Aging effects on resting state networks after an emotional memory task

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Abstract

Aging is one of the primary health concerns in nowadays world, being memory decline an important worry that affects daily functioning of healthy adults. This work presents a study of this kind of decline in normal aging, by processing and analysing electroencephalographs (EEGs) of 72 healthy subjects, categorized as either young or older adults. These biosignals are first pre-processed using a customized pre-processing pipeline using the EEGLAB tool in Matlab. Once the signals have been pre-processed, two different analyses are carried out: a frequency analysis, obtaining the powers for each band of the EEG signals, and a time-frequency analysis. The data obtained from these studies is analysed using R, obtaining some important results and conclusions.

1. Introduction

Aging is one of the primary health concerns in the entire world. Healthy adults experience memory declines that affect their daily functioning, yet their ability to process emotion is well-preserved [1]. During the last decades, there have been several aging studies exploring brain plasticity in relation to cognitive and motor improvement [2-5]. However, the benefit of utilizing spared emotional abilities to help mitigate the memory decline that occurs with age has not been previously explored.

This is the premise of the MEMOTION project [1]. One of the main goals of this project is to analyse age-related neural networks underlying emotional and memory processes. Furthermore, the project presents a ground-breaking methodology to train brain plasticity and transfer those benefits to daily life. This way, the importance of age-related preserved emotions to improve memory deficits is enhanced.

The study design consists on a series of task-related and resting state EEG scans (rs-EEG) recorded before and after an eight-week training program in positive emotions to later examine the neuronal changes that occur in young and older individuals as a result of training. This article describes the analysis of rs-EEG before the training program in positive emotions.

The work presented in this paper has been developed in the context of a graduate-level project following the Project-based learning (PBL) methodology at Mondragon Unibertsitatea.

2. Materials and methods

This first chapter describes how the EEG recordings and data acquisition have been carried out.

2.1. Subjects

The study included 72 right-handed and healthy participants divided into two groups: 34 young and 38 older adults. The age range of young adults was between 18 and 26 years, while older adults ranged between 60 and 75 years.

2.2. Experimental setup

EEG recordings occurred twice: before (pre-test session) and after (post-test session) ten training sessions (training period), distributed across 8 weeks. The rest-task-rest EEG design of both EEG sessions was identical with a total duration of 1.5 h. Therefore, the overall experimental procedure was as follows: the pre-test session included a rest scan (rs1), followed by a task-related scan (tr1), after which another rest scan (rs2) was obtained. The pre-test session was followed by a training program in positive emotions for an 8-week period. Following completion of this training program, the post-test session included a rest scan (rs3), followed by a task-related scan (tr2), and subsequently another rest scan (rs4). See Figure 1 for data acquisition protocol. The current work focuses on the analysis of the rs-EEG scans before the training program (rs1 and rs2). All rest scans had the same protocol and lasted 5 min, in which participants were instructed to keep their eyes open and to fixate a target point.

2.3. EEG recordings and pre-processing

EEG is an electrophysiological monitoring system to record electrical activity of the brain, specifically from the post-synaptic pyramidal neurons [6]. It is typically non-invasive and acquired by means of electrodes that are placed along the scalp. These electrodes measure voltage variations resulting from ionic currents within the neurons of the brain.

EEG signal analysis generally focuses either on Event-Related Potentials (ERP) or on the spectral content of the biosignal. The former investigates potential variations time locked to an event-like stimulus, while the latter analyses the type of neural oscillations or brain waves that can be observed in the frequency domain [7]. As opposed to the ERPs, this type of neural oscillations can be analysed in a

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Figure 1. *Data acquisition pipeline*

Brain wave	Frequency band
Delta	0.5 – 4 Hz
Theta	4 – 8 Hz
Alpha	8 – 12 Hz
Beta	12 – 30 Hz
Gamma	30 – 48 Hz

Table 1. *Brain waves and their frequency bands [8]*

resting-state. Resting-state EEG refers to the recording of the brain's electrical activity when a subject is not performing an explicit task. The frequencies of the brain signals are classified in different waves depending on the frequency band and the state where they appear (*Table 1*).

The EEGs were recorded with a BioSemi Active Two high density system with 128 electrodes. Additionally, four electrodes in the vicinity of the eyes were used to capture two electroculogram (EOG) signals that recorded the vertical and horizontal eye movements. The data were digitalized at a sampling rate of 1024 Hz. Finally, data were offline re-referenced to the nose tip, giving a total number of 133 acquired channels.

3. Signal processing

In this chapter the techniques used for the pre-processing of the EEG signals are described, as well as the frequency and time-frequency analysis techniques.

3.1. Signal pre-processing

EEG signals contain multiple artifacts and noise sources that must be removed before these biosignals can be used for analysis. For that purpose, the signal pre-processing method used in this work is a customized version of the Makoto's pre-processing pipeline, adapted for EEGLab software [9].

3.1.1. Down-sampling

The first step is to reduce the sampling frequency of the signals from 1024 Hz to 256 Hz. This way, the computational load of the algorithm is reduced.

3.1.2. Bandpass filtering

Bandpass filtering is necessary for the elimination of noise and artefacts that are located outside the band of interest. In the works [10 - 11] the pass band of the resting state is considered to be between 1 and 45 Hz, so these cutting frequencies have been used for the realization of the first filtering stage.

3.1.3. Removal of bad channels

Channels that show erroneous or badly acquired information are eliminated and then interpolated using the signals of the adjacent channels.

3.1.5. Re-reference data to average

In this step, the signals of the electrodes are re-referenced. The new reference becomes an imaginary point obtained as the average of all the electrodes.

3.1.6. Independent Component Analysis (ICA)

Using the ICA, the EEG signal is separated into independent components. Then, the SASICA tool (Semi-Automated Selection of Independent Components for Artefact correction) of the EEGLAB library is used for eliminating the components containing artefacts.

3.1.7. Interpolation of removed channels

Finally, the channels that have been eliminated in previous steps are interpolated again.

3.2. Frequency analysis

With the aim of analyzing the spectrum of the EEG, the mean power of each of the EEG frequency bands presented in Table 1 has been computed. This calculation is carried out for each of the 128 EEG signals, for both rs1 and rs2.

3.3. Time-frequency analysis

When analyzing biosignals it is often interesting to see how the frequency content of the signal changes over time. These changes can be noticed by using time-frequency analysis techniques, such as the Short Term Fourier Transform (STFT), Cohen's classes of distributions or the Wavelet transform. In this study, the Morlet Wavelet Transform (MWT) was used in order to carry out the time-frequency analysis of the EEG signals. The MWT is a complex wavelet, comprising real and imaginary sinusoidal oscillations, which is convolved with a Gaussian envelope so that the wavelet magnitude is largest at its center and tapered toward its edges [12-13].

In this study, a wavelet factor of 7 [14] has been used and the spectrum has been divided into 124 frequency bins. Once the time-frequency maps using the MWT have been obtained, the power present in each frequency band has been calculated for 30 second intervals.

4. Data analysis

Once the power data from the different frequency bands was obtained, two different studies were carried out. First statistically significant changes were sought in frequency, and then, time-frequency changes were studied.

The main objective of this step is to determine whether there is any interaction between the two age groups (young vs. older) and the two different resting states (rs1 and rs2). For this, a two-way mixed analysis of variance (ANOVA) was carried out considering as intra-subject variable the rs-EEG scan, and as inter-subject variable the age group. The p-value of the relationship between age group and rs-EEG scan was observed.

A different ANOVA was performed for each of the EEG channels and each frequency band. The process was carried out in three different steps: i) Group the data based on the channel number, ii) Filter the desired number of channels, and iii) Make the ANOVA test for which an error term that accounts for natural variation from subject to subject was specified.

As multiple comparisons are being performed, it is necessary to control the expected proportion of falsely rejected hypotheses. For this, the False Discovery Rate (FDR) method of Benjamini and Hochberg [15] was used with a corrected p-value of 0.05.

Finally, in order to identify the type of change observed in those positive results, the average values of the observations were calculated by group and condition. This process was repeated for both frequency and time-frequency analyses.

5. Results

This section summarizes the results obtained through statistical analysis of frequency band power and time-frequency power data.

5.1. Frequency analysis results

The results of the ANOVA tests showed statistically significant differences in the alpha frequency band of 42 EEG channels regarding the interaction between age group and rs-EEG scan (*Table 2*).

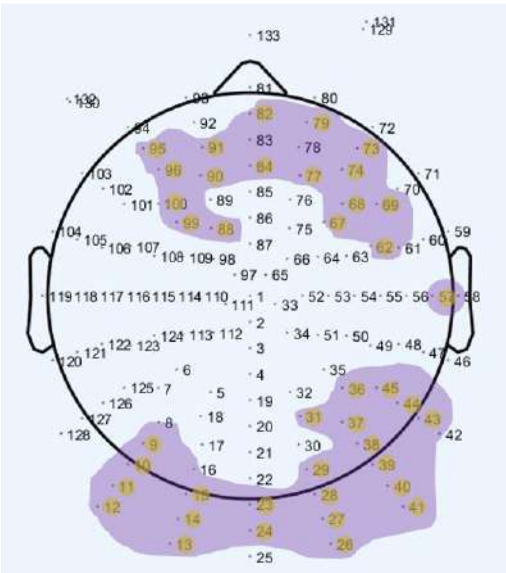

Figure 2. *Map of the scalp showing the channels with a statistically significant difference regarding the interaction between age group and rs-EEG scan in the Alpha waveform*

The underlying areas of the brain where these interactions are identified are the frontal, prefrontal, occipital and posterior areas (*Figure 2*). Regarding the delta waves, six channels were identified with significant statistical differences grouped in the occipital part of the brain. These differences however, may be due to artifacts that were not completely suppressed in the pre-processing stage.

Differences between the values of young and older adults between rs1 and rs2 follow the same trend in all cases without exception. On the one hand, the values for the young group are in all cases higher than for the elderly. On the other hand, the values increase from rs 1 to rs2 following the same trend for both young and older individuals , being this increase greater in the case of young adults.

These results can be observed in Figure 3, which shows results for each age group for the Alpha waveform in the 27th channel. As depicted in Figure 3, changes from rs1 to rs2 are more prominent in the young group compared to the older participants.

CH	p-value	CH	p-value	CH	p-value
9	0.016*	36	0.01547*	73	0.00695**
10	0.0167*	37	0.010406*	74	0.01405*
11	0.00084***	38	0.00234**	77	0.00834**
12	0.004803**	39	0.001**	79	0.00830**
13	0.000667***	40	0.00149**	82	0.008006**
14	3.81e-05****	41	4.99e-05****	84	0.01072*
15	0.00281**	43	0.0145*	88	0.00929**
23	0.009079**	44	0.00242**	90	0.00314**
24	0.002683**	45	0.000264***	91	0.006696**
26	0.00359**	57	0.01476*	95	0.010938*
27	4.42e-05****	62	0.010679*	96	0.0011**
28	0.0022**	67	0.00138**	99	0.0122*
29	0.009567**	68	0.01082*	100	0.01503*
31	0.00287**	69	0.00627**	108	0.0148*

Table 2: *Statistically significant results for the Alpha waveform case per channel (CH).*

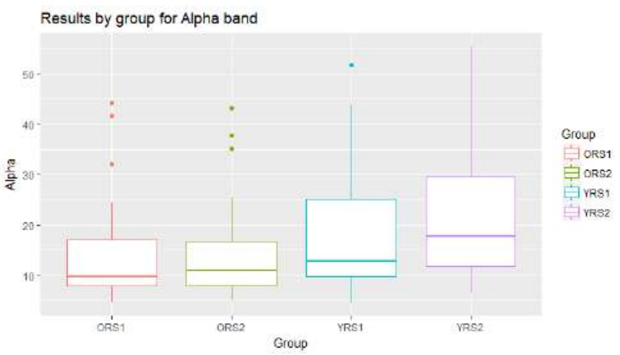

Figure 3: *Boxplots of the Alpha bandpower results for each group.*

5.2. Time-frequency analysis results

The results obtained from the analysis of the time-frequency data are not as prominent as in the previous case. In this instance, only 15 significant values are found after applying the FDR, as can be seen in Figure 4. However, it can be clearly seen that the alpha band is strongest in the third (Alpha3) and sixth (Alpha6) windows (intervals from 1:00-1:30 min and 2:30 -3: 00 min). After calculating the grand mean between the different windows, no relevant trend is seen.

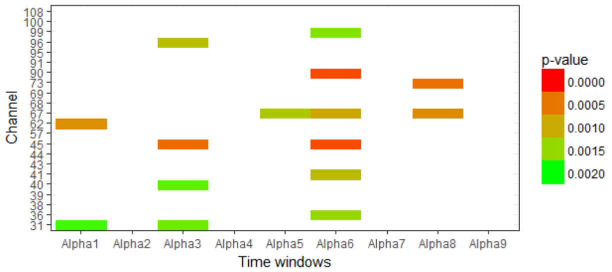

***Figure 4**: Statistically significant results for each time window in the Alpha waveform per channel.*

6. Conclusions

Due to the rapid population aging that most developed countries are experiencing, the search for techniques that allow to ameliorate the loss of cognitive abilities that older individuals face is a general priority. The innovative nature of the project MEMOTION is two-folded. First, we have designed a training program that benefits from well-preserved emotional processes to mitigate memory problems that occur with age. Second, we have used rs-EEG to predict age-related changes in the resting brain as a result of training. The current work is a preliminary approach that focuses on rs-EEG scans before the training program.

The main conclusions have been drawn from the data analysis of the frequency content of the analyzed signals. Statistically significant differences in the alpha band between rs1 and rs2 were found in the frontal, prefrontal and occipital zones for both young and older individuals. As for the delta waveform, statistically significant differences were found in the occipital area, although these may be a consequence of artifacts that were not completely removed in the pre-processing stage. The analyzed data shows that there is a significant increase in the power values from the first resting-state to the second one in both groups. This finding suggests that resting state can be used as a predicting tool to assess changes in neural activity after task performance. What is more, resting state changes as a result of the memory task are more prominent in the young adult group than in the elderly, showing that age is a significant factor that affects the resting state networks in the brain.

Regarding the results obtained for the time-frequency analysis, no statistically significant difference between the values for the different time windows have been obtained for all channels. This may be due to the window length selected for the analysis (30 seconds). Reducing this window length may throw significant results when data analysis techniques are applied on the time-frequency data.

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