Early Diagnoses of Alzheimer using EEG data and Deep Neural Networks classification

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***Abstract*—Alzheimer's disease has always been a challenge to be detected at early stages as it has always been mistaken as normal aging. It can be recognized when the patient starts to have Mild Cognitive Impairment (MCI) and by that stage, only little can be done as no treatment can reverse its effect but only to delay its progression. In this work, we present a method for early diagnoses of AD by creating a low-cost EEG device along with using a deep neural network that can classify the suspected patients into three classes: MCI patients, AD patients, and healthy patients. This is done using collecting brain wave signals using Electroencephalography (EEG) device during a 3 level N-Back working memory test. This is called event-related potential (ERP), later the data will be cut into small frames, FFT transformed to extract brainwave subbands (theta, alpha, and beta) and then projected to 2D images where it will be used in training convolution neural network for classification. Early detection of Alzheimer will reduce the progression of AD at early stages. We implement and evaluate our hardware and classification with an accuracy of 90.36% for MCI and 92.52% for Alzheimer's disease detection.**

Keywords—Alzheimer, Mild Cognitive impairment, early detection, Electroneuronography, Hardware, N-Back Test, Convolutional Neural Network, classification.

I. Introduction

Alzheimer's disease is one of the severe diseases; it is an incurable and progressive brain disorder. Alzheimer slowly destroys memory parts of the brain and the ability to carry out regular life tasks. Alzheimer disease symptoms start to appear in their mid-60s category. While estimates vary, experts suggest that more than 5.5 million may have Alzheimer's. [1]

It is one of the dementia types, especially among elders. Dementia is the degradation of the brain and loss of cognitive functions like thinking and remembering abilities[1] [2].

Arising from the previous point, there are other options to deal with the disease. Early diagnosis was the optimal strategy to tackle the problem of the incurable Alzheimer's disease, not only because the patient's level of function will be preserved for a more extended period, but also because patients with AD incur more societal cost than those who require long-term institutional [6][2]. Our Objective was developing an affordable high-performance system used for early detection of Alzheimer, which collects brain wave signals by mean of a custom implemented EEG sensor, followed by a set of preprocessing and convolutional neural network classification is done on the collected data to early diagnose the disease.

In this context and depending on research done in finding biomarkers like Event-Related Potential (ERP) and Event Sync/Desync in EEG brain wave data to distinguishing healthy persons from MCI and AD, this paper will be discussing the implementation of a system for early diagnosing AD. The need for early detecting Alzheimer comes from believing in the vital role it plays in slowing or preventing the disease from reaching late stages. [2] [8]

Evoking ERP analysis and event sync/desync, EEG data collected had to be gathered during N-Back working memory (WM) Test which will focus on increasing the load on the person working memory with visual stimuli.

Accordingly, pre-processing the EEG signals collected during an N-Back working memory (WM) test. This data is cut into event-related potentials (ERP) bands; they are cut into smaller sub-bands and converted to the frequency domain where it is projected to 2D images of the brain, passing the images to a convolutional neural network (CNN) for training and later classification.

II. Related Work

A. approach

Our approach was to create an EEG brain wave sensor with low cost and high accuracy, this sensor will focus on the application of Alzheimer disease where it will have 10 channels placed on the brain lobes that are most affected by Alzheimer disease.

The proposed system will use the implemented EEG device incorporated with the work done in [7] for a higher representation of EEG data. This representation is based on neural networks due to its high accuracy of the classification and its ability to keep the temporal and spatial data.

B. Related work in the field of EEG device hardware

Cyton Biosensing board, a development board providing the user with 8 channel EEG data sampled at 250Hz. Moreover, the channels are connected to multiple instrumental amplifiers. then to a 24-bit ADC. The operating frequency range from 0 to 100 Hz and it has controllable gain from 3 to 24. which was sold for a price of 550 euro. [13]

The ganglion board like the Cyton board is produced from the same manufacturer as a cheaper solution for biosensing where it has a sampling rate of 200Hz and a bandpass filter from 0.3 to 100, but it can only operate with batteries. Moreover, it only has four channels. Compared to the Cyton board this one is sold for 250 euro. [13]

C. Related work is done in the classification software

The related work in early detection for Alzheimer based on 2 of the latest research which uses EEG data

1. Alzheimer's Early Prediction with Electroencephalogram.
2. Diagnosis of Alzheimer's disease with Electroencephalography in a differential framework.

The first method uses a surrogate decision tree classifier. achieving 93.4% accuracy, an affectability of 86.19% and an exactness of 94.88% using 19 channel EEG data [1]

The second method uses a database containing the EEG data of 169 patients. The dataset includes (AD) patients,

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(MCI) patients, subjective cognitive impairment (SCI) patients and patients with other pathologies. This was tested to be 88.8% which was obtained for the classification between 3-class of SCI, possible AD, and other patients. [2]

III. Material Used

A. *For the Hardware implementation*

The EEG sensor implementation required to have EEG wet electrodes, instrumental amplifier (AD621), Operational amplifier, precession resistors, capacitors and lastly an Arduino MKR1000 as MCU and ADC.

B. *Dataset for training*

Dataset used composed of two parts; the first was got from Alzheimer Disease Neuroimaging Initiative (ADNI) which composed of 20 Healthy, 20 MCI and 20 AD participants, while the second part was ten healthy participants.

IV. Proposed Method

In this chapter, the implementation of our method for the early diagnosis of Alzheimer is explained in two main parts.

A. *EEG Electrode placement and data collection*

EEGs are a non-invasive way to examine the brain. The intensity of brain waves depends on the mental and physical state of the brain. We will focus on theta, alpha, and beta waves occurring 4-8 Hz, 8-12 Hz, and 12-30 Hz respectively.

The EEG electrodes used are the wet electrodes with placement following 10/20 electrode placement. The fixed points are found by dividing this area into 10% and 20% sections as in Fig 1, the location for electrodes are frontal lobe (FPz, Fz, F7, F8), Temporal lobe (T3, T4, T5, T6) and partial lobe (P3, P4), which focuses on areas affected by Alzheimer.

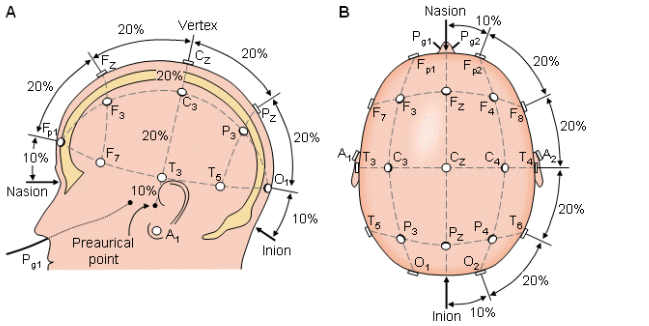

Fig 1. Brain 10/20 international electrode placement *[3]*

Each differential amplifier takes two electrodes as input, first, potential measurement electrode and second, reference electrode. The reference electrode is used for all channels and the locations used for the reference electrode are A1 or A2, the ear electrodes.

Finally, the connection of the electrodes to the system has three main configurations, the common reference, average reference, and the bipolar configuration, in this implementation common reference is used.

B. *Hardware implementation*

Fig 2 shows the flow chart of the hardware. It consists of electrodes inputted to the instrumental amplifier, then to a group of filters to filter the power supply noise and limit the frequency band of the system finally to MCU for sampling.

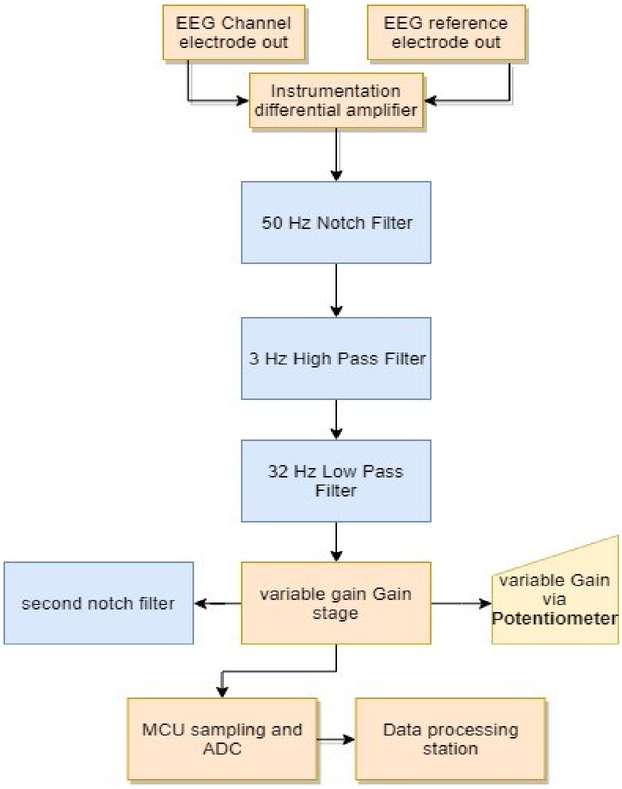

Fig 2. EEG hardware implementation flow diagram

In the EEG implementation, instrumental amplifiers are used instead of standard differential amplifiers due to buffered inputs canceling the need for impedance matching and provides Very High CMMR.

Instrumental amplifiers have an internal feedback resistor that is effectively isolated from its input terminals as the input signal is applied across two buffers.
Shown in Fig 3 the internal design of the instrumental

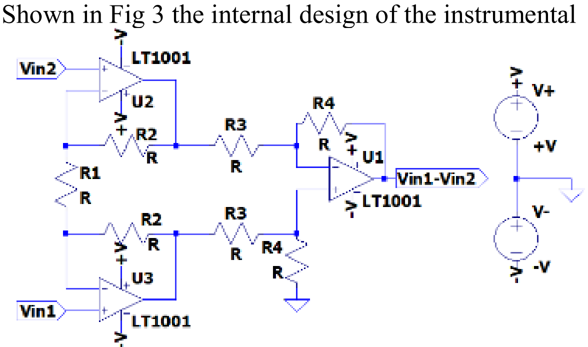

Fig 3. Instrumentational amplifier model on LTspice

$$A_d = \frac{V_{out}}{V_{in}^{+} - V_{in}^{-}} = \left(1 + \frac{2R_2}{R_1}\right)\frac{R_3}{R_2} \qquad (4.1)$$

Instrumentation amplifiers gain shown in Eq. 4.1 and can be realized as in Fig 3, the implemented system uses 10 instrumental amplifiers. One for each EEG channel.

The instrumental amplifier used is AD621 from Analog Devices due to its High CMRR (80dB) over a wide frequency range, Low drift and skew with Simple gain selection.

1) *Filters **used***

All the filters used in the implementation where active filters. For the filter implementation, TL084 operational amplifiers from Texan Instruments were used where each integrated circuit contains four operational amplifiers.

a) Notch filter

Notch filters are bandstop filters with high selectivity for the stop frequency; used to suppress 50 Hz supply noise.

Suppressing supply noise requires the use of two filters one after the Instrumentation amplifier and the other at end of the circuit to further remove the 50 Hz. [4] [5] [6]

The used Notch filter design is the active twin T design with variable Q realized using 2 Op-amps, giving high attenuation for the notch frequency, shown in Fig 4.

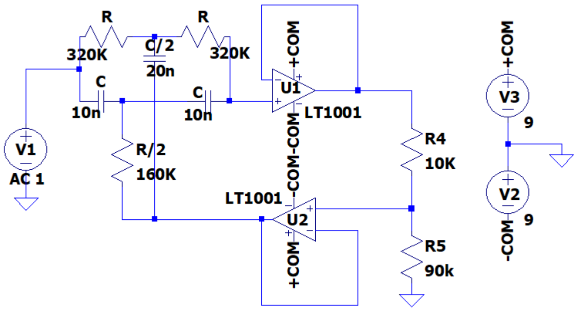

Fig 4. Op-amp twin T notch filter LTspice model

$$f_{notch} = \frac{1}{2\pi\sqrt{R_1R_2C_1C_2}} \quad (4.2)$$

$$Q = \frac{R_4+R_5}{4R_4}, \Delta f_{notch} = \frac{f_{notch}}{Q} \quad (4.3)$$

Notch filter cutoff frequency Calculation showed in Eq4.2 While notch filter quality factor and bandwidth are shown in Eq4.3

f_{notch} notch frequency, R symmetric resistors, C symmetric capacitor, Q quality factor, and Δf_{notch} is the bandwidth.

For the implementation of the filter for 50 Hz, C was chosen to be 10 nF leading to the calculation if R to be 320KΩ.

With the Twin T design, Q is variable by using R_4 *and* R_5 which is useful for controlling the bandwidth of the notch.

To have minimal effect on the EEG band, the notch filter bandwidth was 20 Hz leading to the calculation of Q = 2.5, and from Q, the values for R4 = 10 KΩ and R5 = 90 KΩ.

b) High pass filter

Second filter HPF is responsible for the rejection of the low frequencies below the 4 Hz. The used HPF design was a 2nd order multiple feedback Butterworth inverting configuration HPF. [4] [5] [6]

We used a 2nd order filter as they have a steeper roll-off of 40dB/decade compared to 1st order filter of 20dB/decade.

To design the filter, the following Equations were used

$$F_c = \frac{1}{2\pi\sqrt{R_1R_2C_2C_3}}, \quad K = -\frac{C_1}{C_3} \quad (Eq.4\text{-}8)$$

$$\frac{V_{out}(S)}{V_{in}(S)} = \frac{(2\pi F_c)^2 K}{S^2 + 2\zeta(2\pi F_c)S + (2\pi F_c)^2}, \quad Q = \frac{1}{2\zeta} \quad (Eq.4\text{-}9)$$

Eq. 4-8 and Eq. 4-9 both show the cutoff frequency of the high pass filter and the transfer function of it

F_c is the cut-off frequency, K is the gain, Q is the quality factor and ζ the damping factor.

For a gain of 1 lead to $C_1 = C_3$ was chosen to be 220 nF also C_2 to be $2C_1$ = 440nF

Solving for F_c= 4 Hz, R_1/R_2= 6/25 meaning assuming R_1= 60 KΩ got R_2= 250 KΩ

Fig 5 shows the HPF schematic designed over LTspice

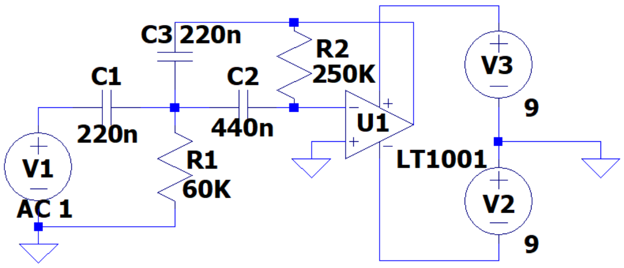

Fig 5. High pass Filter LTspice model

c) Low pass Filter

Following the same topology of the HPF, we use the same filtering design but configured as a low pass filter.

Fc = 37 Hz, C_1/C_2= 25/6 meaning assuming C_1 = 500 nF got C_2 = 120 nF.

Fig 6 shows the schematic of a 2nd pole inverting lowpass filter used in the hardware implementation.

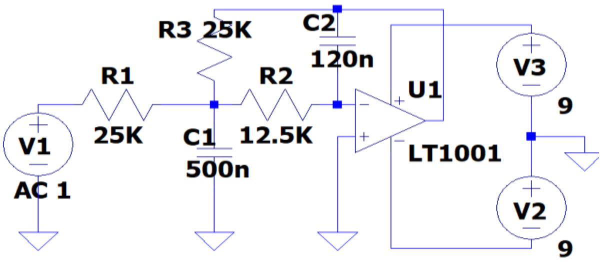

Fig 6. Low pass filter LTspice

d) Gain stage

Gain is responsible for the configurable gain of the EEG device; it uses a non-inverting op-amp amplifier. [4] [5] Fig 7 schematic using the potentiometer R1 to control gain.

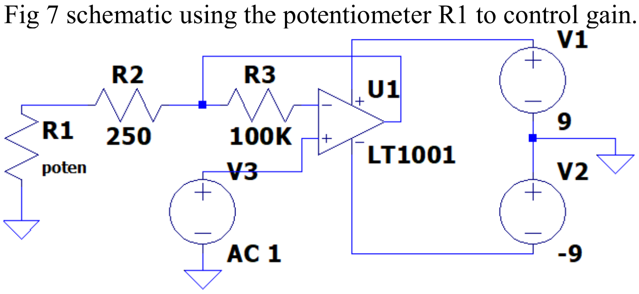

Fig 7. Op-amp noninverting amplifier LTspice model

As seen from Fig 7, $V_{out} = A(V_+ - V_-)$ where V_- is a function of the output due to the negative feedback where it depends on the voltage division between R3 and (R1+R2)

$$V_{out} = V_{in}\left(1 + \frac{R_3}{(R_1 + R_2)}\right) \quad (Eq.4\text{-}12)$$

From the previous function Eq. 4-12, the gain depends on the ratio of R_3 to $(R_1 + R_2)$ where R1 is 1 KΩ potentiometer

With the gain = $(1 + \frac{R_3}{(R_1+R_2)})$.

For potentiometer value of 0 Ω, gain = 401 while for potentiometer value of 1 KΩ, gain = 81.

The total gain of the device depends on the gain of the instrumentational amplifier of 100 and the selectable gain of the gain stage ranging from 8100 to 40100. Choosing a wide range of large gain due to the small potential detected by the EEG electrodes. Ranging from 10uV to 30 uV while the used ADC is only 12-bit meaning it has a 4096 values resolution of 1.22mV with a range of 0-5.

2) MCU

The last phase where the data will be inputted to the ADC pins of Arduino MKR1000 for the conversion from the analog to the digital using 12-bit ADC at a rate of 1KHz then transferred to the processing using serial communication.

C. Pre-Processing and classification

All the preprocessing steps will be done individually for each channel; Fig 8 shows an example of outputted data from the Collected EEG hardware. Where the y-axis is the signal amplitude while the x-axis is the sample number. [7] [8]

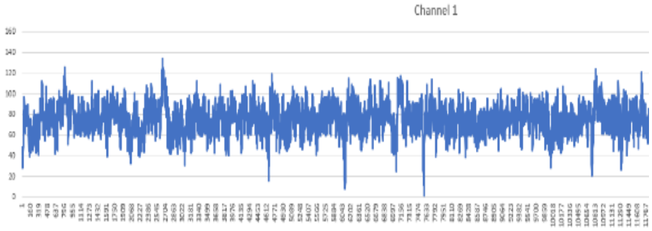

Fig 8. EEG data collected example for one channel.

1) Extracting the ERP

Data preprocessing includes getting segments of data based on the N-Back WM test timestamps of the correct answered sessions by the user, dividing the EEG data into 2 sub-sessions (ERP). An example of the ERP data in Fig 9. the y-axis is the measured ADC value from the controller.

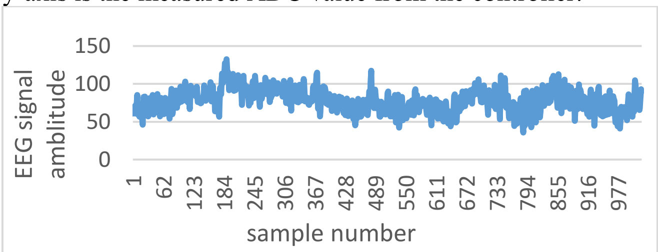

Fig 9. ERP data section of 2 seconds long

2) Dividing the extracted ERP to sub-frames

The ERP data will be divided into subframes using a moving window with a width of 250 msec and with 50% overlap which will divide ERP data it into an array of sub-frames

Following is an example of the data segment or sub-frames in Fig10, the Y-axis is again the amplitude read by ADC.

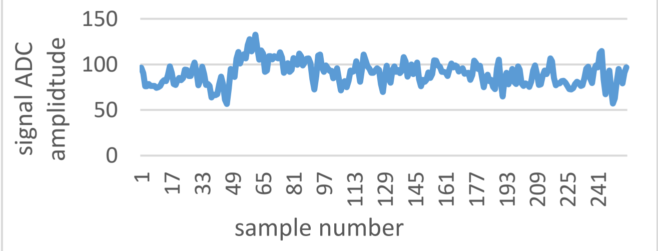

Fig 10. 1st sub-frame of the ERB data with 50% overlap

3) Fast Fourier Transform (FFT) of subframes

This section is for converting the time domain signals to the frequency domain using the known fast Fourier transform, shown in Fig 11.

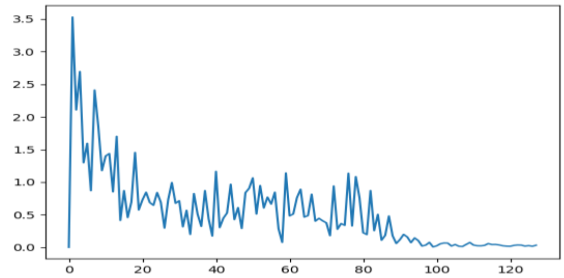

Fig 11. ERB Sub-frame FFT transformation by python

4) Projecting the sub-bands on 2D brain images

Relying on previous EEG research done by [7]. Our implementation will convert the raw EEG data to image representation by projecting EEG sub-band data to a 2D image of the brain where these images will be given to a CNN for video classification [7].

Taking an input, the number of channels, the location of each channel (electrode) and an ERP data session, composed of multiple sub-frame frequency band scalar values.
Example Subframe frequency data = (theta1, theta2, ..., alpha1, alpha2, ..., beta1, beta2, ...).

For each ERB sub-frame, the respective feature array will be used for creating an image representation of the EEG data where the output of the ERP session will be an array of images.

The EEG image Conversion will be realized in 2 steps:

1. Convert the 3D brain image to a 2D projection of the brain image for the respective placement of the electrodes while keeping spatial data preserved leading to the 2D electrode locations.

   Fig 12 the conversion of the 3D to the 2D brain image

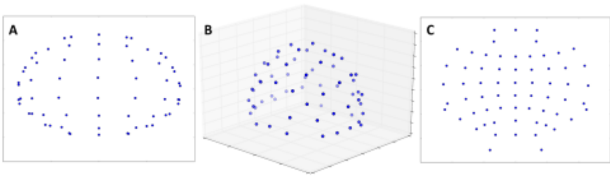

Fig 12. 3D image probe location converted to 2D *[7]*

2. Apply the azimuth projection of the scalar feature array of each ERP sub-frame on a 2D image the brain electrode image like in Fig 12 C. Each frequency sub-band will be represented as RGB channel, As shown in Fig 13.

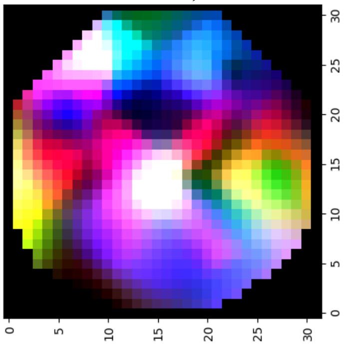

Fig 13. EEG Image Azimuth projection of frequency sub-bands

V. RESULTS

the Result section is divided into two main parts, the results in the hardware and software implementation

A. Hardware results

The implemented hardware has the following specs, 10-channel EEG sensor, 1KHz sampling rate, The use of instrumental amplifiers eliminating the need for impedance matching, Hardware 2-pole active Butterworth inverting filters for frequency band selection, Notch filter for suppressing with AC power supplies noise, controllable Gain, High-resolution 12-bit ADC and the cost of the hardware implementation and components cost 80 euros.

B. Software results

For testing the overall system, two tests were done, but first, CNN was trained with three different models

1. Healthy vs. MCI
2. Healthy vs. AD

First was testing the classifier with a known dataset for Alzheimer's and MCI disease which was collected during the WM test (N-Back test) to train the neural network.

The use of a ready dataset was due to the inability to do clinical trials with AD and MCI patients.
The dataset used for training and testing consisted of

1. 20 healthy participants
2. 20 MCI patients
3. 16 Alzheimer patients

The data collected during the N = 3 back Test using numbers as a visual stimulus and consisted of 30 images for each test, also the training was done in groups of two, Healthy vs. MCI and Healthy vs. AD. finally the results for different architectures were shown in Table 1.

Table 1. Classification accuracy with multiple architectures

	Healthy vs. MCI	Healthy vs. AD
ConvNet+1D-Conv	85.52%	87.82%
ConvNet+ LSTM	89.61%	90.15%
MIX of both	90.36%	92.56%

The second testing for classification was done using the implemented hardware over ten healthy participants. Each participant did the test 4 times giving 40 data sessions. Later, the data were used as follows, 20 for training, 10 for validation and 10 for testing the classification accuracy.

The results: out of the 10 participants 1 was falsely classified as Alzheimer, leading to an accuracy of 90%.

VI. CONCLUSION

As discussed in this paper. One of the ways to tackle the uncurable Alzheimer disease is to early diagnose the disease which will give a chance to the doctors to slow down the progress of the Alzheimer, which in terms decreases the healthcare cost over the long term and gives a chance for the patient for extra time. To detect Alzheimer early, we need to identify the early stages of the disease which starts by MCI. MCI is the decrease in the cognitive functions of the brain. This Paper discusses the implementation of a system to early detect Alzheimer disease based on EEG brain signals.

The proposed approach depends on previous research in the field of detecting specific biomarkers in the EEG signals which are detected in the ERP analysis of the EEG and the Sync/Desync of the frequency sub-bands of the brain waves. The system uses these ERP collected during an N-back test using the implemented low cost high-performance EEG hardware, these data is then preprocessed and projected on a 2D brain images, which allows to train a Convolutional neural network for video classification handling EEG data as a video, the CNN will be trained with different sets of data for healthy, MCI patients and Alzheimer patients, then used for disease classification. The proposed approach gave consistent results compared to the related work. Classification accuracy of 90.36% for healthy vs. MCI and 92.56% for healthy vs. AD patients.

REFERENCES

[1] Pedro Miguel Rodrigues, João Paulo Teixeira, Carolina Garrett, Dílio Alves, Diamantino Freitasa. "Alzheimer's Early Prediction with Electroencephalogram", Conference on ENTERprise Information Systems / International Conference on Project MANagement / Conference on Health and Social Care Information Systems and Technologies, CENTERIS / ProjMAN / HCist 2016, October 5-7, 2016.

[2] François Vialatte, Esteve Gallego-Jutglà, Gérard Dreyfus. "Diagnosis of Alzheimer's disease with Electroencephalography in a differential framework", PLoS ONE 13(3): e0193607. https://doi.org/10.1371/journal.pone.0193607, 2018.

[3] "Sharbrough F, Chatrian G-E, Lesser RP, Lüders H, Nuwer M, Picton TW (1991): American Electroencephalographic Society Guidelines for Standard Electrode Position Nomenclature. J. Clin. Neurophysiol 8: 200-2.".

[4] Zumbahlen, H. Basic Linear Design. Ch. 8. Analog Devices Inc. 2006..

[5] Zumbahlen, H. "Analog Filters." Chapter 5, in Jung, W., Op Amp Applications Handbook. Newnes-Elsevier (2006)..

[6] Williams, A. B. Electronic Filter Design Handbook. McGraw-Hill. 1981..

[7] "Bashivan, et al. "Learning Representations from EEG with Deep Recurrent-Convolutional Neural Networks."," in *International conference on learning representations (2016)*.

[8] "Yamashita, R., Nishio, M., Do. et al. Convolutional neural networks: an overview and application in radiology," *Insights Imaging (2018).*

[9] "Lama RK, Gwak J, Park JS, Lee SW. "Diagnosis of Alzheimer's Disease Based on Structural MRI Images Using a Regularized Extreme Learning Machine and PCA Features"," *J Healthc Eng. 2017.*

[10] "Long X, Chen L, Jiang C, Zhang L. "Prediction and classification of Alzheimer disease based on quantification of MRI deformation."," *Alzheimer's Disease Neuroimaging Initiative, PLoS One. 2017.*

[11] Francisco J Fraga, Godofredo Quispe Mamani, Guilherme Tavares, and Natalie A Phillips. "Early diagnosis of mild cognitive impairment and Alzheimer's, with event-related potentials and event-related desynchronization in N-back working memory tasks." In:Computer methods and programs in biomedicine164(2018), pp.1–13..

[12] Krizhevsky et al., 2012; Graves et al., 2013; Karpathy and Toderici, 2014; Zhang and LeCun, 2015; Hermann et al., 2015.

[13] OpenBCI, https://shop.openbci.com/collections/frontpage