SoundStim: EEG Connectivity analysis during sound stimulation

PDSB 2019 – Group 7
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1. ABSTRACT

Auditory stimuli have proven to have an important role in brain activity [4]. One way to analyse it consists of understanding how different areas of the brain are connected after the application of a stimulus. The concept of Connectivity refers to the magnitude of couplings between neurons inside our brain. Coherence-based methods have proved to be efficient in the investigation of connectivity, in particular the Direct Transfer Function and the Partial Directed Coherence are able to overcome the volume conduction problem. The main goal of this project is to analyse brain connectivity of different subjects (musicians and non-musicians) that have been submitted to different sound stimuli consisting of different frequencies and different types - monaural and binaural. The results have shown that musicians have a higher number of interhemispheric connections than non-musicians and present greater difference in the number of connections between monaural and binaural stimuli. Furthermore, musicians and non-musicians present different connectivity results across different brain regions.

2. PROBLEM AND MOTIVATION

Over the years a great number of studies has been developed in order to analyse the variation in the cerebral activity provoked by sound stimuli [4]. In fact, it has been demonstrated that auditory stimulation is able to elicit a series of electric signals in the nervous system which can be used for neurologic diagnosis, intraoperative monitoring, and neurophysiologic research. For this purpose, useful information can be obtained from the analysis of activity pattern generated in anatomically separated regions of the brain. The goal of this project is to analyse the functional connections between different cerebral areas when subjected to auditory stimulation and, in particular, investigate the possible different reactions between non-musicians and well-trained musicians. A great number of studies have revealed important insights into the possible benefits of long-term music training for musicians, such as enhancement of sensory perception and of long-term memory, suggesting a different cerebral response [4]. The ultimate purpose is to generate cortical maps indicating the connectivity between neural populations of the brain, which can contribute to the clinical research. In fact, they can be useful in the development of procedures of neurostimulation for the treatment of neurological and psychiatric disorders. In addition, a distinction between monaural and binaural excitation is performed. The application of these two different sets of stimuli has proved to be a promising tool in decreasing anxiety levels, as well as in treating cranioencephalic trauma and ADHD (attention deficit hyperactivity disorder). [7]

3. BACKGROUND AND RELATED WORK

Electrical impulses – Action Potentials (AP) and Postsynaptic Potentials (PSP) - and associated chemical exchanges are the way the nervous system communicates within itself – synapses - and other systems [8]. Therefore, by analysing the variations in the electrical signals generated by the brain, it is possible to draw some conclusions about neural phenomena and apply them to the human behaviour scale. In this context, it is collocated the concept of brain connectivity. Brain connectivity can be defined as a pattern of links of a different nature between the units of a nervous system. In other words, connectivity can be referred to as the magnitude of couplings between neurons inside our brain. It can be subdivided into a structural and a functional domain, with each categorized further into static and dynamic components. The static component refers to the regions and wirings in which communication occurs, while dynamic components represent the functional relationship between static components. Static connectivity can be measured by anatomical properties using a number of imaging methods, including high-resolution magnetic resonance (MR), diffusion tensor imaging (DTI), and histology. Dynamic connectivity can be measured by a wide variety of techniques, such as resting-state functional connectivity MRI (rs-fcMRI), which is able to provide information about the spatial distribution and strength of dynamic connections, or methods capable of measuring causality, such as EEG (ElectroEncephaloGram). The current project focuses the attention on the functional domain of connectivity in order to analyse possible connections arising in the brain when the subject is submitted to sound stimuli of different nature. In particular, different causality methods involving processing EEG data are analysed. EEG serves this purpose by recording the changes in potential of electrodes positioned in the scalp. These changes arise from the simultaneous firing of cortex pyramidal neurons (aligned perpendicular to the surface of the cortex - figure (1-B)).

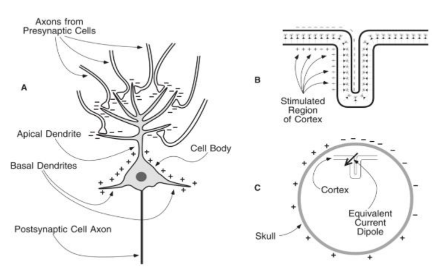

Figure 1 – *Basic principles of an EEG measurement*

More specifically, the post-synaptic potentials of these neurons are recorded, being this the same as currents resulting from synaptic excitations. Important to note that these neurons must fire simultaneously so that the currents are large enough to generate electrical activity possible to record. An amplification system is always required.

A set of different methods have been developed to quantify the degree of coupling between different EEG recording positions, with the specific aim to characterize the functional interaction between neural populations within the cortex. One of the common measures of such dynamics is *Coherence.* Coherence is a measure of synchronization between two signals based mainly on phase consistency [2]; that is, two signals may have different phases (as in the case of voltages in a simple linear electric circuit), but high coherence occurs when this phase difference tends to remain constant. From a mathematical point of view this parameter measures the linear correlation between two variables as a function of the frequency, f. It is the squared module of the coherency function (C), which is the ratio between the cross power spectral density, Yij(f), between channels i and j ($i \neq j$), and their individual power spectral densities Yii(f) and Yjj(f):

$$Cij\ (f) = \frac{Yjj(f)}{\sqrt{Yii(f) * Yjj(f)}}$$

thus, Coherence is defined as:

$$COHij\ (f) = |Cij(f)|^2 = \frac{|Yij(f)|^2}{Yii(f) * Yjj(f)}$$

and it can vary from 0 to 1.

The coherence analysis, though, is distorted by the phenomenon of volume conduction. Because of this phenomenon two nearby EEG electrodes can appear coherent across all frequency bands just because they record potentials generated by the same source, not because there is an actual connectivity between them. The volume conduction effect is independent of frequency and depends only on the electrode locations and electrical properties of the head.

Recently, different methods regarding the MVAR modelling have been proposed [1] in order to provide a more reliable esteem of neural interactions.

The main characteristic of an MVAR model is related to the fact that it is capable of describing directed causal relationships between channels. First of all, in order to obtain the possible methods based on a multivariate autoregressive model, its necessary to consider the transformation from the time domain into the f-domain and the z-domain:

$$H(z) = \frac{Y(z)}{X(z)} = \lfloor I - \sum_{k=1}^{p} (z^{-k} * Ak) \rfloor^{-1}$$

where ($\lfloor\ \rfloor$) is the floor function, and :

$$H(f) = A^{-1}(f) = \frac{Y(z)}{X(z)}$$

Where A_k are the k-th autoregressive parameters, Y is the observed EEG data, X is the innovation process (a multivariate white noise process), p is the order of the model and

$$H(z; z = e^{\frac{2 * \Pi * i * f}{f0}})$$

given the sampling rate f0.

A useful approach in order to remove volume conduction effects is based on the partialization of coherence (pCOH). The pCOH between channels i and j represents the coherence between channel i and j, removing the (partial) components common to any other channel combination. The pCOHij(f) is defined as:

$$pCOH_{ij} = \frac{g_{ij}}{\sqrt{g_{ii}(f) * g_{jj}(f)}}$$

where: g(f)= $|g_{ij}(f)|$= A(f) Σ^{-1}_{x} A(f).

The pCOH is symmetric, this means that it is not able to provide directional information. For this reason, the concept of pCOH has been extended to obtain information about directionality, leading to the definition of Partial Directed Coherence (PDC):

$$PDC_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{i=1}^{M} \left|A_{ij}(f)\right|^2}} = \frac{A_{ij}(f)}{\sqrt{A_{:j}^{H}(f) * A_{:j}\ (f)}}$$

Another method that is able to provide directed information id the Directed Transfer Function (DTF), defined as:

$$DTF_{ij}(f) = \frac{|H_{ij}(f)|}{\sqrt{\sum_{k=1}^{M} |(H_{ik}(f))^2|}} = \frac{|H_{ij}(f)|}{\sqrt{H_{i:}\ (f) * H_{i:}^{H}\ (f)}}$$

It has been demonstrated that DTF extracts direct as well as indirect connections, while PDC reveals exclusively direct connections between EEG channels. Nevertheless, it is still not clear to the scientific community which of these last two methods is more efficient in the analysis of directional information. However, it is evident that DTF and PDC are the most interesting measures for describing couplings between EEG signals.

In the current work the brain connectivity is analysed differentiating between two different kinds of stimuli: monaural and binaural. The effects of their application have been studied using monaural and binaural beats. Auditory beats are amplitude-modulated signals, which can be generated by the superposition of two auditory sine waves with neighbouring frequencies [7]. Monaural beat stimulation is achieved by applying the same amplitude-modulated signal to both ears simultaneously. This physical beat signal is modulated first in the cochlea and then relayed via brain stem neurons to the auditory cortex. As both ears receive the same beat wave, perception of the beat does not require an integration of information from the two ears. On the other hand, binaural beats occur when sine waves with neighbouring frequencies are presented to each ear separately. For example, presentation of 145 Hz oscillations to the left ear and 155 Hz oscillations to the right ear results in the perception of an amplitude-modulated (“beat”) stimulus of 10 Hz. The binaural beat sensation is often described as being subjectively located “inside” the head and is understood to be modulated at the level of the brainstem in the superior olivary nuclei, whereas monaural stimuli are modulated at the level of the cochlea. These phenomena are shown in figure (2) where the left figure represents the application of a monaural beat, while the right one shows the effects of the application of a binaural stimulus.

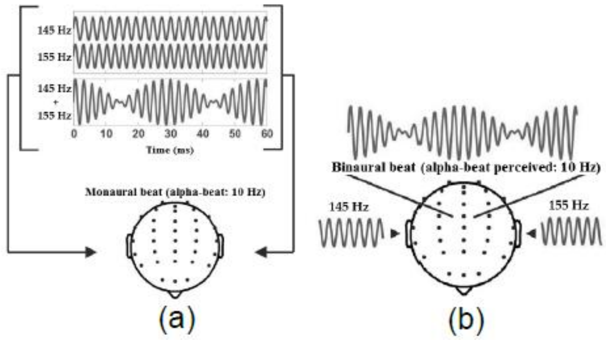

Figure 2. *In figure (a): application of a monaural beat, in figure (b): application of a binaural beat.*

4. APPROACH AND UNIQUENESS

4.1 Material

The data analysed in this project derive from an EEG test and were recorded as part of the study carried out by Marco Miranda at Instituto Superior Técnico [7]. The procedure involved the use of the International 10-20 System [8], which is currently the most used convention to dispose the electrodes in the context of an EEG exam. In figure (3) an up view of the system is shown. The odd electrodes are positioned in the left hemisphere and the even electrodes are in the right hemisphere. P- Parietal, C- Central, T-Temporal, A-Auditive, F-Frontal, O-Occipital. Some of these brain areas are associated with specific functions: F7 – Rational Activity; F2 – Intentional & Motor Centres; F8 – Emotional Impulses; C3, C4, Cz – Sensory & Motor Functions; P3, P4, P2 – Perception & Differentiation; T3, T4 – Emotional Processes; T5, T6 – Memory Functions, O1, O2 – Vision. In the case of our experience, electrodes A1 and A2 are not present and two additional electrodes - M1 and M2 - were collocated and used as reference.

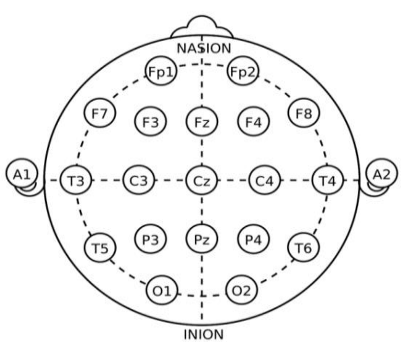

Figure 3. *Representation of the 10-20 System for the electrode positioning.*

The test was performed on four people differentiating between musicians and non-musicians (Table (1)). This distinction was based on the following questions: 1) whether they had any musical training, 2) whether they could play a musical instrument, and 3) whether they composed music. In order to be considered a musician, the volunteer would have had to reply positively to, at least, two questions, or simply to question 3). All other replies placed the volunteer in group NM.

Table 1. *Subdivision of subjects between the musician and non-musician cathegories.*

Musicians:	Non-musician:
Subject ZMAP	Subject FOPK
Subject XNOA	Subject HAOK

Following the 10-20 System configuration, a number of 19 EEG channels was recorded with a sampling frequency of 250 Hz and saved in a .edf file. Channel 20 and 21 correspond to the references, while in channel 22 the audio with the stimuli was saved.

The auditive stimulation, originally containing 51 stimuli, was divided into three sets, each containing 17 different stimuli, corresponding to 17 different trials. For the aim of this project just the first set of trials was selected, corresponding to the application of the monaural-binaural stimuli, according to figure (4).

EA	Type	Description of the EA/ Excerpt (10 seconds)
SEQ1-EA1	-	Pink Noise
SEQ1-EA2	-	Creek (fluvial environment)
SEQ1-EA3	Monaural	FP = 150 Hz [149 Hz + 151 Hz : L+R] FB = 2 Hz (delta)
SEQ1-EA4	Binaural	FP = 150 Hz [149 Hz (L) + 151 Hz (R)] FB = 2 Hz (delta)
SEQ1-EA5	Monaural	Pink Noise + FP = 150 Hz [149 Hz + 151 Hz : L+R] FB = 2 Hz (delta)
SEQ1-EA6	Binaural	Pink Noise + FP = 150 Hz [149 Hz (L) + 151 Hz (R)] FB = 2 Hz (delta)
SEQ1-EA7	Monaural	Riacho + FP = 150 Hz [149 Hz + 151 Hz : L+R] FB = 2 Hz (delta)
SEQ1-EA8	Binaural	Riacho + FP = 150 Hz [149 Hz (L) + 151 Hz (R)] FB = 2 Hz (delta)
SEQ1-EA9	Monaural	FP = 150 Hz [147 Hz + 153 Hz : L+R] FB = 6 Hz (teta)
SEQ1-EA10	Monaural	FP = 440 Hz (Lá-A4) [437Hz + 443Hz : L+R] FB = 6 Hz (teta)
SEQ1-EA11	Binaural	FP = 150 Hz [147 Hz (L) + 153 Hz (R)] FB = 6 Hz (teta)
SEQ1-EA12	Binaural	FP = 440 Hz (Lá-A4) [437Hz (L) + 443Hz (R)] FB = 6 Hz (teta)
SEQ1-EA13	Monaural	FP = 150 Hz [145 Hz + 155 Hz : L+R] FB = 10 Hz (alfa)
SEQ1-EA14	Binaural	FP = 150 Hz [145 Hz (L) + 155 Hz (R)] FB = 10 Hz (alfa)
SEQ1-EA15	Binaural	FP = 150 Hz [143 Hz (L) + 157 Hz (R)] FB = 14 Hz (low-beta)
SEQ1-EA16	Binaural	FP = 150 Hz [141 Hz (L) + 159 Hz (R)] FB = 18 Hz (beta)
SEQ1-EA17	Binaural	FP = 150 Hz [136 Hz (L) + 164 Hz (R)] FB = 28 Hz (high-beta)

Figure 4. *First set of trials corresponding to the monaural-binaural stimulation. Each EA represents a different aural stimulus. For each trial the carrier frequencies and the beat frequency are presented.*

Each stimulus has a duration of about 10 seconds and it is preceded by a 2-second sinusoid. The duration of each stimulus was registered in a matlab file as well as the time offset from the beginning of the first sinusoid of each set. With the use of *Fieldtrip* the corresponding matlab files (*sdata.mat*) for each patient were generated from the .edf files, containing also information about the event type. Fieldtrip is an open source software package developed for the analysis of EEG, MEG, and other electrophysiological data. The software is implemented as a MATLAB toolbox and includes a complete set of consistent and userfriendly functions to analyse experimental data. The same toolbox contains a module to compute measures of connectivity in the frequency domain. For this reason, it was also exploited to apply the selected connectivity measures.

4.2 Methods

4.2.1 Data preprocessing

The starting point of this project, after selecting the data relative to a specific patient, consists in cleaning up the data obtained from the EEG and removing the possible artifacts. For this reason, a pre-processing procedure is applied using the FieldTrip function ft_preprocessing, implementing a band-pass filter to select the frequencies in a range from 0.5 to 30 Hz. The following figure presents the EEG data before and after the filter.

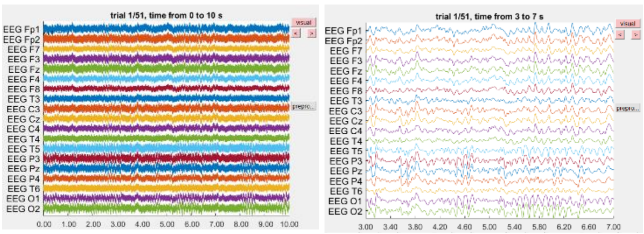

***Figure 5**. In the left figure: representation of the signal for all channels and for the first trial before the application of the filter, in the right figure: representation of the post-processed data for all channels and for the first trial.*

In order to reduce the computational time and the variability of the signal, only the middle segment of each trial was analysed, going from 3 sec to 7 sec. The segments should be long enough to comprise the period of the lowest frequency being anlysed (0.5 Hz), and not too long, so that only stationary segments are captured.

4.2.2 Connectivity Analysis

To analyse the connectivity between EEG channels different methods were studied, including coherence, granger causality, DTF and PDC. Given the characteristics of the data and the results given by each measure, it was possible to conclude that the DTF and the PDC were the most suitable for our analysis. For each of the selected methods, the connectivity measure was computed for each trial at a time, using the Fieldtrip function ft_connectivity analysis. This function returns a struct containing the computed spectrum for each frequency and for each combination of channels.

The results were separated for each EEG band (Delta, Theta, Alpha, Beta), which correspond to the frequencies shown in table 1. For each band the average value is obtained in order to make the comparison of the results easier.

Table 1. *Initial and final frequency for each EEG frequency band.*

Frequency band:	Initial frequency (Hz)	Final frequency (Hz)
Delta	0.5	3.5
Theta	3.5	7.5
Alpha	7.5	12
Beta	12	30

4.2.3 Network Analysis

The next step consists in computing the whole-brain connectivity networks from connectivity matrixes obtained. To do that, the matrixes must be binarized, by setting the most relevant connections to 1 and the remaining connections to 0. Different methods are referred in the literature to perform such binarization, including surrogate data tests and the use of absolute and proportional thresholds. The generation of surrogate data is computationally expensive and requires a fair amount of data to be generated, in order to obtain stable connectivity results, so that option was excluded. The absolute threshold approach considers just those connections that exceeds the selected value and for this reason, even if it is simple and potentially powerful, it leads instability in network metrics between datasets. On the other hand, the proportional threshold approach aims at selecting the strongest percentage (PT%) of connections in each individual network. This represents a more reliable method and results in more stable network metrics [5]. Based in literature results and on a comparison with some surrogate data tests, the selected value for the threshold (PT) was 20%. This value should be sufficient to prevent the instability of metrics observed for lower thresholds, and to keep only the most relevant connections. In order to implement this method, a function called *connections* was created. As an input, aside from the threshold value and the *sdata* structure, it receives the connectivity matrix for all the EEG channels and the 4 frequency bands. It returns a binary matrix containing the connections associated to each channel for each frequency band.

The following part of the projected consists of defining metrics to study the connectivity networks obtained for each trial in order to find potential differences between the groups under analysis: musicians vs. non-musicians and monaural vs. binaural stimuli. Two of the metrics studied are presented in this paper: the strength of the outwards connections from each channel and the percentage of connections that cross brain hemispheres (PCH). The first one corresponds to the sum of weights of outward links connected to the channel, where weights correspond to the connectivity values computed using DTF. The second one is the percentage of connections between channels that are located in the left and right brain hemispheres, out of all the connections. For this measure, the connectivity matrix was first computed using the PDC. For this purpose, a different function is created to investigate the detected connections for each frequency band and for each trial. The results are then saved in an Excel file in order to investigate the presence of possible patterns. To conclude, the functions ft_connectivityplot, ft_topoplotCC and imagesc are exploited to visualize the connectivity results between different channels for the most relevant frequency bands and trials.

5. RESULTS AND CONTRIBUTIONS

The connectivity matrixes for two subjects (1 musician and 1 non-musician) for trial 17, for the frequency band corresponding to the stimuli that is being received, are shown in figure 6 (a) and (c). In these figures it is clear that the intensity of the connections from channel 14 (P3) to other channels are the strongest when compared to other channels.

In other to investigate for a pattern across trials, the plots in figure 7 were obtained, which correspond to an average of the strength of the outwards connections from each channel over the binaural and monaural trials separately. The connectivity between channels for such measure was computed for the frequency bands of interest using DTF. That computation was performed for the four subjects. It is not possible to observe significant differences between musicians and non-musicians or monaural and binaural stimuli. However, it is possible to see that the intensity of the connections from channels 14 (P3) and 16 (P4) to other channels are the stronger when compared to most of other channels. These channels correspond to perception and differentiation, so it could be a point for further investigation.

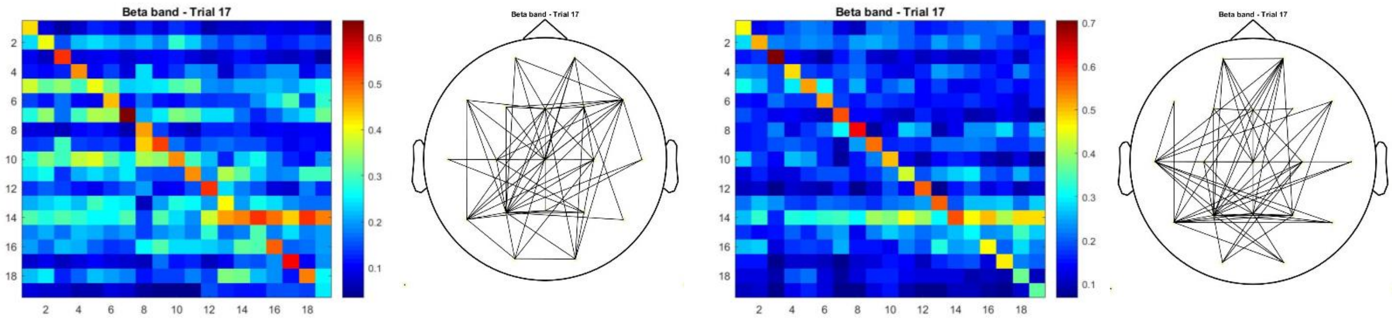

Figure 6 – *(a), (c) Functional connectivity matrixes corresponding to the intensity of connectivity computed between each pair of channels (1 to 19) using DFT. The direction of the connections is from the channels in the vertical axis to the channels in the horizontal axis. Both matrixes correspond to the results obtained for trial 17, for two different subjects. The results in figures (a) and (b) are for a non-musician subject (FPOK) and the results in figures (a) and (b) are for a musician subject (XNOA). Correspondence between channel number and EEG channel: Fp1=1; Fp2=2; F7=3; F3=4; Fz=5; F4=6; F8=7; T3=8; C3=9; Cz=10; C4=11; T4=12; T5=13; P3=14; Pz=15; P4=16; T6=17; O1=18; O2=19 .(b), (d) - Graph-based representations of network connectivity, generated by applying a proportional threshold of 20% to the functional connectivity matrix, such that each channel is represented as a node and each supra-threshold correlation as a connecting edge.*

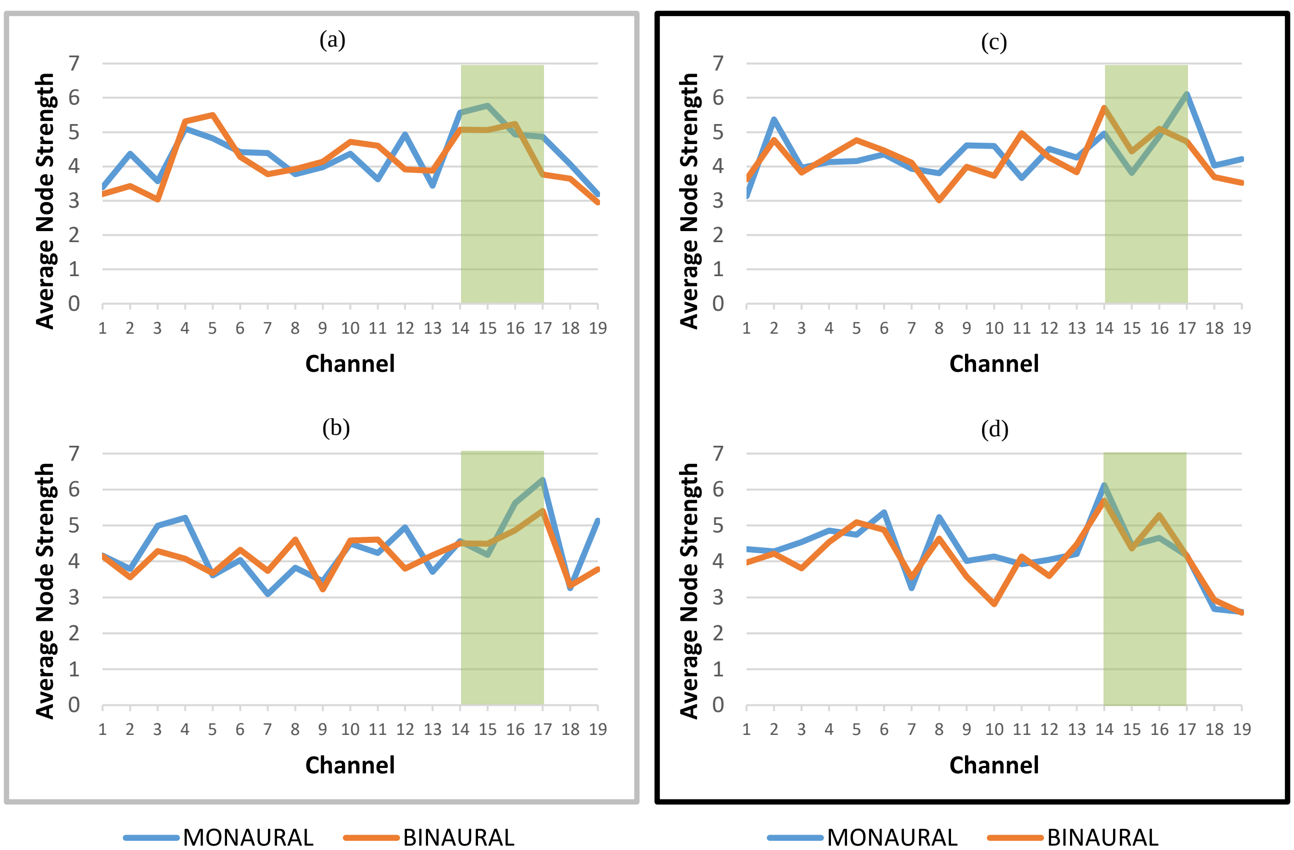

Figure 7 - *Average node strength for each channel, where the node strength is the strength of the outwards connections from each channel. Averages were computed over binaural and monaural trials only for the frequency band of the corresponding auditory stimuli. (a) and (b) correspond to musicians (FOPK and HAOK, respectively); (c) and (d) correspond to musicians (ZMAP and XNOA, respectively). Correspondence between channel number and EEG channel: Fp1=1; Fp2=2; F7=3; F3=4; Fz=5; F4=6; F8=7; T3=8; C3=9; Cz=10; C4=11; T4=12; T5=13; P3=14; Pz=15; P4=16; T6=17; O1=18; O2=19.*

Another parameter than can be used in order to assess connectivity results is the PCH. The Partial Direct Coherence method was used for this purpose as it outputs better results for analysis compared to the DTF method. The musician and non-musician results were averaged and considered as a group result in this section.

PCH was computed for trials 3 to 14, which are the ones that have both binaural and monaural data for the same frequency range. These trials were grouped according to their rhythm frequency (FB) and, consequently, denominated as delta, theta or alpha. Beta trials are only from the type binaural, not being used for this analysis. Furthermore, the results were averaged for the four different range of frequencies (from delta to beta) for the same FB. The results for musicians and non-musicians are plotted in figures 8 and 9.

According to the results, it is possible to conclude that the distribution of interhemispheric connections is approximately uniform for the non-musicians, not having a clear distinction for the monaural and binaural types and the different frequency bands. Furthermore, there is not a direct relation between the FB of the trial and its respective band, from the connectivity point of view. On the other hand, musicians do present significant differences between the monaural and binaural trials as it is possible to visualize in figure 8. For the alpha range, musicians tend to have higher values of PCH in the binaural type compared to the monaural. In the lower frequency ranges – delta and theta – the inverse occurred, the musicians presented a greater number of connections crossing hemispheres in the monaural trials than in the binaural trials.

In addition, the musicians present, in average, a greater number of connections crossing hemispheres than the non-musicians. No relevant statistical conclusions can be taken from the results as there are only two subjects for each group and there is not available literature to confirm the results.

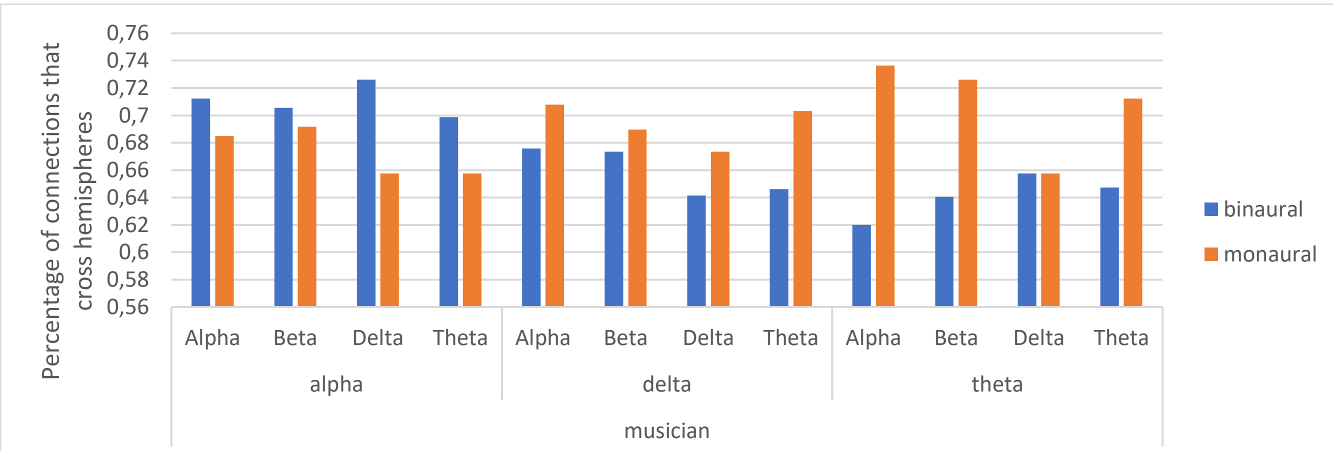

Figure 8. *Percentage of connections that cross hemispheres for the group musicians. The results are grouped according to the rhythm frequency of the trial – alpha, delta and theta – and averaged across the different frequency bands, from delta to beta. The results were also distinguished between binaural and monaural according to the trial type. The vertical scale represents the average percentage of connections that cross hemispheres and the horizontal scale represents the different groups of frequency bands for different trials.*

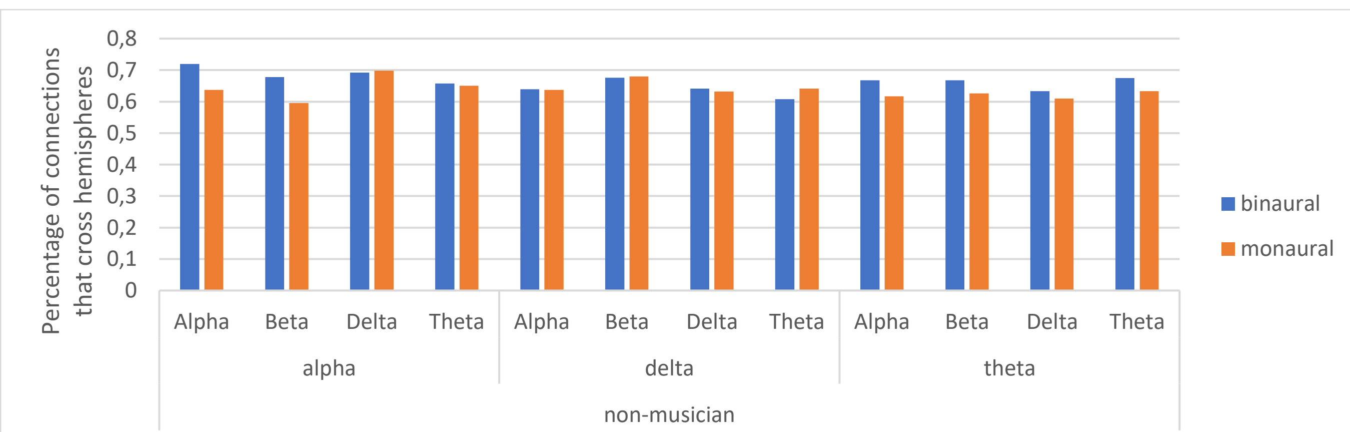

Figure 9. *Percentage of connections that cross hemispheres for the group musicians. The results are grouped according to the rhythm frequency of the trial – alpha, delta and theta – and averaged across the different frequency bands, from delta to beta. The results were also distinguished between binaural and monaural according to the trial type. The vertical scale represents the average percentage of connections that cross hemispheres and the horizontal scale represents the different groups of frequency bands for different trials*

6. DISCUSSIONS AND CONCLUSIONS

As Martínez et al suggest in the article '*Role if inter-hemispheric connections in functional brain networks*', the human brain can be modelled as a graph where nodes represent different regions and links stand for statistical interactions between their activities. An adequate graph analysis can, therefore, give relevant information about how the human brain works and how it reacts to different types of stimuli. Not having any background in connectivity analysis or network analysis, it was challenging to learn enough about these topics at the same time as we had to decide which were the best parameters to analyse the data available. Given the lack of knowledge and experience in these topics, only a simplistic analysis could be performed, and there is no guarantee that no other relevant information is present in the data analysis. In fact, given the amount of parameters that could be analysed (variation between frequency bands, subjects – musicians and non-musicians, types of stimuli, different connectivity metrics, different possibilities to binarize connectivity matrixes and different metrics to analyse the resulting networks) one could not evaluate all possible results in due time.

In the present paper, only two parameters for connectivity analysis are discussed: strength of connection and percentage of connections that cross hemispheres. The strength parameter suggested that different channels of the brain interact more with others. According to the brain structure-function relationship, it was possible to conclude that the subjects in analysis had a higher intensity of connections from channels 14 and 16. The results of the analysis of the number of connections that cross hemispheres showed that these are higher for musicians. Molly Gebrian, in the paper The Differences Between Musicians' and Non-musicians' Brains refers that musicians' motor and auditory cortices are interconnected. In addition, she explains that 'For most people, what they hear doesn't cause them to have automatic associations with movement and moving certainly doesn't cause them to hear things in their heads but if a musician listens to a recording of a piece they know and play well, not only does their auditory cortex light up on a brain scan'. Despite dealing with stimuli that are pure sinusoids and not music pieces, the justification for our findings can be related with this phenomenon. To conclude, it is important to enhance that only four subjects were analysed, which by itself is not sufficient to take any statistically significant information, even if some patterns are observed. For these reasons, no significant conclusions can be taken from our work and a more in-depth analysis would be required.

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