राष्ट्रीय मस्तिष्क अनुसन्धान केंद्र
(समविश्वविद्यालय)
(जैव एवं प्रोद्योगिक विभाग का स्वायत संस्था,
विज्ञान एवं तकनीकी मंत्रालय, भारत सरकार)
एन० एच०-8, नैनवाल मोड़, मानेसर- 122051, (हरियाणा)

National Brain Research Centre
(Deemed University)
(An Autonomous Institute of Deptt. of Biotechnology,
Ministry of Science and Technology, Govt. of India)
NH-8, Nainwal Mode, Manesar-122051(Haryana)

CERTIFICATE

This is to certify that the dissertation entitled "Dynamics of resting state transient spectral alpha bursts with age" is the result of work carried out by **Mr.Darshit Mahesh Thakar** in National Brain Research Centre, Manesar, Haryana, India.

The work presented herein is original and has not been submitted previously for the award of any degree or diploma to **National Brain Research Centre (Deemed to be University)** or to any other University. This work is completely based on the guidelines given by **National Brain Research Centre** and is a record of the candidate's own efforts.

Supervisor

Director, NBRC 01/6/20

Place : Manesar

Date :29/05/2020

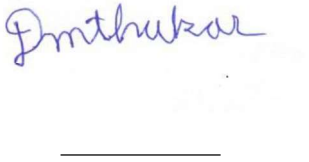
दूरभाष / Telephone: +91-124-2845 200 फैक्स / Fax : +91-124-2338910
ईमेल / Email : Info@nbrc.ac.in Website : www.nbrc.ac.in

DECLARATION

I, **Darshit Mahesh Thakar** hereby declare that the work presented in the dissertation entitled " Dynamics of resting state transient spectral alpha bursts with age" is carried out by me under the guidance of Prof. Arpan Banerjee, **National Brain Research Centre (Deemed to be University),** Manesar, Haryana, India.

I also declare that no part of this dissertation has been previously submitted for the award of any degree or diploma to **National Brain Research Centre** or any other University.

Place : Manesar



Date :29/05/2020

ACKNOWLEDGEMENT

First of all, I would like to thank my thesis supervisor Dr.Arpan Banerjee for guiding me through my master's thesis. He imparted quality ideas whenever necessary and also pursued me to think on my own to tackle problems. All the professors of NBRC played an indispensable role during the coursework in building my foundations of knowledge. I express my gratitude towards Dr.Dipanjan Roy for his valuable suggestions in the project. My lab mates helped me by discussing research ideas and also by motivating me whenever needed. I thank Neeraj Kumar who helped me in academics from the day I joined NBRC to helping me troubleshoot MATLAB codes and research papers. My batch mates are amazing and I got to learn a lot from them. It was a memorable experience with the batch of 2018. I express my gratitude towards all in NBRC who have directly or indirectly helped me during my stay at the institute.

My heartfelt thanks to my parents, my brother Arpit and all my other family members. They have supported me through all phases of life and their life itself has inspired me to keep on going in spite of any adverse circumstances. Finally, with Almighty's grace I wish to find happiness and satisfaction in my career ahead.

DARSHIT
THAKAR

ABSTRACT

Author: Darshit Mahesh Thakar

Title: Dynamics of resting state transient spectral alpha bursts with age

Institution: National Brain Research Centre

Dissertation Advisor: Dr.Arpan Banerjee

Degree: Master's in Neuroscience

Year: 2020

Brain oscillations are fluctuations in the potential difference if measured by EEG or fluctuations in the magnetic field if measured by MEG. Resting state in the absence of external stimulus leads to self-evolving oscillations in the brain. Brain is never at rest. In the absence of external stimuli, brain is functioning by planning future events and tasks, recalling past experiences hence consolidating memory and is ready to receive a unique stimulus which can draw our attention towards it. Alpha oscillation is known to play a role in drawing attention towards a salient stimulus. Neuroimaging studies and autopsy studies have shown that even healthy aging leads to atrophy of the nervous tissue. One can speculate that this will certainly have an impact on the brain oscillations. Alpha oscillation is most prominent during resting state and is known to change many of its properties with increasing age. Hence the dynamics of oscillations at rest does have a lot of clinical applications. We look for such dynamics of the alpha waves over various regions of the brain and analyse changes in it with age. The subjects are healthy individuals with age from 18 years to 88 years. For our alpha oscillation dynamics, we defined alpha burst. It is a spectral event which crosses a statistical z score threshold for the

alpha power at 10 Hz and is sustained for 1 second or more. We then looked on the number of these spectral events and then compared it between three age groups i.e. young, middle aged and old. We did find some differences between the age groups mainly in the occipital sensors, prefrontal sensors and global i.e. all sensors. A general trend observed across all the sensors is that the total duration and number of such spectral events increases with age i.e. from young to middle-age and then decreases again for the old age across most of the sensors. This is just one way of defining a spectral event. By collecting empirical data from a huge population of healthy and population suffering from neurodegenerative diseases, we can compare the oscillations in healthy aging with that of neurodegeneration. Healthy aging brain shows some atrophy and hence some researchers term Alzheimer's disease as rapid aging. If we look into the perturbations of the resting state dynamics, we can draw a model of healthy aging which can be used for diagnostic purposes like early prediction of diseases. In case of disorders we can predict the extent of progression by non-invasive techniques like MEG and EEG.

Contents

List of figures

List of tables

1 Introduction

1.1 Brain Oscillations

In humans, brain waves were first discovered in 1932 by Hans Berger. In his publication in 1929 he wrote “The electroencephalogram represents a continuous curve with continuous oscillations in which one can distinguish larger first order waves with an average duration of 90 milliseconds and smaller second order waves of an average duration of 35 milliseconds. The larger deflections measure at most 150 to 200 microvolts” (Buzsáki, 2009). Berger named the waves with high amplitude at an approximate frequency of 10Hz alpha waves. Berger didn’t know anything thing about technical and physical basis of the waves and the mechanics to extract further information from the waves (MCCRUM, 1964). Since then we have come a long way. The analysis of brain waves has found its way in diagnosis of epilepsy (Uhlhaas & Singer, 2006) and research is going on to further elucidate its implication in other psychiatric disorders like schizophrenia (Uhlhaas, Haenschel, Nikolić, & Singer, 2008). The right tools are required to accomplish a task, similarly to record the brain waves one needs some sophisticated equipment that serve as a window for us to have a peek into the brain. EEG (electroencephalogram), MEG (magnetoencephalogram), ECog (electro cortigogram), and LFP recordings with microelectrodes are the methods widely used to record brain oscillations. The former two are non-invasive while the latter two are invasive techniques requiring surgical implantation of electrodes into the brain. EEG records fluctuations in the potential difference, while MEG records the fluctuations in the magnetic field as brain waves.

1.2 Origin of Brain oscillations

Any excitable membrane whether it is a spine, dendrite, soma, axon or axon terminal and any type of transmembrane current contributes to the extracellular field (Buzsáki, Anastassiou, & Koch, 2012). Neurons transmit information through action potentials. This action potential is a result of change in voltage across the membrane. This leads to the release of neurotransmitter which again causes change in membrane potential at the dendritic spines. Only if thousands of cells contribute their small voltage, the signal becomes large enough at the scalp to be measure by the EEG electrode at the scalp. This process occurs across the brain and leads to fluctuation in the potential measured at the scalp. The EEG recorded from the scalp

samples mostly the synaptic activity that occurs in the superficial layers of the cortex. The contribution of deeper layers is scaled down substantially, whereas the contribution of neuronal activity from below the cortex is, in most cases, virtually negligible (Buzsáki, 2009).

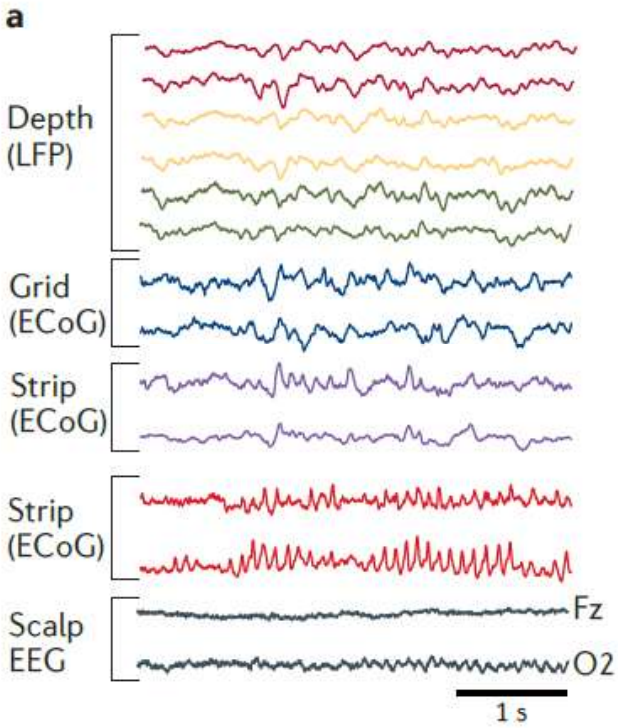


Figure 1. 1- Brain oscillations at varying depths in brain tissue

The diminishing magnitude of the wave shows the dampening of signal away from the source due to resistance from the tissue (Buzsáki et al., 2012). This dampening is not observed in case of MEG, but if far from the source the magnitude of field does decrease as shown in figure below.

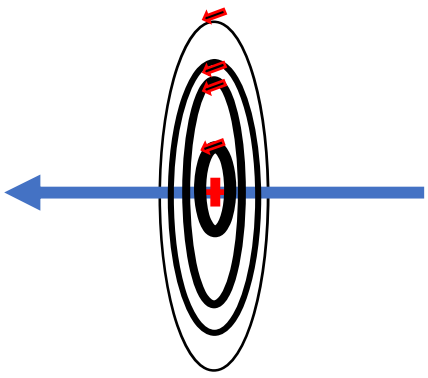


Figure 1. 2- Magnetic field around a moving positively charged particle.

The blue arrow shows the direction of movement. The direction of magnetic field can be determined by the right-hand rule. The thinning of magnetic field lines shows diminishing magnitude of magnetic field with distance.

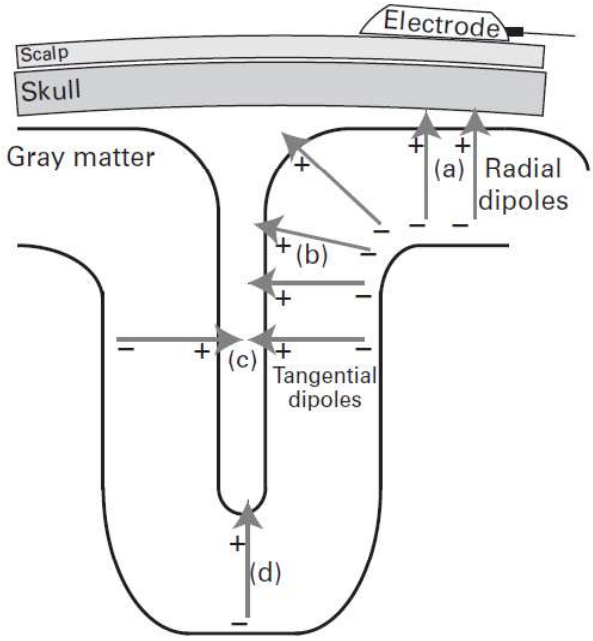


Figure 1. 3- dipoles contributing to EEG and MEG signals (M. X. Cohen, 2014)

a) dipole is a radial dipole and contributes the most to the potential difference recorded in EEG. The b) dipole is a tangential dipole and it generates magnetic field perpendicular to it. This magnetic field is recorded by the magnetometers in the MEG sensors. The tangential dipoles cancel each other's electric field and are not recorded by the EEG electrodes. The dipole at d contributes to EEG signal but its magnitude is very less as it is located away from the scalp.

1.3 Measuring the magnetic field of the brain

The magnetic field generated by the neurons is extremely minute. It is in the units below 10^{-12} Tesla, which is way beneath the earth's magnetic field ($0.5x10^{-4}$ T) and urban magnetic noise (10^{-7} T) (D. Cohen & Halgren, 2003). A comparison with EEG shows is shown below.

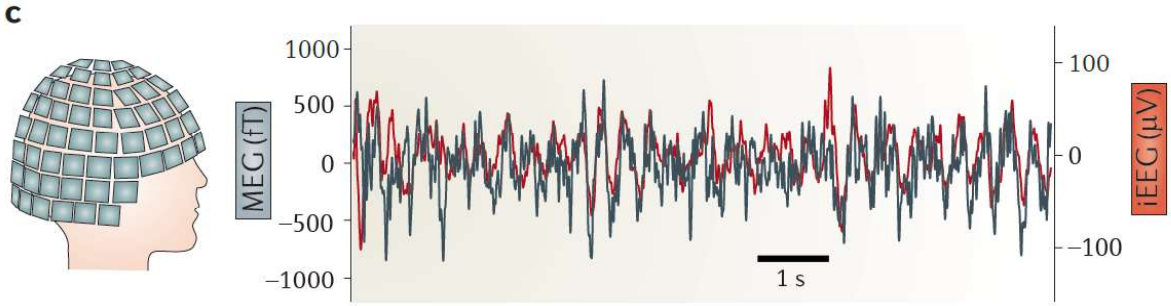


Figure 1. 4- schematic comparision of MEG and EEG signal.

On the left the units are in femto tesla(10^{-15}) while on the right the units are in microvolts(10^{-6}). To measure such a minute magnitude of magnetic field, there are sophisticated magnetometers called SQUID (superconducting quantum interference device). MEG setup contains these SQUID arranged in the shape of a helmet to fit the human headshape (Figure 1. 4). The room is magnetically shielded to minimise external magnetic interference. Each SQUID measures the magnetic field with a temporal resolution of 1 ms, which varies with the manufacturer and settings of equipment. When plotted against time, it gives us the raw MEG signal.

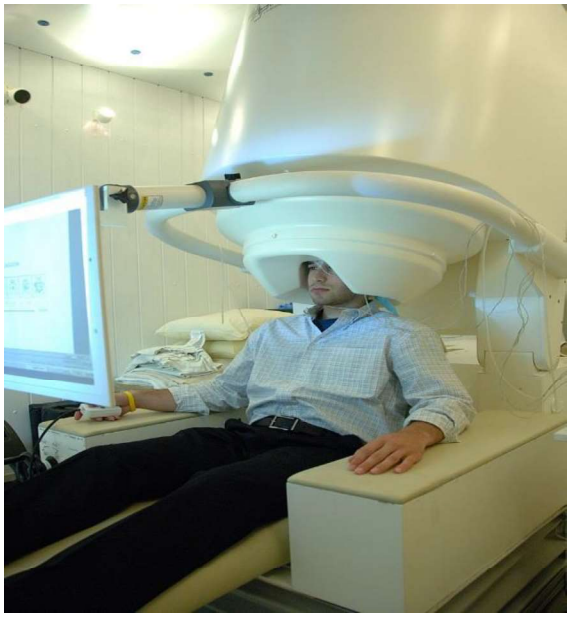


Figure 1. 5- Magnetoencephalogram recording machine. An array SQUID is located in the helmet like structure supercooled with liquid helium. In front of the participant is the screen for stimulus display

1.4 Oscillations and spectral analysis

The raw signal recorded by EEG and MEG is a mixture of frequencies up to the Nyquist (Sampling rate/2). The frequencies of interest in the brain oscillations are Delta waves (0.1 to 4Hz), Theta(4-7Hz), Alpha(8-12Hz), Beta(13-30Hz) and Gamma(30-90Hz). The raw signal is a mixture of all these frequencies. To delineate these individual frequencies from the raw signal one needs to perform the transformation of the signal. Here the key of extracting the information is to transform the data from time domain to frequency domain. Most widely used transformation is the Fourier transform. It provides amplitude of sine functions of various frequencies up to the nyquist that exist throughout the entire duration of the signal (Le Van Quyen & Bragin, 2007).

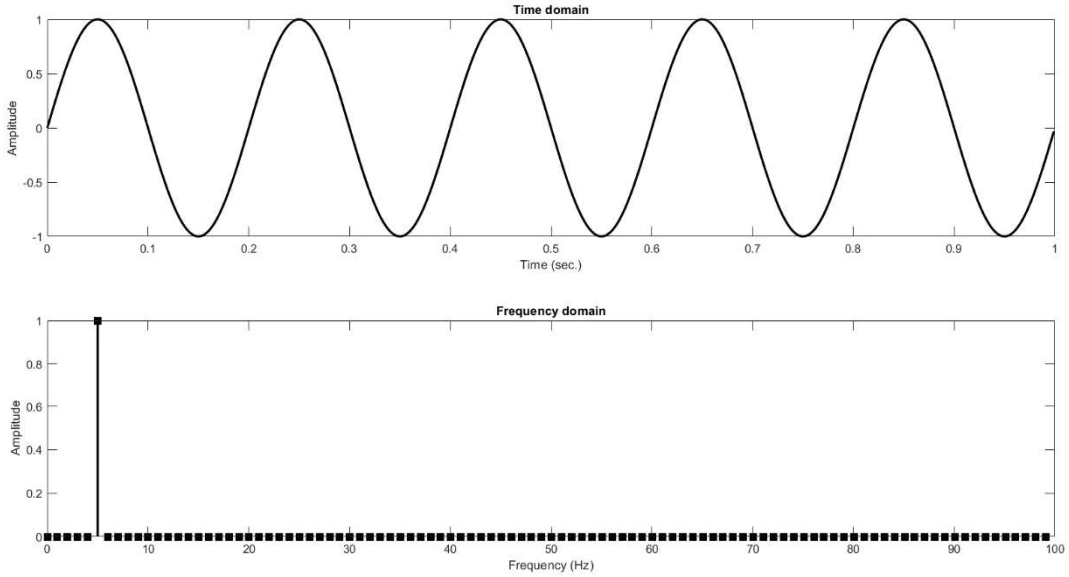


Figure 1. 6- sine wave with frequency 5 Hz and its Fourier transform showing amplitude 1 at 5Hz

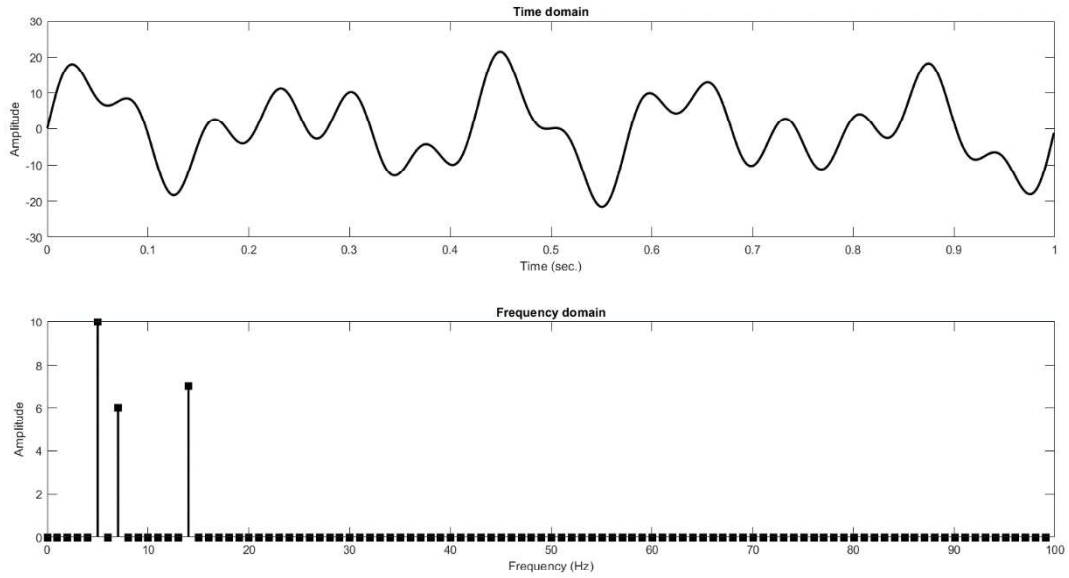


Figure 1. 7- mixed sine waves with frequency 5, 7, 14 Hz and its Fourier transform showing amplitude 10, 6 and 7 at their respective frequency.

2 Methods

2.1 Participants

The data was collected by Cambridge Centre for Ageing and Neuroscience. Cam-CAN is a multi-modal, cross-sectional adult life-span population-based study. There were 650 participants ranging from age 18 to 88. These participants were tested for cognitive measures and neuropsychological test like vision, hearing, verbal intelligence etc. For our study I have selected 240 participants from three age groups. The participants were divided into three groups young, middle-aged and old by us. Each group consisted of 80 participants with young group from age 18 to 32, middle-aged 49 to 57 years and old aged group from 79 to 88.

2.2 Stimulus and Trials

During the whole recording the participant was at rest with eyes closed. No stimulus was presented hence it is termed resting state recording. The recording was a single length for each participant with an average duration of 550 seconds.

2.3 Neuroimaging Technique

The neuroimaging technique used in the study was MEG. The data was acquired using Elekta Neuromag with 306-channel system consisting of 102 magnetometers and 204 gradiometers with a sampling frequency of 1000 Hz or 1 ms. The data from the magnetometers was used for spectral analysis.

2.4 The question

With researchers reporting the slowing of alpha power with age in power spectrum, changes in network oscillations (Sahoo, Pathak, Deco, Banerjee, & Roy, 2020) and bistability in the alpha power distribution (Freyer, Aquino, Robinson, Ritter, & Breakspear, 2009), we decided to look into the dynamics of alpha burst with increasing age. I was given raw MEG data which was acquired from Cam-CAN and I began my preliminary analysis. I performed spectral density estimation of a single participant and the plotted a spectrogram of a single channel.

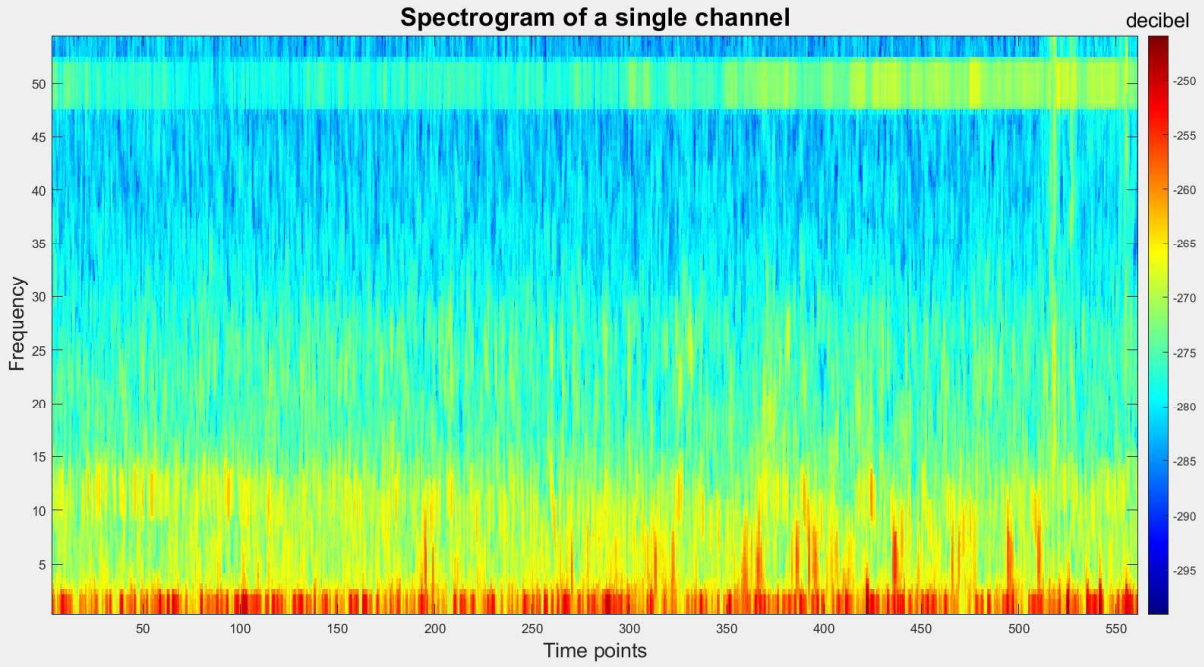


Figure 2. 1- Spectrogram of a single magnetometer channel

We noticed a repeating alpha activity, the yellow and red patches between 8 to 12 on the Y axis. Hence, we decided to look into the dynamics of alpha oscillations. We asked questions like whether the duration of these high-power alpha activity change with age? Whether the number of such high-power alpha activity change with age? We called this high-power alpha activity as alpha burst.

2.5 Data Analysis

The raw data was already ICA corrected for head movements. Field trip toolbox for MATLAB was used to read the raw files and chronux toolbox was used for Spectral density estimation.

Spectral density estimation has some advantages over the Fourier transform for analysis of neural time series data. Practically neural oscillations are dynamic. Fourier transform provides the spectral content of the signal but it does not provide the information about the time at which the dynamics take place (Le Van Quyen & Bragin, 2007). Hence, time-frequency analysis helps us delineate each spectral component with a specific time and frequency. The method used for spectral density estimation is multitaper method. The tapers in multitaper analysis was set to [3 5] and the moving window set to [1.2 0.01]. This operation was performed for 102 magnetometers channels for each subject.

Division of the sensors

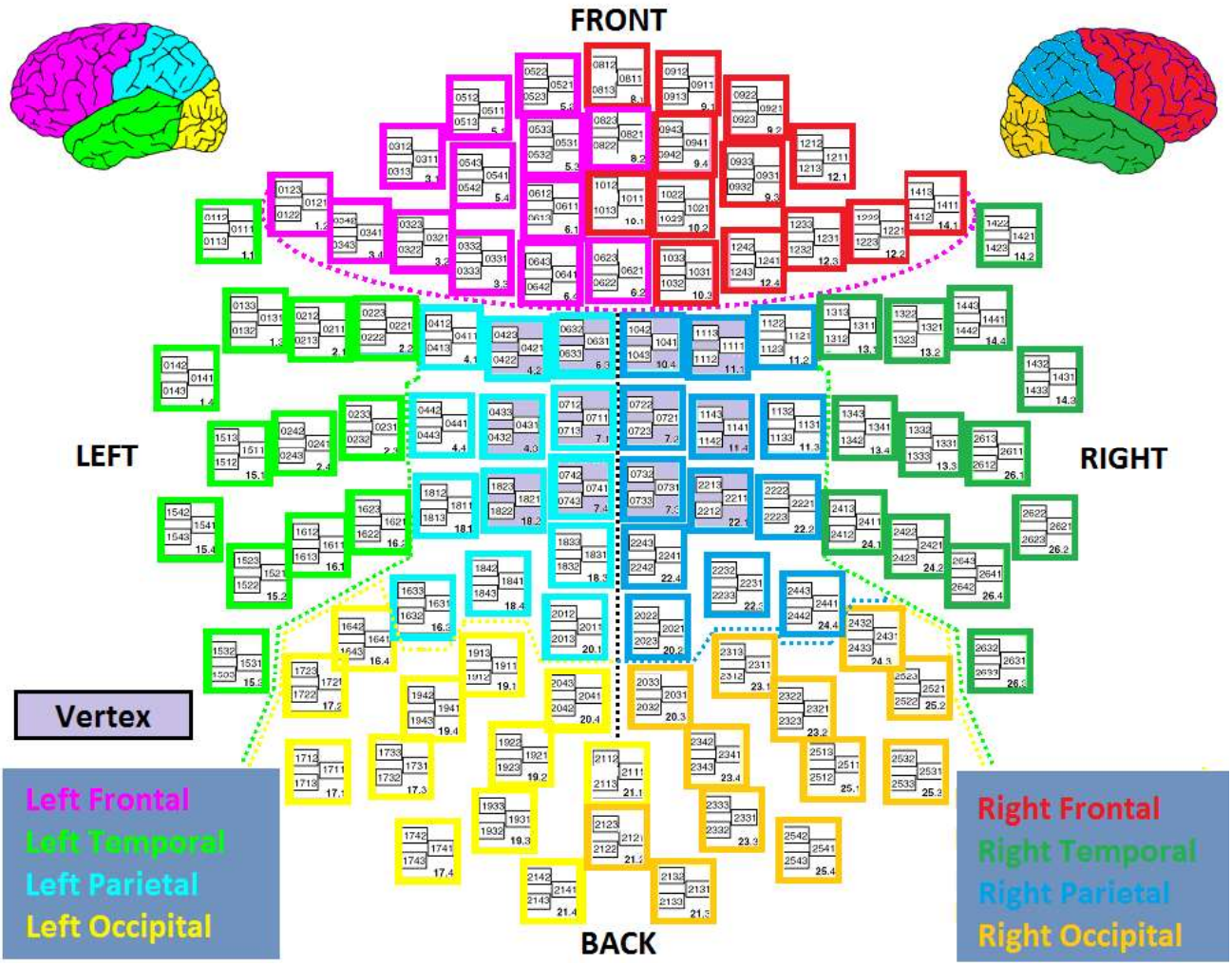


Figure 2. 2– Layout of the MEG sensors, Elekta Neuromag MEG channel positions (Abadi et al., 2015)

The sensors were classified according to their location. Global sensors – included all the 102 sensors, occipital sensors included sensors from the occipital cortex, prefrontal sensors included sensors from the prefrontal cortex, motor cortex, occipital cortex and sensory cortex. Once the sensors were divided the power was averaged across the extracted sensors

For e.g. for global alpha power grand average was performed across 102 sensors, for occipital sensors the average was performed across 22 sensors and so on.

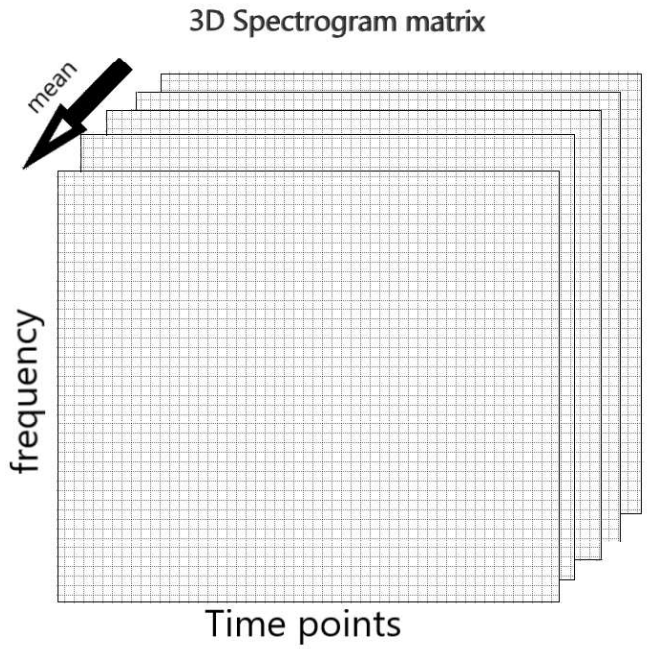


Figure 2. 3- Representation of a 3D spectrogram matrix. The third dimension contains individual sensors

Each 2D matrix represents spectrogram matrix of one sensor. The row is represented by the frequency while the columns by time points. The value in the corresponding cell, indicates the power at that frequency and time. The sensors were indexed out according to their location above the head and then the power was averaged across the sensors. The power at frequency 10 Hz was extracted based on the frequency indices.

2.5.1 Defining Alpha burst

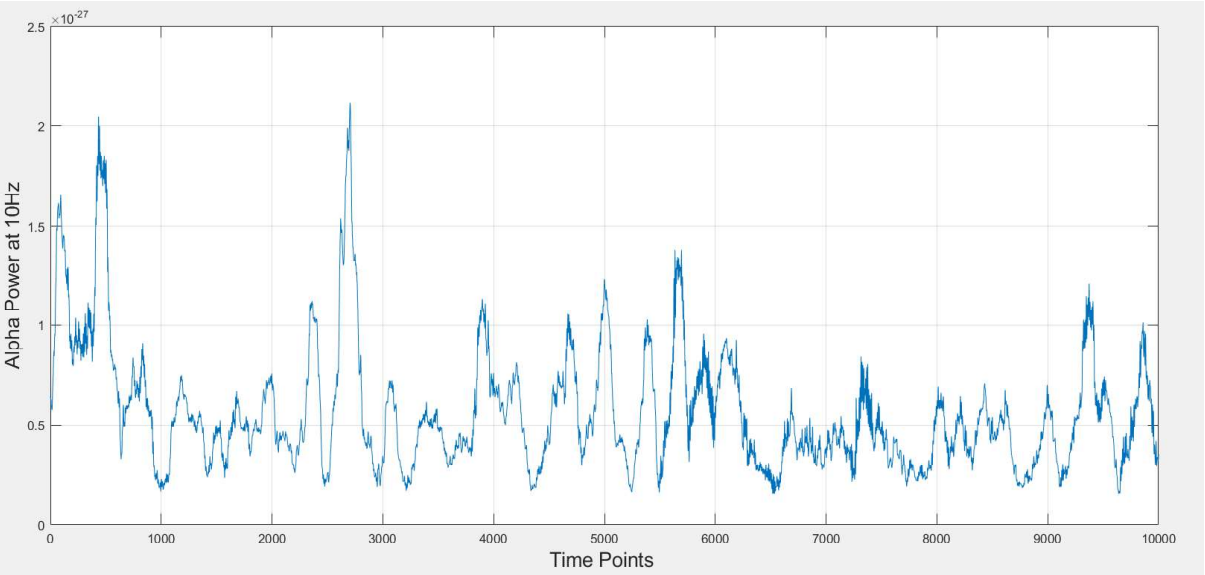


Figure 2. 4- Power at 10 Hz for a typical subject It has some periods of high amplitude phases followed by low amplitude phases.

On performing spectral analysis and plotting a scatter plot for maximum and minimum alpha power across age we found the maximum and minimum alpha to be highly variable among the same age group. Hence, we decided to define an alpha burst by the z score threshold method to normalise the alpha burst threshold among subjects. For e.g. if the alpha power at a particular time point crosses a z-score of 2.5 and is sustained for more than 1 second is termed an alpha burst. The number and time of each of those bursts is recorded and then compared across ages.

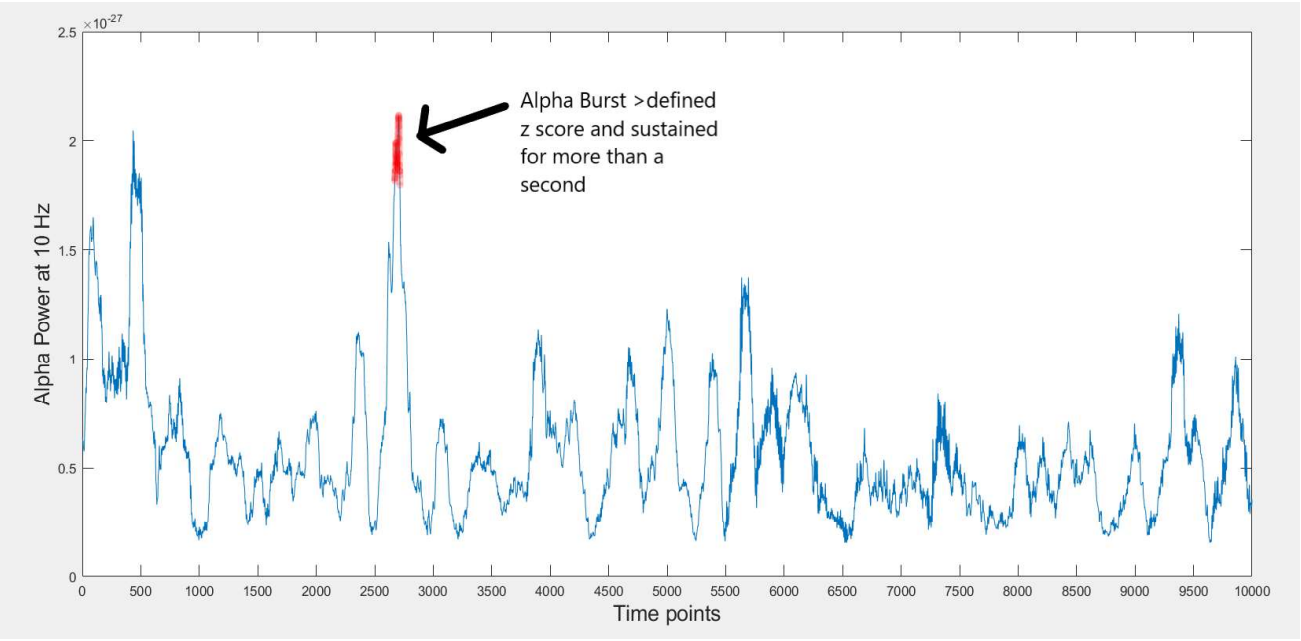


Figure 2. 5- Schematic representation of the alpha burst, defined as the alpha power which crosses a defined z-score(threshold) and is sustained for a set period of time.

2.5.2 Dynamics of the Alpha Burst

Three parameters of the alpha burst were analysed in this study, then statistically tested to check for the difference in the data.

1. Mean Power of each burst – A burst consists of a vector in which the dimension is time points and the values in the cells is the corresponding power. Mean of all the cells in that vector gives mean alpha power of that burst. This value is concatenated with other bursts to form a vector for each group. The length of the vector is the total number of bursts for that group
2. Length of Burst – The total time points in one burst is the length of each burst. From the parameters set for multitaper analysis, the time resolution is 10 milli second, hence the time between two adjacent time points is 10 milli sec.
3. Number of Bursts - Bursts classified based on the above criteria are counted for each subject.

3 Results

The number of bursts increases for the middle-aged population and then decreases for the old aged, so does the total length of the burst. This observation is consistent across all the sensors. The trend followed by the average alpha power across subject groups, is not in consensus with the length and number of bursts. (table 3. 1)

ANOVA – One-way ANOVA with a significance level of 0.05 was performed to check for the difference in the distribution of data between the age groups. Only the sensor groups which showed a significant difference in distribution in any one of the dynamics mentioned above are displayed as figures and ANOVA table.

Groups	Number of Subjects	Burst Count	Average Length $x10^{-2}$ sec	Average Alpha Power(averaged over burst count)	Standard Deviation
Global Y	80	251	414.9875	6.60695E-27	5.11693E-27
Global M	80	281	491.4	5.54819E-27	5.08391E-27
Global O	80	262	428.125	6.31342E-27	5.12137E-27
Occipital Y	80	253	426.275	9.84668E-27	8.02759E-27
Occipital M	80	298	521.4125	8.23376E-27	8.15389E-27
Occipital O	80	300	488.225	7.83395E-27	6.91987E-27
Motor Y	80	290	447.55	2.84721E-27	2.61179E-27
Motor M	80	342	541.85	3.37086E-27	3.36284E-27
Motor O	80	301	481.575	3.18198E-27	2.2729E-27
Frontal Y	80	240	366.025	1.76987E-27	1.38777E-27
Frontal M	80	298	460.3375	1.91773E-27	1.82598E-27
Frontal O	80	264	414.125	1.94802E-27	1.26353E-27
Sensory Y	80	300	464.4	5.49616E-27	5.25658E-27
Sensory M	80	346	562.225	5.73602E-27	5.69349E-27
Sensory O	80	321	521.0625	5.42215E-27	4.7362E-27

table 3. 1- Summary of results – alpha burst Dynamics

ref Y – Young, M – middle-age , O - Old

Observation – The mean total time is lowest for the young population. As the age increases, we observe an increase in the mean total time of the alpha burst and it decreases for the old population. On performing one factor ANOVA with a significance level of 0.05, we get a p value of 0.03758. The data in the groups is non-normal, hence on performing a Wilcoxon rank sum test we find that the young population is significantly different from middle-aged group. There is no significant difference between the middle-aged and the old and between young and old (figure 3. 1 table 3. 2).

A similar trend is observed in the number of alpha bursts in the prefrontal sensors. The mean number of bursts increases for the middle-aged group and it decreases for the old group. On performing one factor ANOVA with a significance level of 0.05, we get a p value of 0.0379. In the post hoc analysis by Wilcoxon rank sum test we find that the young group is significantly different from the middle-aged group while the there is no significant difference between the middle-aged and old and also between young and old (figure 3. 2 table 3. 3). While there is an increase in the mean alpha power with age, the ANOVA results show no significant difference in distribution (figure 3. 3 table 3. 4).

The trend shown for the total time points of global sensors is similar to that of frontal sensors. The ANOVA does not result in a significant difference in the distribution (figure 3. 4 table 3. 5). The trend shown for the total number of bursts of Global sensors is similar to that of frontal sensors. The ANOVA does not result in a significant difference in the distribution (figure 3. 5 table 3. 6).

The mean power (global sensors) for each burst shows a decrease in the mean power for the middle-aged group and then an increase for the old aged group. One-way ANOVA results in a significant difference in distribution between the groups. Post hoc analysis by Wilcoxon rank sum test reveals that young age group is significantly different from the middle-aged, but not from the old aged group. The middle aged and the old aged groups show significant difference (figure 3. 6 table 3. 7).

The trend shown for the total time points of occipital sensors is similar to that of frontal sensors and global sensors. The ANOVA does not result in a significant difference in the distribution (figure 3. 7 table 3. 8).

The trend shown for the total number of bursts of occipital sensors is little different of frontal sensors and global sensors. The mean number of bursts does not decrease for the occipital sensors. The ANOVA does not result in a significant difference in the distribution (figure 3. 8 table 3. 9).

The Occipital sensors show a decrease in the mean power with age. One-way ANOVA results in a significant difference for the distribution between the groups. Post hoc analysis reveals that the young group is significantly different from the other two. Hence, we can say that the mean power of each alpha burst decreases with age but there is an uncertainty for the transition from middle aged to old aged group (figure 3. 9 table 3. 10).

3.1 Prefrontal cortex sensors

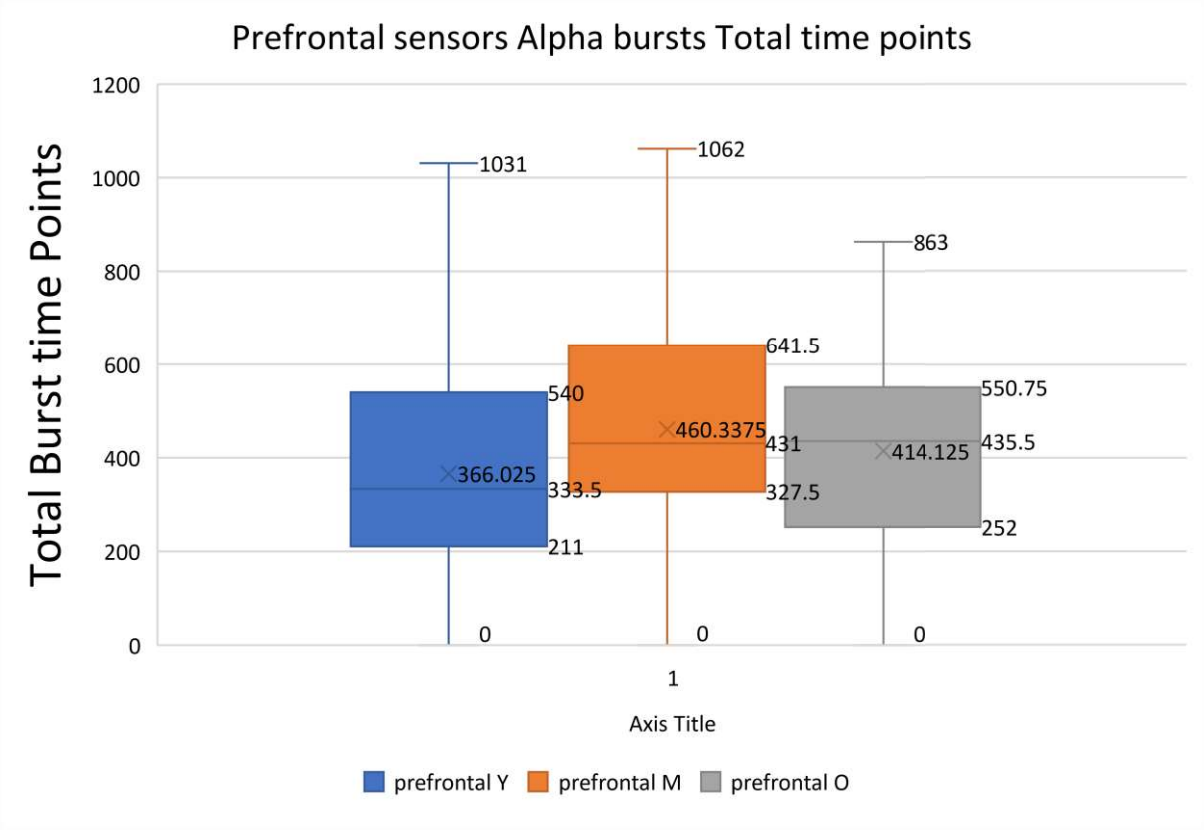


figure 3. 1- prefrontal cortex alpha burst total time points

SUMMARY				
Groups	Count	Sum	Average	Variance
Frontal Y	80	29282	366.025	62126.58
Frontal M	80	36827	460.3375	62639.01
Frontal O	80	33130	414.125	35664.31

ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	355841.408	2	177920.7	3.327074	0.037582	3.03392
Within Groups	12673962.6	237	53476.64			
Total	13029804	239				

Post hoc Wilcoxon test	P value
P Young-middle-aged	0.017999729
P middle-aged- Old	0.379516343
P Young- Old	0.098903206

table 3. 2- Anova table Prefrontal sensors alpha burst total time points

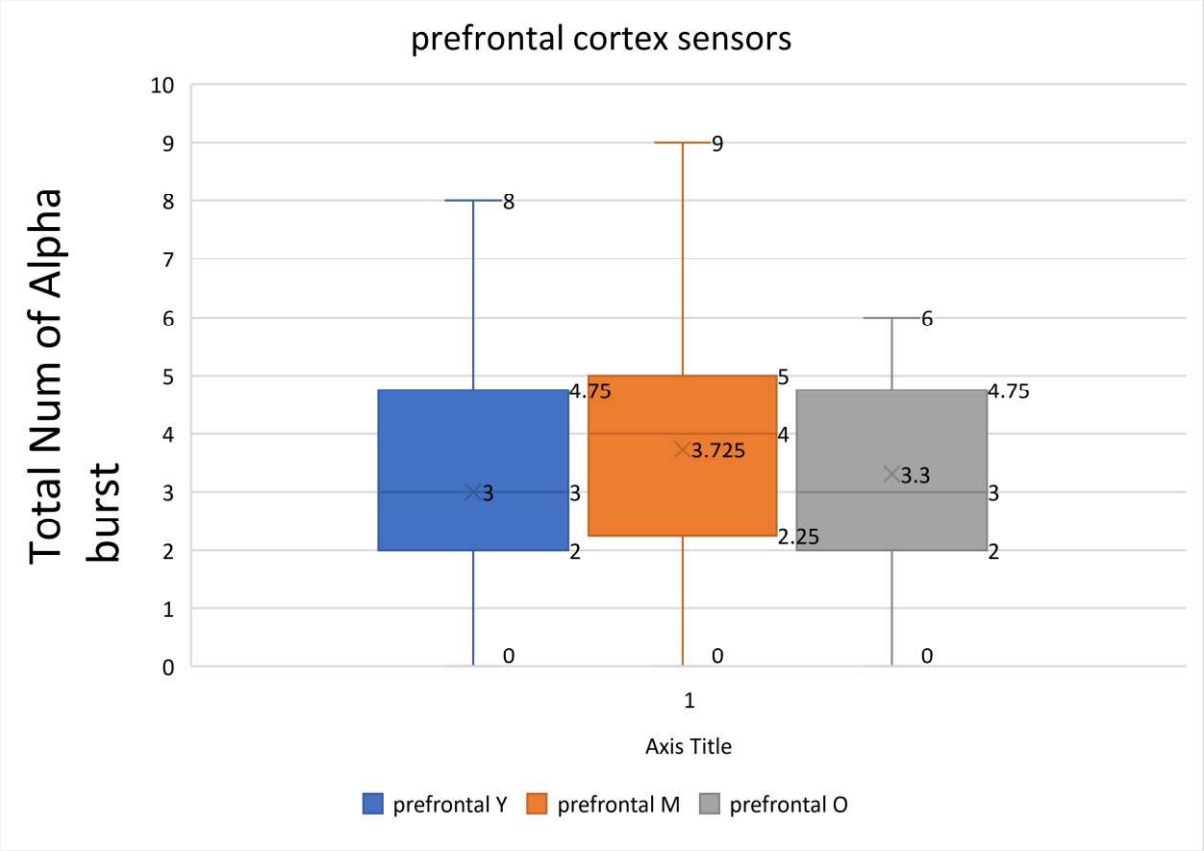


figure 3. 2- prefrontal cortex number of alpha bursts

SUMMARY

Groups	Count	Sum	Average	Variance
Frontal Y	80	240	3	3.974684
Frontal M	80	298	3.725	3.568987
Frontal O	80	264	3.3	2.060759

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	21.23333	2	10.61667	3.316178	0.037983	3.03392
Within Groups	758.75	237	3.201477			
Total	779.9833	239				

Post hoc Wilcoxon test	P value
P Young-middle-aged	0.011981
P middle-aged- Old	0.14917
P Young- Old	0.158024

table 3. 3- ANOVA prefrontal cortex number of alpha bursts

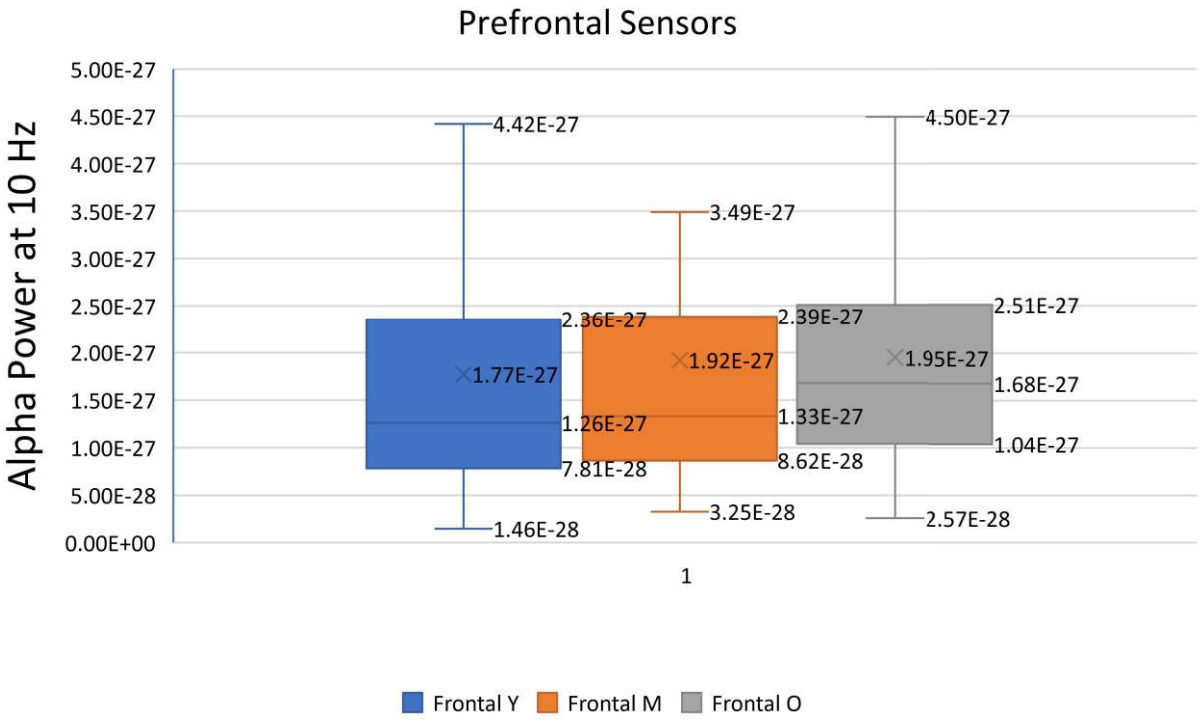


figure 3. 3- Prefrontal sensors mean power of bursts.

Anova: Single Factor

SUMMARY

Groups	*Burst Count*	*Sum*	*Average*	*Variance*
Frontal Y	240	4.25E-25	1.77E-27	1.93E-54
Frontal M	298	5.71E-25	1.92E-27	3.33E-54
Frontal O	264	5.14E-25	1.95E-27	1.6E-54

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	4.55E-54	2	2.27E-54	0.971194	0.379077	3.006992
Within Groups	1.87E-51	799	2.34E-54			
Total	1.87E-51	801				

table 3. 4- ANOVA Prefrontal sensors mean power of bursts

3.2 Global sensors

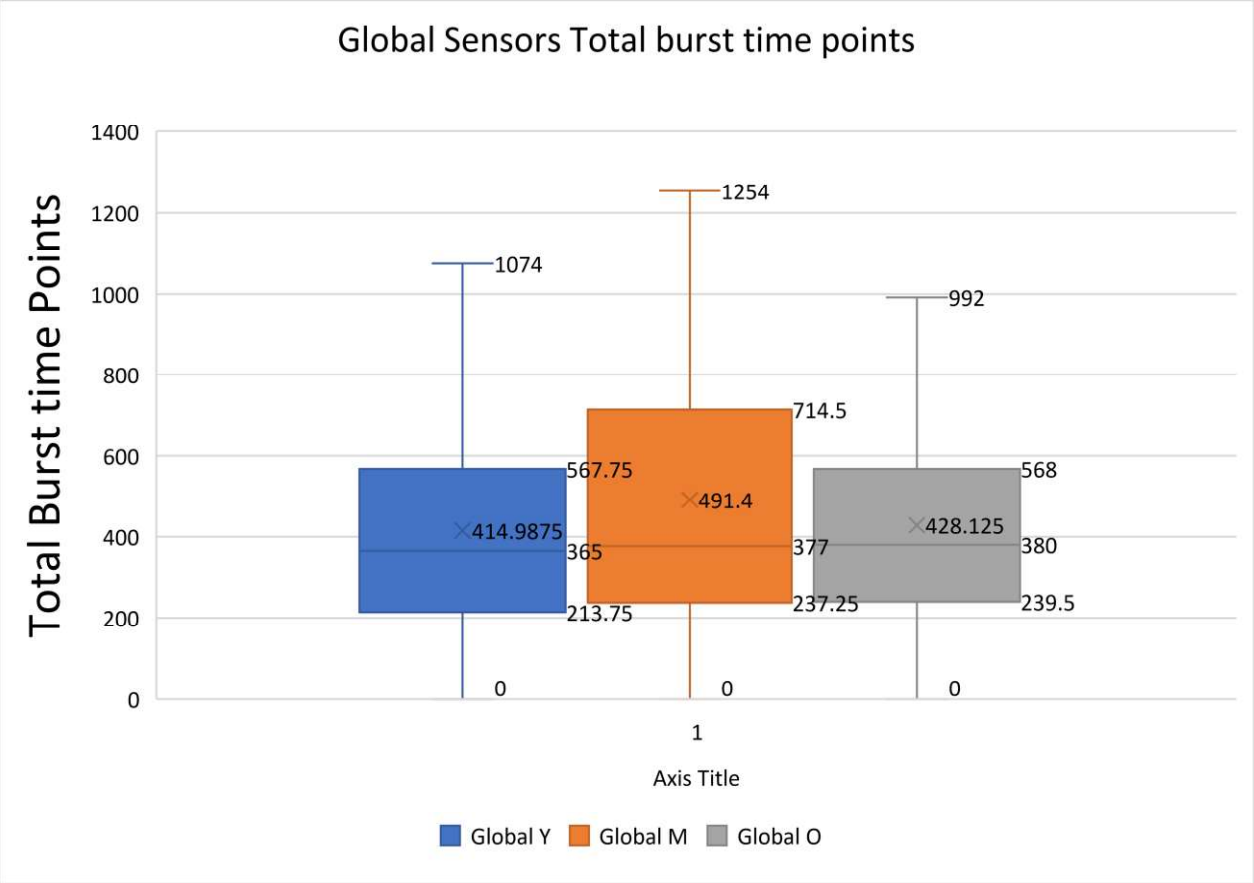


figure 3. 4- Global sensors total burst time points

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Global Y	80	33199	414.9875	84170.57
Global M	80	39312	491.4	124772.8
Global O	80	34250	428.125	77441.73

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	267071.725	2	133535.9	1.398842	0.248913	3.03392
Within Groups	22624422.9	237	95461.7			
Total	22891494.7	239				

table 3. 5- ANOVA Global sensors total burst time points

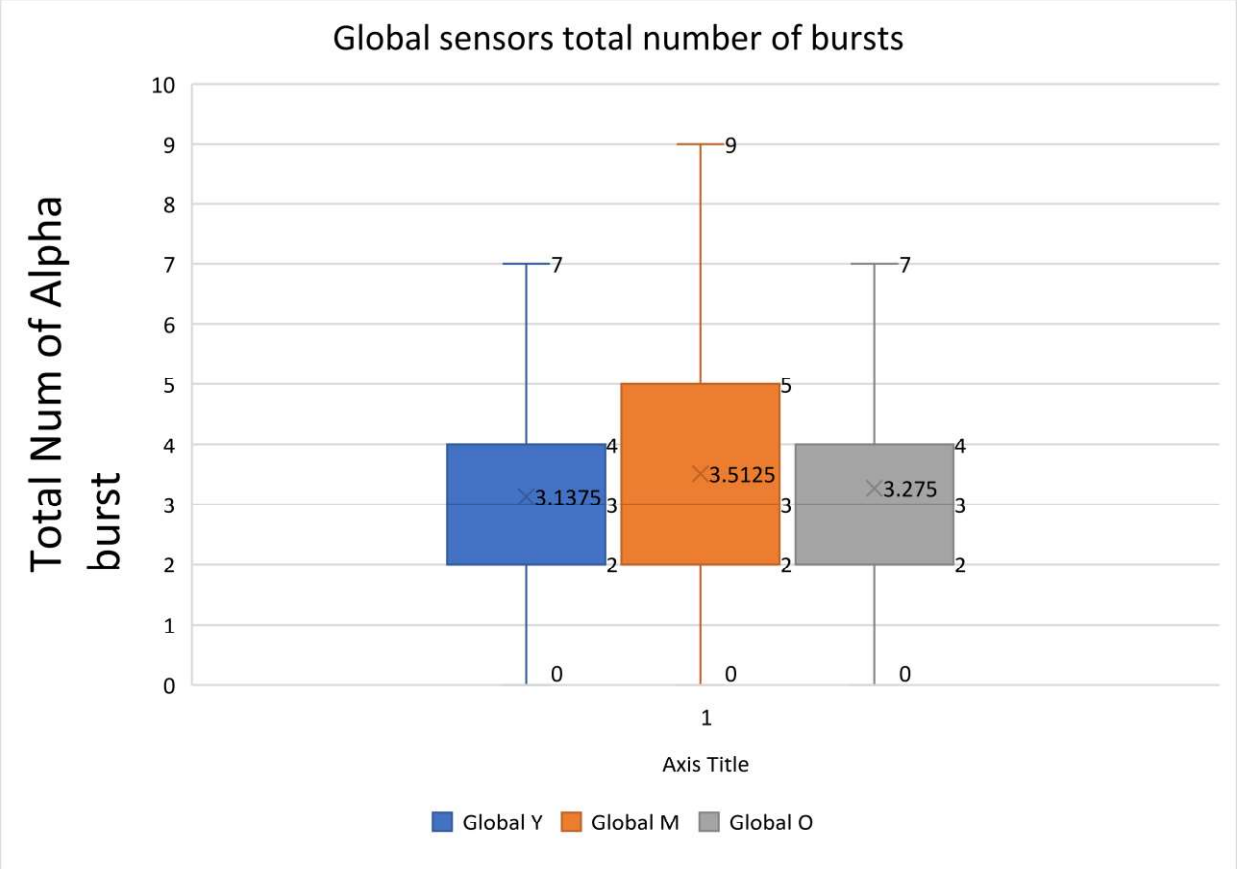


figure 3. 5- Global sensors total number of bursts

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Global Y	80	251	3.1375	3.715032
Global M	80	281	3.5125	5.139082
Global O	80	262	3.275	4.303165

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	5.758333	2	2.879167	0.656481	0.519614	3.03392
Within Groups	1039.425	237	4.385759			
Total	1045.183	239				

table 3. 6- ANOVA Global sensors total number of bursts

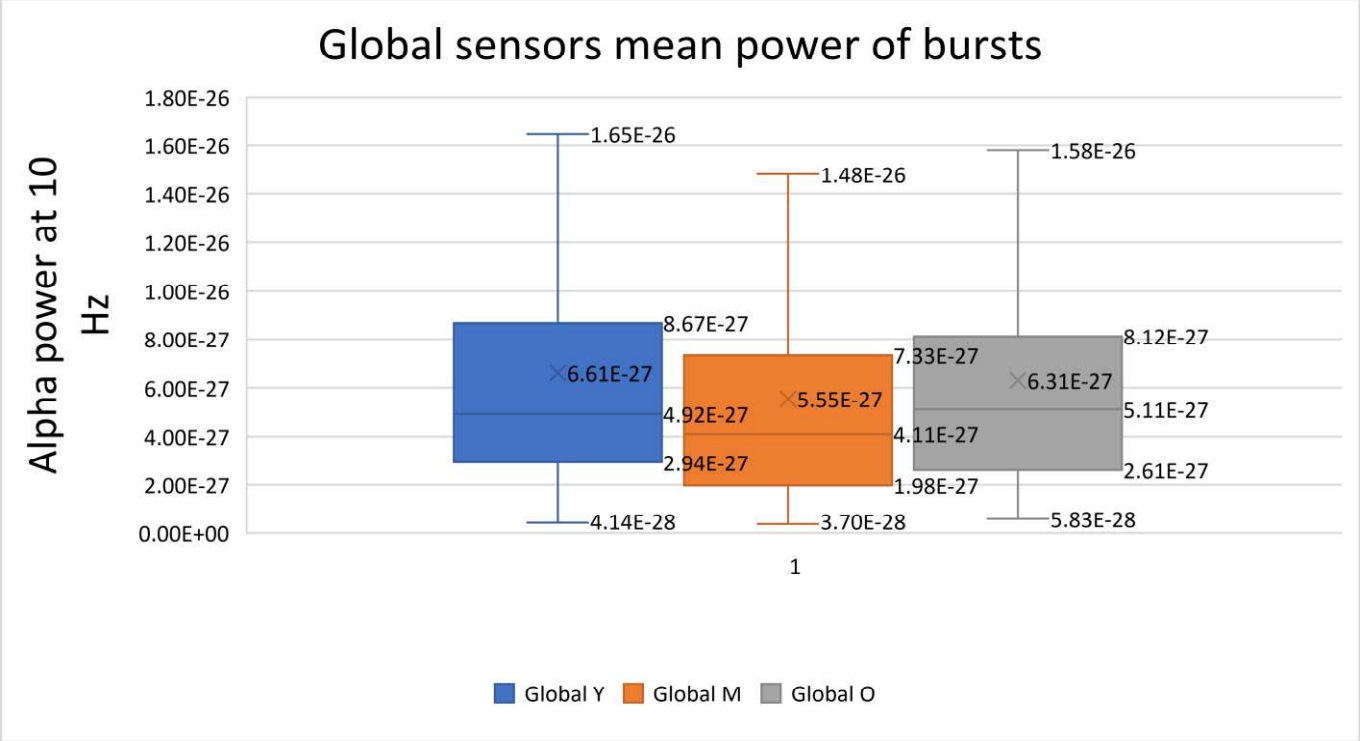


figure 3. 6- Global sensors mean power of bursts

SUMMARY

Groups	Count	Sum	Average	Variance
Global Y	251	1.65835E-24	6.60695E-27	2.62E-53
Global M	281	1.55904E-24	5.54819E-27	2.58E-53
Global O	262	1.65412E-24	6.31342E-27	2.62E-53

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	1.61E-52	2	8.05052E-53	3.08700	0.046189	3.00710
Within Groups	2.06E-50	791	2.60787E-53			
Total	2.08E-50	793				

Post hoc Wilcoxon test	P value
P Young-middle-aged	0.00161
P middle-aged- Old	0.01935
P Young- Old	0.4642

table 3. 7- ANOVA Global sensors mean power of bursts

3.3 Occipital sensors

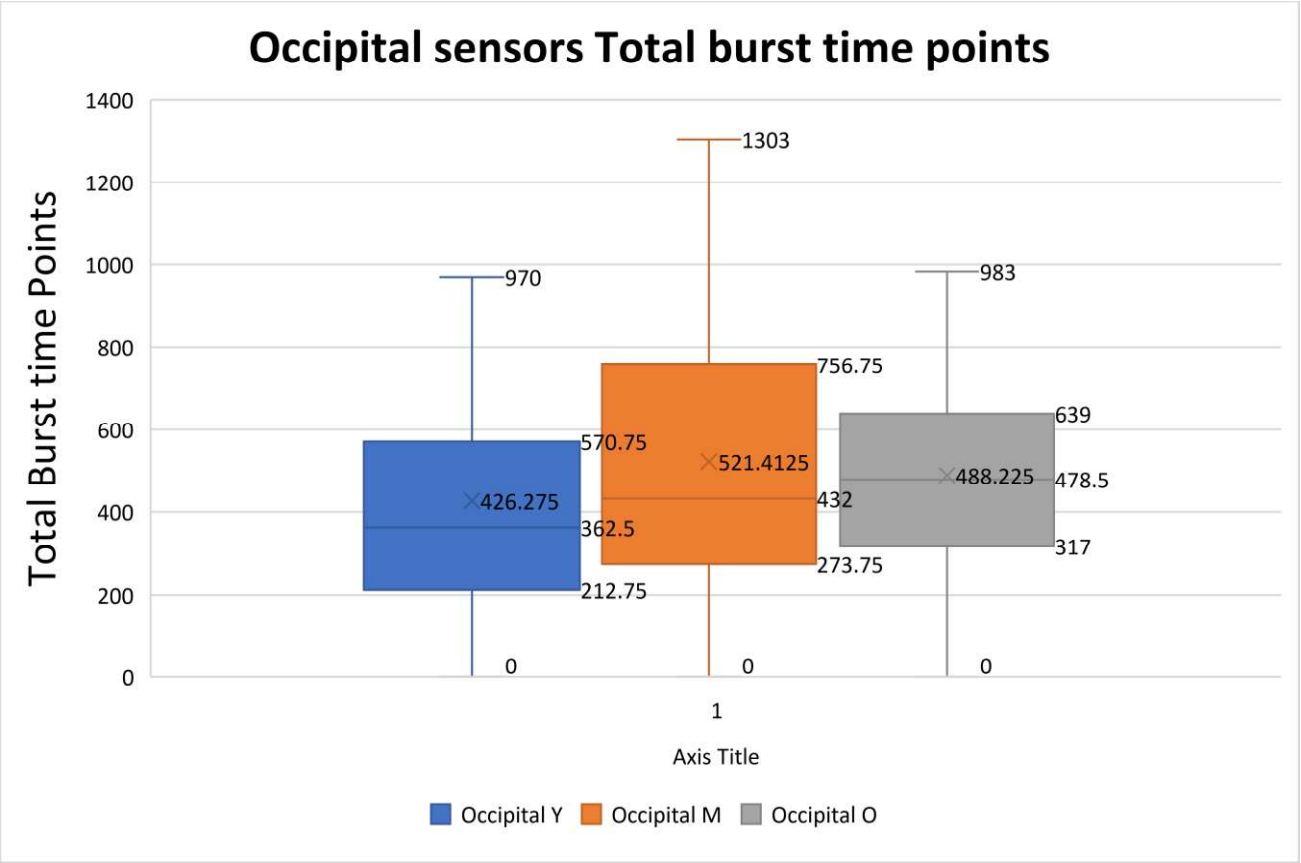


figure 3. 7- Occipital sensors total burst time points

SUMMARY				
Groups	*Count*	*Sum*	*Average*	*Variance*
Occipital Y	80	34102	426.275	102993.7
Occipital M	80	41713	521.4125	117199.2
Occipital O	80	39058	488.225	78623.24

ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	373076.2	2	186538.1	1.872771	0.155965	3.03392
Within Groups	23606479	237	99605.4			
Total	23979555	239				

table 3. 8- ANOVA Occipital sensors total burst time points

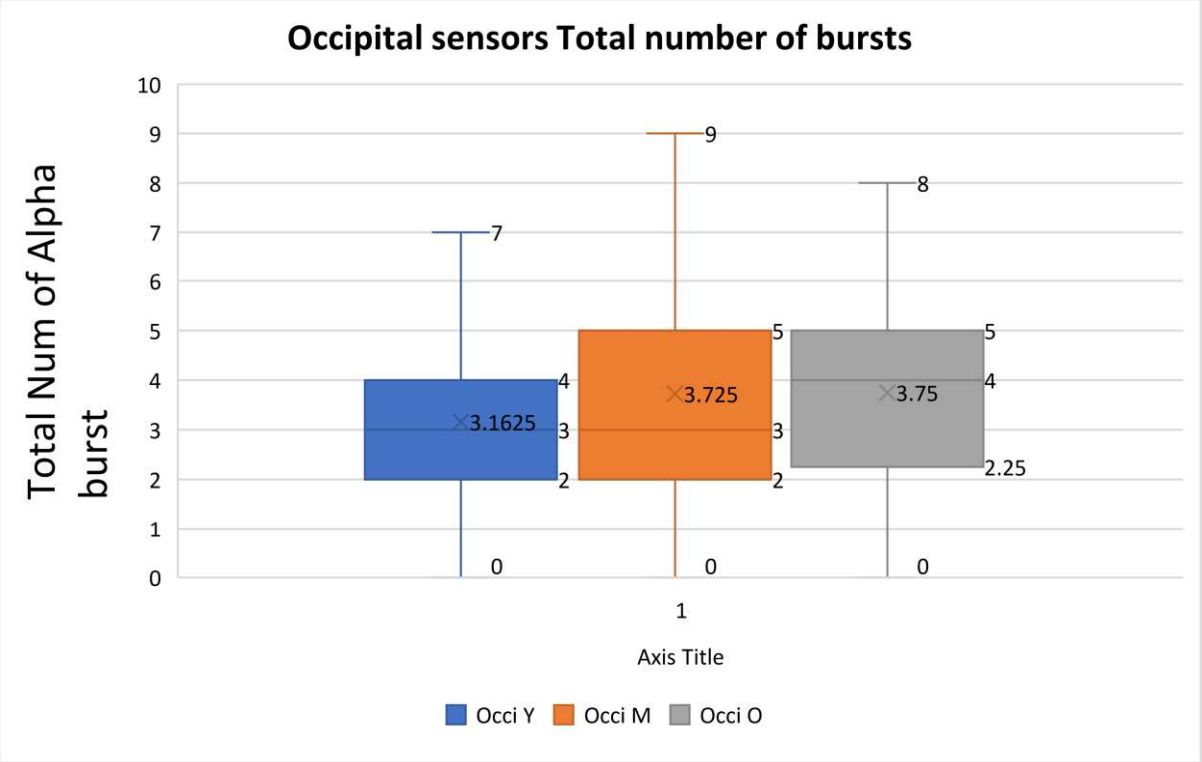


figure 3. 8- Occipital sensos total number of bursts

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Occi Y	80	253	3.1625	4.188449
Occi M	80	298	3.725	4.83481
Occi O	80	300	3.75	4.088608

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	17.65833	2	8.829167	2.020117	0.134918	3.03392
Within Groups	1035.838	237	4.370622			
Total	1053.496	239				

table 3. 9- ANOVA Occipital sensors total number of bursts

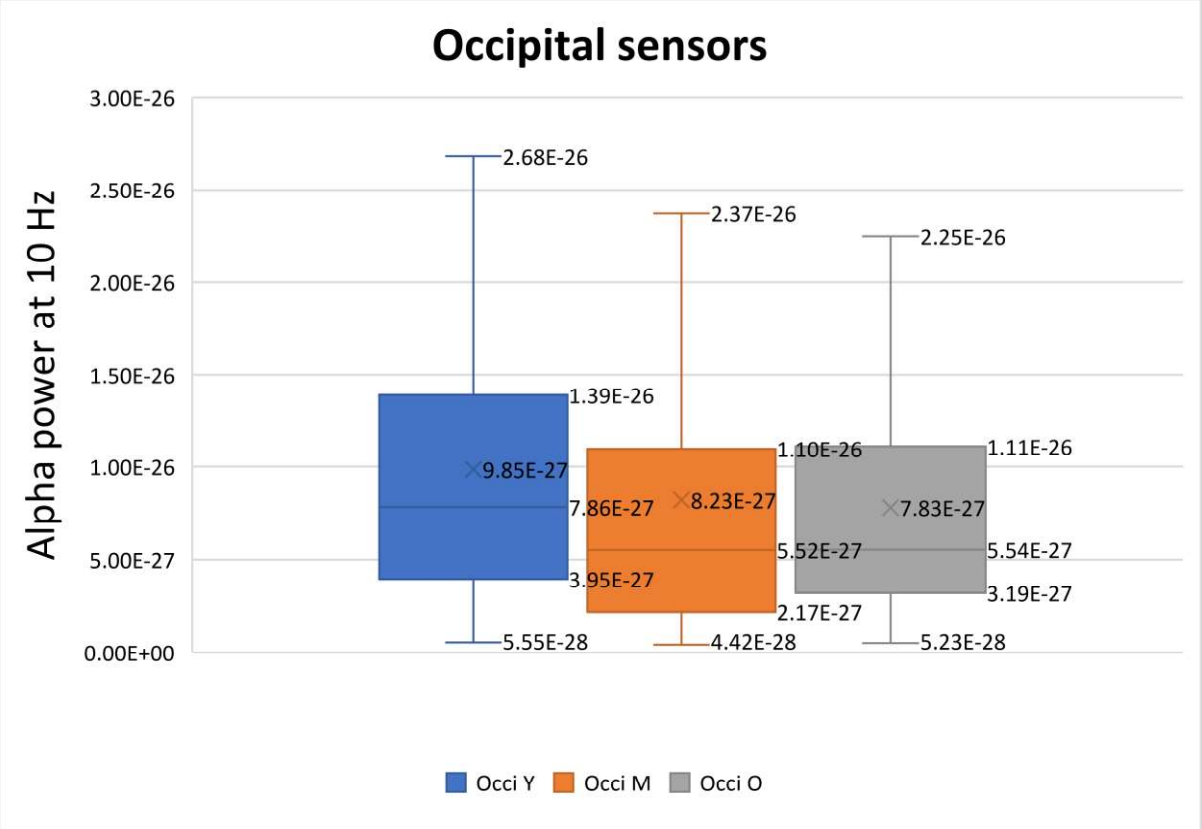


figure 3. 9- Occipital sensors mean power of burst

SUMMARY

Groups	Count	Sum	Average	Variance
Occi Y	253	2.49E-24	9.84668E-27	6.44E-53
Occi M	298	2.45E-24	8.23376E-27	6.65E-53
Occi O	300	2.35E-24	7.83395E-27	4.79E-53

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	6.09E-52	2	3.04294E-52	5.12970	0.00610	3.00634
Within Groups	5.03E-50	848	5.93199E-53			
Total	5.09E-50	850				

Post hoc Wilcoxon test	P value
P Young-middle-aged	0.001434
P middle-aged- Old	0.325156
P Young- Old	0.003015

table 3. 10- ANOVA Occipital sensors mean power of burst

4 Conclusion and Summary

Important Observations

1. There is decrease in mean alpha power of the bursts in the Occipital regions. For the global sensors the trend differs from the occipital i.e. the mean power decreases for the middle-aged group and then again increases for the old aged, whereas there is an increase in the mean alpha power with age in the prefrontal sensors but with no statistical significance is seen in the prefrontal sensors.
2. The trend observed in the total length of bursts and the total number of bursts is similar for all the sensors except for number of bursts in occipital sensors. Mean length and number of bursts increases for the middle-aged group and then decreases for the old group, with significant difference observed only in the prefrontal sensors.
3. When the mean burst power from the global sensors is compared with its number of bursts and total alpha time data, we observed a reverse trend. For the middle-aged group the mean length of bursts and number of bursts is more.
4. Here from the trends, we can conclude that globally the middle-aged population has more frequent alpha burst with lower amplitude. We have to take this with a pinch of salt as the ANOVA of number of bursts and total length of bursts for the global sensors has shown an insignificance between the groups.

4.1 Prefrontal sensors

Coming to the prefrontal cortex sensors there is an increase in the mean power of alpha bursts with age. Though it fails a statistical significance test the trend is different from other sensors. Prefrontal cortex is involved in planning, thinking, creativity, logical reasoning etc. Increase in mean power of alpha burst indicates robust neural oscillations of the network in alpha frequency. More alpha power at rest can imply a focused, calm and composed brain. In the middle-aged population due to maturity, experience and more knowledge and a physiologically healthy prefrontal cortex this effect can be seen in the number of alpha bursts in the prefrontal cortex. This effect should be checked for replicability in some task positive MEG studies which challenge the prefrontal cortex's innate functions like working memory,

attention or simple arithmetic tasks. If a similar result is found in the task positive studies, the above statement made can be said with conviction.

Now coming to number of alpha bursts and total length of the bursts, we find that for the prefrontal sensors their mean increases for middle aged population. Post hoc analysis for both dynamics suggests the young group to be significantly different from the middle-aged population. There is no significant difference between the middle-aged and the old groups and also between young and the old groups. But looking at the distribution in the figure we see that the old aged group lies in between the young and middle aged, with some proximity to the young group's distribution. We can infer that in spite of a reduction in the number and length of alpha bursts, the old group has sustained a high mean power of alpha burst. We can think of this as a compensatory mechanism of decreased alpha power in other regions of the brain due to age related atrophy. The brain is trying to compensate the lost alpha with high power alpha burst. Age related atrophy and Alzheimer's disease mainly degenerates the temporo-parietal cortex, and the prefrontal cortex does not undergo the same degree of degeneration (Montez et al., 2009).

4.2 Occipital sensors

There is a decrease in the mean power of alpha bursts in these sensors. This observation at least in the occipital sensors is in consensus with the previous findings of slowing of alpha waves age (Sahoo et al., 2020). There researchers have reported shifting of alpha peak to the lower frequencies with age. Here we performed the spectral analysis at 10Hz, hence we can see a significant reduction in alpha power with age due to the underlying shift of peak at lower frequencies with age. Previously some studies have noted alpha oscillations in corticothalamic networks (Bollimunta, Mo, Schroeder, & Ding, 2011) . The mean power of burst reduction in the occipital sensors can infer to demyelination of posterior thalamocortical connections and also of the pyramidal cells in the primary visual cortex, or it could be just a collateral of desynchronization in the network. This needs to be verified with other approaches to determine peak alpha like Hidden Markov model (HMM) (Seedat et al., 2020) or an automated multi-site algorithm (Chiang, Rennie, Robinson, van Albada, & Kerr, 2011). Neurodegenerative diseases have shown slowing of alpha and many researchers term Alzheimer's disease as rapid aging of the brain. The current burst detection approach used here and other methods like HMM can be

applied to subjects with neurodegeneration and on comparing the results one can paint a larger picture.

4.3 Global sensors

The mean alpha power of the bursts shows an unusual trend from what one would expect. Generally, it has been observed slowing of alpha with age in the power spectrum but here at 10Hz we see an increase in the mean power of alpha burst. This observation needs to be checked for replicability in data sets and even the data recorded with EEG. Looking at the length the trend is similar to other sensors, but average number of bursts are similar for the middle-aged and the old-age population.

4.4 Clinical perspective

Various studies have found a decrease in the alpha power in Alzheimer's disease (Nimmrich, Draguhn, & Axmacher, 2015). By assessing the dynamics of alpha oscillations from the empirical data of healthy individuals we can draw a model of healthy aging. To make the model more robust, empirical data from a large population can be drawn and methods involving HMM and other algorithms to delineate the spectral dynamics can be looked upon. This model can be used to look for any perturbations in the alpha dynamics hence can be used for early prediction of neurodegeneration.

5 Bibliography

Abadi, M. K., Subramanian, R., Kia, S. M., Avesani, P., Patras, I., & Sebe, N. (2015). DECAF: MEG-Based Multimodal Database for Decoding Affective Physiological Responses. *IEEE Transactions on Affective Computing*, *6*(3), 209–222. https://doi.org/10.1109/TAFFC.2015.2392932

Bollimunta, A., Mo, J., Schroeder, C. E., & Ding, M. (2011). Neuronal mechanisms and attentional modulation of corticothalamic alpha oscillations. *Journal of Neuroscience*, *31*(13), 4935–4943. https://doi.org/10.1523/JNEUROSCI.5580-10.2011

Buzsáki, G. (2009). Rhythms of the Brain. In *Rhythms of the Brain*. https://doi.org/10.1093/acprof:oso/9780195301069.001.0001

Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents-EEG, ECoG, LFP and spikes. *Nature Reviews Neuroscience*, *13*(6), 407–420. https://doi.org/10.1038/nrn3241

Chiang, A. K. I., Rennie, C. J., Robinson, P. A., van Albada, S. J., & Kerr, C. C. (2011). Age trends and sex differences of alpha rhythms including split alpha peaks. *Clinical Neurophysiology*, *122*(8), 1505–1517. https://doi.org/10.1016/j.clinph.2011.01.040

Cohen, D., & Halgren, E. (2003). *Magnetoencephalography (Neuromagnetism)*. *i*(January 2003).

Cohen, M. X. (2014). Analyzing Neural Time Series Data. In *MIT Press* (Vol. 1). https://doi.org/10.1017/CBO9781107415324.004

Freyer, F., Aquino, K., Robinson, P. A., Ritter, P., & Breakspear, M. (2009). Bistability and non-Gaussian fluctuations in spontaneous cortical activity. *Journal of Neuroscience*, *29*(26), 8512–8524. https://doi.org/10.1523/JNEUROSCI.0754-09.2009

Le Van Quyen, M., & Bragin, A. (2007). Analysis of dynamic brain oscillations: methodological advances. *Trends in Neurosciences*, *30*(7), 365–373. https://doi.org/10.1016/j.tins.2007.05.006

MCCRUM, W. R. (1964). The Living Brain. *American Journal of Psychiatry*, *120*(10), 1038-

a-1038. https://doi.org/10.1176/ajp.120.10.1038-a

Montez, T., Poil, S. S., Jones, B. F., Manshanden, I., Verbunt, J. P. A., Van Dijk, B. W., … Linkenkaer-Hansen, K. (2009). Altered temporal correlations in parietal alpha and prefrontal theta oscillations in early-stage Alzheimer disease. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(5), 1614–1619. https://doi.org/10.1073/pnas.0811699106

Nimmrich, V., Draguhn, A., & Axmacher, N. (2015). Neuronal Network Oscillations in Neurodegenerative Diseases. *NeuroMolecular Medicine*, *17*(3), 270–284. https://doi.org/10.1007/s12017-015-8355-9

Sahoo, B., Pathak, A., Deco, G., Banerjee, A., & Roy, D. (2020). Lifespan associated global patterns of coherent neural communication. *NeuroImage*, *216*(August 2019), 116824. https://doi.org/10.1016/j.neuroimage.2020.116824

Seedat, Z. A., Quinn, A., Vidaurre, D., Liuzzi, L., Lauren, E., Hunt, B. A. E., … Brookes, M. J. (2020). The role of transient spectral 'bursts' in functional connectivity: A magnetoencephalography study. *NeuroImage*, 116537. https://doi.org/10.1016/j.neuroimage.2020.116537

Uhlhaas, P. J., Haenschel, C., Nikolić, D., & Singer, W. (2008). The role of oscillations and synchrony in cortical networks and their putative relevance for the pathophysiology of schizophrenia. *Schizophrenia Bulletin*, *34*(5), 927–943. https://doi.org/10.1093/schbul/sbn062

Uhlhaas, P. J., & Singer, W. (2006). Neural Synchrony in Brain Disorders: Relevance for Cognitive Dysfunctions and Pathophysiology. *Neuron*, *52*(1), 155–168. https://doi.org/10.1016/j.neuron.2006.09.020