and closed-eye recordings were segmented into nonoverlapping 5 second segments.

To avoid overfitting, the maximum number of segments per patient file was set to 45, taking into account that the number of good quality segments per subject varied. The segmentation into chunks also facilitated the dimensionality reduction procedure (see section 2.3), as it was applied in flattened segments of length N=*channels x segment_size.*

2.2.2 Signal Filtering

The data segments with a much higher standard deviation than an adapted average threshold were automatically removed from the sample to remove possibly significant artifacts.

In addition, in this research, we used two types of filters. The first was a low-band Finite Impulse Response (FIR) filter to keep delta and theta signals, and the second filter was a high-band FIR filter for alpha and beta signals. Those FIR filters were used to create two different data schemes. In addition, although channels Fp1 and Fp2 are informative, they were removed to avoid potential artifacts, a necessary step since segments were not manually inspected. Thus, a scheme with 17 channels was employed. An alternative scheme with a reduced number of channels (10 channels in the central-temporal zone) was also considered.

2.3 Dimensionality Reduction

In search of a method that will use the flattened segments of length N=*channels x segment_size* as sample inputs, and produce a much-reduced number of features to be used for the classification, the typical dimensionality reduction methods, PCA and t-SNE (van der Maaten and Hinton; 2008) were initially considered, with moderate results.

Kernel PCA (KPCA), an extension of PCA using kernel methods, was adopted as a much better choice. KPCA is used for multivariate datasets and performs better in non-linear data. With kernel methods, KPCA can protrude data to a higher dimension where there are linearly separable (Wang, 2012). We chose heuristically 160 components and radial basis function kernel (rbf) for KPCA, with gamma parameter to be by default 1/number of features. These 160 KPCA components, resulting from the transformation of each multichannel segment, are used as classification inputs.

3 CLASSIFICATION

3.1 Segment Classification

The classification of each multichannel segment, employing the KPCA components, employs Random Forest (RF). RF is an ensemble method based on Decision Trees. RF aggregates the outcome of many individual decision trees operating as one.

In the RF classifier algorithm, we applied 80 decision trees, 5 jobs to run in parallel, balanced class weight, and random state value=1, which is the parameter controlling the randomness of samples when building the trees. An SVM was considered alternatively (Awad & Khanna, 2015), but potentially due to the fact that the data were already transformed via an RBF kernel, did not add better results and was not further pursued,

The number of segments used for the classification were 871 closed-eyes and 891 open eyes for Healthy subjects, 2008 closed and 2096 open eyes for MCI, 1034 closed and 1034 closed, and 1197 open eyes for AD.

3.2 Subject Classification

In order to move from segment classification to patient classification, a hard voting scheme was applied as a second step. The classification of each patient’s segment contributes a vote to the classification of a patient. The performance recall TP/(TP+FN) was calculated among the classified segments per patient, and a threshold >=0.6 is applied to denote the majority and suggest whether the patient is correctly classified based on the majority of segments or not.

For instance, if at least 60% of a patient's segments were classified as AD, the patient was categorized as an AD patient.

3.3 Training and Testing

We chose to run three different binary classifiers for our prediction, one for AD vs. MCI, one for Healthy vs. AD, and one for MCI vs. AD. For completeness, a 3-class classifier was also presented.

A cross-validation strategy was followed. The classifiers were trained 20 times, leaving in each iteration a set of 2 patients out (one from each class) for testing, in a leave-one-subject-out scheme. For example, we run the classifier for Healthy and MCI patients, and for every run, the classifier left out all the segments of a different patient from the Healthy and MCI class. After each run, the RF classifier returned the training and test set accuracy and a confusion matrix, and the two-step classification procedure was applied for the two subjects to classify the and Healthy or MCI. The average performance metrics per patient were used for comparison.

4 RESULTS

This section presents the results for the binary classifiers for AD vs MCI, Healthy vs AD and MCI vs Healthy patients for open and closed eyes with low and high band filter, as well as the three-class model performance

In order to illustrate the transition from the segment-wise classification to the patient-based classification, a histogram of the classification recall per patient is provided (Figure 1). The recall per patient (TP/TP+FN) shows the percentage of TP vs FN of the classified segments per patient, and in the hard voting scheme selected, a recall threshold >=0.6 as selected to suggest a correct patient classification. As seen in the figures, most of the segments are well above the 0.6 threshold in all cases. Only in Figure 1a, in the Healthy class, one can see 2 out of the 20 cases where recall is between 0-5 and 0.6, in which cases we do not conclude with a correct subject classification.

Table 1 presents the summarised performance metrics in the testing set regarding the three binary classification models, with closed eyes and low-pass filter. In each run, all segments of the 1st class belong to a single subject of this class that is left out for testing, and the same stands for the 2nd class. The

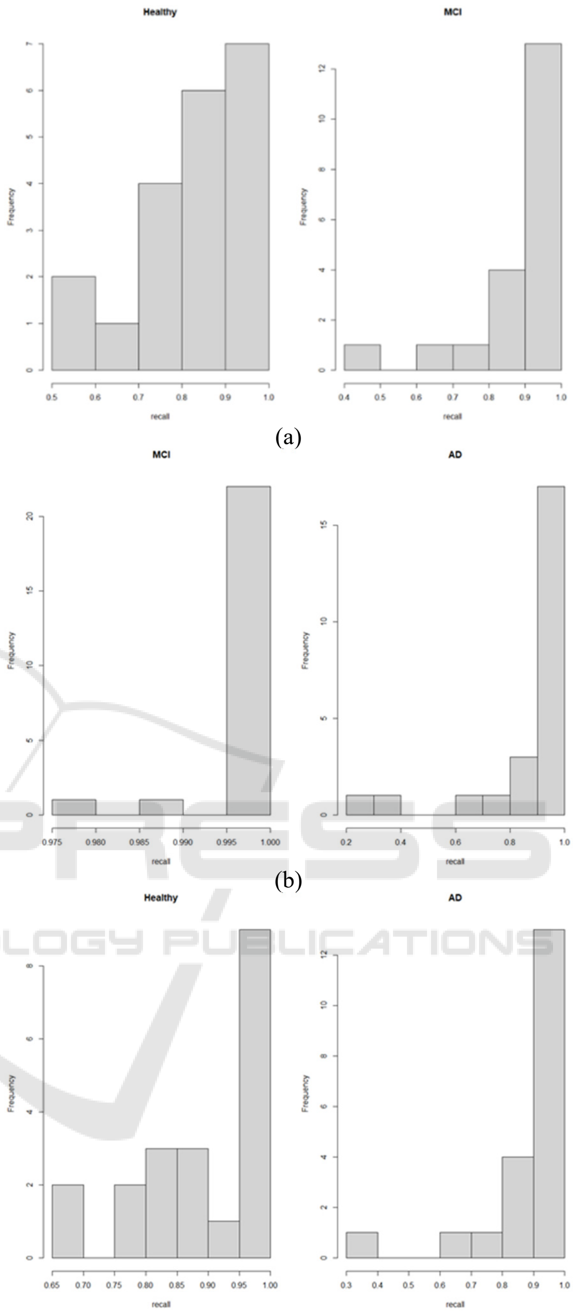


Figure 1: Distribution of classification recall per patient. a) Healthy-MCI closed eyes, low band, b) MCI-AD closed eyes low band, c) Healthy-AD closed eyes low band.

precision and recall metrics are depicted as median and (1st -3rd quantile), corresponding to the percentages of correctly and falsely classified segments per subject. The correctly classified subjects per class are calculated based on recall >0.6 in each run.

Table 1: Patient Classification performance metrics for the three binary classification models, using RF classifier and the majority voting per patient. H stands for Healthy, M for MCI, A for AD. #C stands for the correctly classified subjects (correct segments > 60%).

H/ M		Precision	Recall	#C
	H	0.97 (0.87–1)	0.84 (0.75-0.93)	18 /20
	M	0.85 (0.74-0.95)	0.97 (0.86–1)	19 /20
H/ A				
	H	0.91 (0.85–1)	0.9 (0.81-0.97)	20/20
	A	0.91 (0.84-0.97)	0.93 (0.86–1)	19 /20
M /A				
	M	0.94 (0.88-0.97)	1 (1-1)	24 /24
	A	1 (1–1)	0.93 (0.86-0.97)	22 /24

Table 2: Classification cross-validation results measured in a range between 0 and 1 in terms of ratio of correctly classified patients for the AD vs MCI, Health vs AD and MCI vs Healthy scenario, with all channels.

AD vs MCI	Closed Eyes		Open Eyes	
	AD	MCI	AD	MCI
High Band	0.42	0.46	0.22	0.52
Low Band	**0.92**	**1.00**	**0.93**	**1.00**
Healthy vs AD	Closed Eyes		Open Eyes	
	Health	AD	Health	AD
High Band	0.20	0.45	0.00	0.57
Low Band	**1.00**	**0.95**	**0.90**	**1.00**
MCI vs Healthy	Closed Eyes		Open Eyes	
	MCI	Health	MCI	Health
High Band	0.70	0.00	0.76	0.00
Low Band	**0.95**	**0.90**	**0.86**	**0.76**

Table 3: Ratio of patients classified correctly in the three binary classification scenarios, with selected channels.

AD vs MCI	Closed Eyes		Open Eyes	
	AD	MCI	AD	MCI
High Band	0.04	0.58	0.07	0.52
Low Band	0.29	0.96	0.44	1.00
Healthy vs AD	Closed Eyes		Open Eyes	
	Health	AD	Health	AD
High Band	0.50	0.40	0.00	0.48
Low Band	0.65	0.80	**0.71**	**0.95**
MCI vs Healthy	Closed Eyes		Open Eyes	
	MCI	Health	MCI	Health
High Band	0.65	0.15	0.76	0.00
Low Band	0.90	0.00	1.00	0.00

More detailed results are presented in Table 2 and Table 3, as regards the different schemes considered. More specifically, these results show percentages of correctly classified subjects per class and correspond to the three binary classification models (based on the 2-stage classifier) and the schemes with 17 vs. 10 channels, open vs closed eyes, and high vs low-frequency bands.

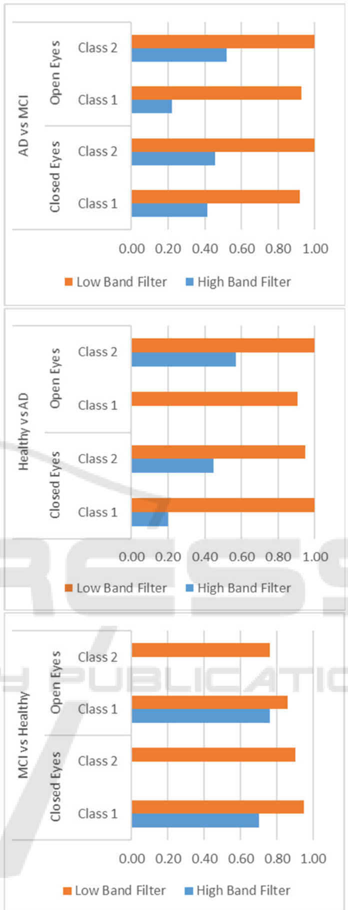


Figure 2: Classification results (correctly patients classified ratio) with low / high band filter, with open / closed eyes and all channels for top) AD vs MCI patients. mid) Healthy vs AD patients, bottom) MCI vs Healthy patients.

The case with ten selected channels (in the central-temporal zone) resulted in inferior results, suggesting that the combined information from all channels was useful. The case of Healthy vs. AD Low Band Open Eyes and closed eyes is the only open-eye case where classification results are quite high.

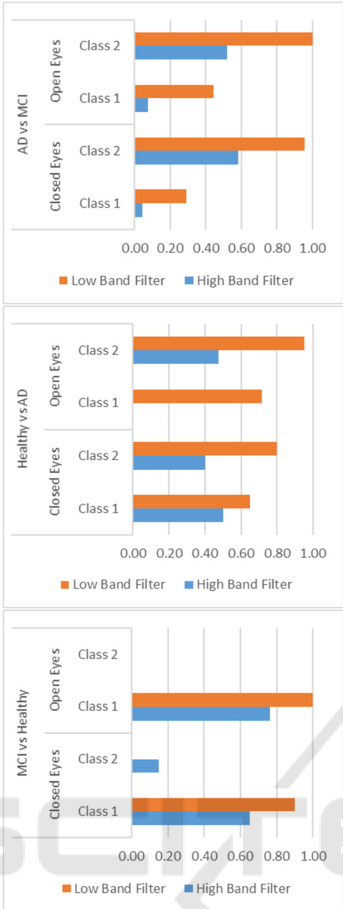


Figure 3: Classification results (correctly patients classified ratio) with low/high band filter, with open/closed eyes and all channels for top) AD vs. MCI patients. mid) Healthy vs. AD patients, bottom) MCI vs. Healthy patients.

As illustrated in Figure 2, the scheme with the low band filter and closed eyes works better for every case in our dataset. In Healthy vs. AD and MCI vs. Healthy examples, the algorithm returned in total the optimal accuracy using the low band filter. Figure 3 presents the correctly classified patients, when selected channels are used, and performance is overall lower.

Overall, when considering together the results of low-frequency closed and open eyes, only one AD and one healthy subject are wrongly classified in both open and closed eye cases, while one healthy subject is wrongly classified vs. AD and vs. MCI in open eyes. All other failures are basically in open eyes, which is probably a more challenging case and lies in the inconclusive area, having around 50% of patients' segments in each class. The combination of both open and closed eyes in a classification scheme might lead to interesting results, and even manage to classify into more subgroups.

Table 4: Summarised performance metrics for the 3-class classification model. Precision and recall are calculated in terms of percentages of correctly and falsely classified segments per subject. Values correspond to median and 1st-3d quartiles. The correctly classified patients are depicted in the #C column.

	Precision	Recall	#C
Healthy	0.96 0.86-1.0	0.85 0.72-0.96	16/20
MCI	0.75 0.69-0.87	0.95- 0.84-1.00	17/20
AD	1.00 0.99-1.00	0.95 0.90-0.98	19/20

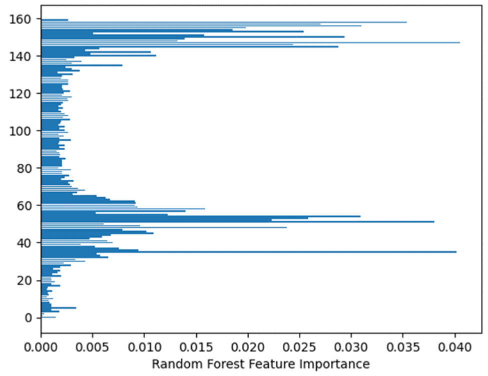
In the case of the three-class classification problem, Table 4 presents similar performance metrics for the 3-class model in the testing set, including segments from two subjects in each run. Metrics include Median (1st -3rd quartile) for precision and recall. Based on recall >0.6 in each run, the last column shows the correctly classified subjects per class. Results are slightly poorer in this case than the binary models as presented in Table 1, especially regarding the Healthy class. The 3-class model may require more data for training.

Finally, an important issue that would need to be addressed is that of exploring feature importance. KPCA is not directly leading to insights about the features that lead to best classification, and the mechanisms behind that, and more sophisticated methods would be required to illustrate results in terms of interpretability.

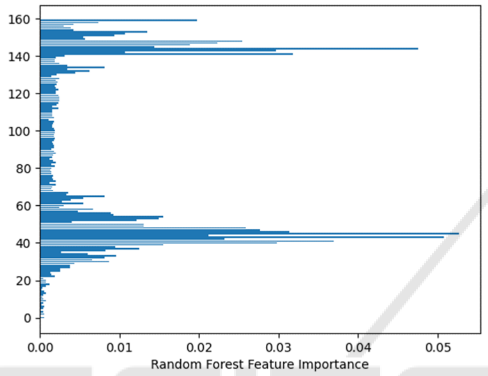
Nevertheless, Figure 4 provides feature importance, as provided by the RF model, based on the Gini importance, to illustrate the contribution of multiple components of the KPCA transform, and how these differ per classification problem. This could potentially help in optimising the features eventually selected in each classification model.

4 CONCLUSIONS

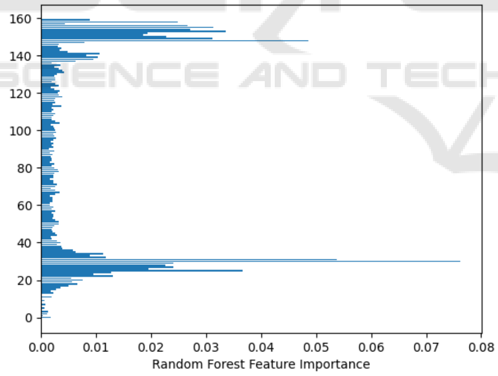
The presented method is based on KPCA for dimensionality reduction of multichannel segments. This method has been used before with EEG analysis (Ye et al, 2018). Considering the classification results, low band filter returns better accuracy for both training and test set. Furthermore, the algorithm works best with AD or MCI vs Healthy patients rather than AD vs MCI. Compared to the results performed in the comparative study of (Lehmann et al, 2007), a rather higher accuracy is achieved. This is probably because MCI and AD signals share some similarities,



(a)



(b)



(c)

Figure 4: Feature importance from the Random Forest model classification results with low band filter, closed eyes and all channels, for a) Healthy-MCI model, b) for MCI-AD model, and c) Healthy-AD model. Y-axis corresponds to 1-160 KPCA components used as features.

and the algorithm faces difficulty to correctly identify patient data as one of those classes.

While the low frequency closed eyes scheme seems to produce a better result than open eyes, it is a matter of further research whether information from both states would result in more stable and safe results. Certainly, a larger training dataset and a more comprehensive evaluation would improve the credibility of the results. A more thorough finetuning of the various parameters would also be of value and would potentially lead to a more optimized outcome.

Furthermore, adding an explainability layer would help better understand and trust the approach. Finally, it would be relevant to address the problem in a continuous space rather than a classification problem and recognize the problem's complexity addressing the different subtypes of the MCI/AD conditions.

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