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EEG analysis and depression: A study considering absolute power, asymmetry, Interhemispheric and Anteroposterior Coherences

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Abstract

Major Depressive Disorder (MDD) will be considered the most common and the most incapacitate psychopathology towards 2020-2030 according World Health Organisation (WHO). Research of electroencephalography (EEG) in mood disorders as well-known history of research, proving to be a useful tool and gaining its importance of being part of a non-invasive procedure and informative of how our brain is functioning, playing a central role in diagnosis. The aim of this study lies on investigate EEG patterns in depression and if other EEG data than EEG asymmetry, such as coherence scores, may play an important role in characterizing depression. Frontal absolute alpha and beta power, anterior alpha and beta asymmetry, delta, theta, alpha and beta interhemipherical and anteroposterior coherence measures derived from spectrally analysed EEGs, exposed to group comparisons. The results found no significate difference concerning alpha and beta absolute power. An inversion pattern is found in lateralfrontal areas, which is in accordance with literature. Regarding interhemipsherical coherences significate results were found in delta, theta and alpha bands in midfrontal and central areas, suggesting also a general decrease in interhemispherical coherence scores in depressives in all studied bands, except for T3-T4 Delta. Anteroposterior coherences showed significate results in delta band for both fronto-parietal sites (F3-P3; F4-P4). Although literature consensus regarding a phenotype isn't well defined, these results suggest that an inversion pattern in lateral frontal areas and the lower functional connectivity between brain regions may be characterizers of depression.

Keywords: EEG; qEEG; Depression; Absolute Power; Asymmetry; EEG Patterns; Inter-hemispherical Coherence; Anteroposterior Coherence;

Resumo

A Depressão Major será considerada o mais comum e incapacitante distúrbio de humor até 2020-2030 de acordo com a Organização Mundial de Saúde (OMS). A investigação eletroencefalográfica nos distúrbios de humor tem um historial de investigação bem conhecido, provando ser uma ferramenta adjuvante e ganhando importância ao ser uma técnica não-invasiva e informativa acerca do funcionamento do nosso cérebro, tendo um papel importante no diagnóstico. O objetivo deste estudo reside na investigação de padrões EEG na depressão e se dados de EEG, como as coerências, podem ter um papel importante na caracterização da depressão. Poderes absolutos de alfa e beta, assimetrias alfa e beta anteriores, coerências inter-hemisféricas e anteroposteriores nas bandas delta, teta, alfa e beta derivaram de análises de EEG, expostas a comparação entre grupos. Não foram encontradas diferenças significativas relativamente aos poderes absolutos de alfa e beta. Um padrão invertido foi encontrado para as áreas fronto-laterais (F7-F8), estando de acordo com a literatura. Relativamente às coerências inter-hemisféricas foram encontrados resultados significativos para as bandas delta, teta e alfa para as áreas frontais e centrais, sugerindo ainda um decréscimo geral das coerências inter-hemisféricas nos depressivos em todas as bandas estudadas, excetuando para delta em T3-T4. Coerências anteroposteriores indicam resultados significativos na banda delta para as conexões frontoparietais (F3-P3; F4-P4). Apesar de existir pouco consenso na literatura no que toca a um fenótipo da depressão, estes resultados sugerem que o padrão invertido da assimetria, assim como a diminuição da conetividade inter-hemisférica entre regiões cerebrais podem ser caracterizadoras da depressão.

Palavras-Chave: EEG; qEEG; Poder Absoluto; Depressão; Assimetria; Padrões EEG; Coerências Interhemisféricas; Coerências Anteroposteriores

Introduction

In a wide range of mood disorders, Major Depressive Disorder (MDD) is one of the most common psychopathologies and it will be considered the most common and the most incapacitate psychopathology towards 2020-2030, based on statistical data of the World Health Organisation (WHO).

MDD is characterised by a depressed mood or a loss of interest or pleasure in daily activities, sadness for more than two weeks in which can have impaired functions in social, occupational, educational contexts (DSM-V; American Psychology Association, 2014). In fact, cognitive deficits, memory processing, learning, attention, and executive function have been reported in depressed individuals (Leuchter, A. F., Cook, I. A., Hunter, A. M., Cai, C., & Horvath, S., 2012). Due to his heterogeneity, depression has a wide "bank" of treatments, from pharmacology to psychotherapeutics. It is known the importance of brain functioning in mood disorders, especially in depression.

Trough years and since the very first studies lead by Hans Berger, EEG (Electroencephalography) has been proving to be a useful tool concerning the understanding of brain functioning. Other than psychological, neuropsychological or medical approaches, the EEG gains its importance of being part of a non-invasive procedure and carrier of many information of how our brain is functioning, playing a central role in diagnosis and management of patients with seizure disorders, combinating a variety of other diagnostic techniques developed over the last years (Smith, 2005).

Yet, the EEG has a number of limitations. The electrical activity recorded by electrodes placed on the scalp or surface of the brain mostly reflects summation of excitatory and inhibitory postsynaptic potentials in apical dendrites of pyramidal neurons in the more superficial layers of the cortex (Smith, 2005).

Nowadays, rather than the simple EEG recording, an incremental tool is used to have a topographic view of the activity in the brain, known as qEEG (Quantitative Electroencephalography). Critical to the use of qEEG profiles is the question of whether qEEG is a reliable measure and whether individual qEEG profiles are stable over time. qEEG profiles may be regarded as intermediate phenotypes who are manifestations between the genome and behaviour (Johnstone, Gunkelman, & Lunt, 2005). The intermediate phenotypes are highly heritable, and reliable indices of brain function.

To better understand the phenotypes and their manifestations trough behaviour, one of them has been on the top of the list, specially to characterize mood disorders. The investigation in the field of frontal electroencephalography asymmetries (EEG) and the relation with emotion, more precisely their traits and states has a well know history of research for the past three decades (Coan, & Allen, 2004).

The EEG asymmetry was vastly studied by Davidson (Davidson, Taylor, & Saron, 1979). The concept of asymmetry suggests that positive and negative affect is associated with different frontal asymmetric patters of brain function (Davidson et al., 1979). Nonetheless, the investigation concerning the neurobiology of depression points to other concepts such as Motivation and Withdrawal. (Davidson, 2004). Neuropsychological observations of affective consequences following brain lesions led to the hypothesis that both hemisphere are differently engaged in emotional functions (Gainotti, 1972; Robinson, Kubos, Starr, Rao, & Price, 1984).

The theory behind these concepts (Motivation; Withdrawal) suggest that one with right-side activation of the anterior cortex might show a vulnerability for the experience of negative emotional states and a tendency to show withdrawal/inhibition behaviours, as, in the contrary, a left-side activation may lead to positive emotional experience and an approach tendency (Davidson, 1993; Wheeler, Davidson, & Tomarken, 1993; Hagemann, Naumann, Thayer, & Bartussek, 2002).

This model steered to one prediction that stands for individual differences in asymmetrical activation in these systems, which might be a major factor in trait-like affective/motivational behaviours, constituting one's affective style (Davidson, 1998; Schaffer, Davidson, & Saron, 1983).

Albeit many studies refer the EEG asymmetry model, very few try to demonstrated it through an experimental way. A study lead by Allen, Harmon-Jones, & Cavender, (2001) examined the effect of frontal EEG biofeedback (Frontal F3-F4 electrode locations) on facial muscle activity and emotional experience responses to happy, neutral and sad films. The sample was constituted by 18 undergraduate women and the results showed that those assigned to a "left asymmetry" biofeedback group reported more positive affect in response to a happy film and a neutral film. Right asymmetry training did not result in a relative increase in negative emotions in response to the sad film.

Further investigations were made pursuing this model and some of the majority studies suggest that depressive mood is characterised by a hyper activation of right-frontal region.

Some studies suggest that greater left alpha absolute power is related with depressive symptoms (Diego, M. A., Field, T., & Hernandez - Reif, M., 2001).

However other showed other asymmetry patterns associated with depression, suggesting a less left frontal activity associated with depression (Stewart et al., 2010) and that pattern was found in depressive males, contrary to females that showed greater right frontal activity associated with unpleasant mood (Hagemann, 2004). Yet, another study suggests that depressed subjects had more significantly delta power than group control and female subjects showed greater values than male subjects (Morgan et al., 2005). Only one study suggests symmetrical frontal activity for depressed subjects and left frontal activity in healthy subjects (Mathersul, Williams, Hopkinson, & Kemp, 2008). Other study suggests the existence of networks of positive mood corresponding to higher activation of right insula (INS), ventral striatum (VS), anterior cingulate cortex (ACC) and ventromedial prefrontal cortex (VMPFC), (Linden et al., 2012).

Hagemann and collaborators (1999) also observed important gender differences during baseline, where females showed relatively less left-hemisphere alpha waves (greater activation) compared to men. This gender difference is consistent with other reports (Davidson, 1994; Kingerly, 2003), but the meaning of these differences is unclear. Nevertheless, a study lead by Kingerly (2003) found that, contrary to the Davidson's model, no support was found for an association between frontal EEG asymmetry and mood or personality.

One of the measures other than physiological asymmetry is EEG coherence. EEG coherence is a frequency-specific amplitude power and phase independent linear index of the degree of synchronicity of neuronal signals between two cortical sites, analogous to a correlation coefficient (Shaw, 1981). Mathematically, it can be defined as the normalized cross power spectrum and phase delay as the phase angle and it is computed between two simultaneously recorded EEG signals from different scalp locations per frequency band (Thatcher, Biver, North, & To, 2004). EEG phase delays are often used to compute "directed coherence" which is a measure of the directional flow of information between two EEG electrode sites. (Thatcher et al., 2004).

Regarding the studies presented before a classical question may emerge. Is EEG asymmetry a well sustained trait and guide to characterize mood, or can other EEG data give us a better view of the cerebral activation and his relation with mood disorders? Precisely, other than frontal asymmetry as a trait characterizer of depression, it might be important

consider other electrophysiological measures to have a wider understanding of EEG patterns and behaviours associated.

Although the heterogeneity of depression, it'll will be considered for the present review the unipolar depression (MDD).

Method and Materials

1. Subjects

This study included 45 subjects, 27 for the experimental group and 18 for the control group. Experimental group subjects were selected from the qEEG database of Neurobios-Instituto de Diagnóstico e Reabilitação Integrada (n=27; M=39.34 years; SD=19.66 years) totalizing 10 female and 17 male participants. All these subjects were selected based on criteria for diagnosis of Major Depressive Disorder and minor depressive disorder, excluding other disorders or any kind of neurological pathology, verified by clinical history, neurological examination and EEG clinical evaluation, as well drug or alcohol consumption, assessed by an experienced psychiatrist who was responsible for clinical evaluation. All this process was based on a comprehensive assessment process, compromising a clinical psychological and symptoms evaluation, as well as a neuropsychologial assessment, consisting of "Bateria de Avaliação Cognitiva Breve – *Brief Cognitive Assessment Battery*" (Alvarez, M. Machado, M., Pastor-Fernandes, R., Marins, N. & Marques-Teixeira, J., 2005). Diagnosis was obtained following the DSM-IV (American Psychiatric Association, 2014) criteria, with all of the 27 subjects presenting a Major Depressive Disorder. Control group subjects were selected from general population that present no history of any mental or neurological disorder, no history of present or past substance consumption, except nicotine, nor taking any type of psychopharmacs, in a total of 10 female and 8 male subjects (n=18; M=37.27 years; SD=13.02 years).

2. qEEG recording

Verbal informed consent was obtained from the patient after the nature and the goal of the qEEG recording had been fully explained in which the patient provided assent to intervention.

The electrophysiological recordings were carried out employing Neuronic (Neuronic SA) hardware and software, in a soundproof room. All subjects were instructed to rest with eyes-closed, seated in a comfortable armchair. Five minutes of eyes closed resting state EEG, followed by 5 minutes of eyes open were acquired, with the sampling rate of 250 Hz. Nineteen sintered Ag/AgCl electrodes were positioned in the cap according to the 10/20 International System with linked ears references. The electrode impedance was under 10 Kohms and impedance was monitored throughout the recording. The raw EEG signal was filtered through a band-pass filter (0.15-30 Hz) before artefact elimination. Artefact-free EEG data epochs (minimum 2 minutes) were selected based on visual inspection and completed with automatic edition included in Neuroguide Deluxe 2.5.1 (Applied Neuroscience St. Petersburg, FL) software for qEEG analysis. Age referenced z-score deviations based on a commercially available normative qEEG database (NeuroGuide Deluxe 2.5.1; Applied Neuroscience;). A Fast-Fourier-Transform was used to calculate absolute and relative power in each of five non overlapping frequency bands: delta (1-4 Hz), theta (4-8 Hz), alfa (8-12 Hz), beta (12-25 Hz), and Hibeta (25-30 Hz) by using NeuroGuide Deluxe 2.5.1 software.

3. Statistical Analysis

Separate t-test student tests were performed for two independent groups, the experimental group and the control group for natural log transformation of raw score for absolute powers, asymmetry and frontal homologous inter-hemispherical electrodes coherences. To analyse the differences in asymmetry patterns between the two groups, an independent measure t-test was performed across the alpha (8-12Hz) and beta (12-25Hz) bands and homologues interhemispheric pairs of electrodes calculated for F3-F4, Fp1-Fp2, C3-C4, T3-T4 and intra-hemispheric pairs of electrodes F3-F7 and F4-F8. Another asymmetry calculation was tested: (F3+F7) - (F4+F8) for beta and (F4+F8)-(F3+F7) for

alpha waves in order to obtain left (F3+F7) and right (F4+F8) frontal absolute power scores for right and frontal areas.

Coherence values were analysed for the same electrode homologous pairs (Fp1-Fp2; F3-F4; C3-C4; F7-F8; T3-T4), for the Delta (1-4 Hz), Theta (4-8 Hz), Alpha (8-12 Hz) and Beta (12-25 Hz) bands coherence raw scores. Raw scores for Coherence were found to be normally distributed only in the control group and no logarithmic transformation was required.

All statistical analysis was assessed by SPSS 24 for the normalized absolute powers, the normalized asymmetry scores and the raw absolute power inter-hemispherical coherences.

4. Research Design

Asymmetries were calculated using the neurometrics formulas proposed by John (1988) to assess the power differences between left (L) and right (R) hemispheres for the alpha (8-12 Hz) and beta (12-25 Hz) bands. To obtain a normal distribution of the absolute power scores a natural logarithmic transformation was done (y = log (Absolute Power) (Gasser, 1982). The calculations were inverted in the alpha band (R – L) / (R + L) and used in its original form for the beta band (L – R) / (R + L), meaning that a negative score refers to increased inversion of the asymmetry in both bands since that alpha waves are inversely related to cortical activation (Ritter, 2006). A positive score for the alpha band means greater power in the right hemisphere and a greater left-sided power for the beta rhythms, pointing towards a physiologic asymmetry.

Results

1. Alpha and Beta Absolute Power normalized data

The logarithmic transformation allowed to normalize the data, in order to make the asymmetry calculations of the difference between intragroup interhemispheric pairs of

electrodes. Concerning the absolute power in alpha band (8Hz-12Hz) between depressive individuals and controls, no significant differences were found (Table 1).

Also, the absolute power in beta band (12Hz-25Hz) (Figure 2) between the two groups shows no significate differences.

Table 1

Alpha absolute power normalized sample LOG (uV Sq) between depressive and control subjects

	Dª	Cº				
Electrodes	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1	0.94 (0.38)	0.90 (0.39)	0.316	43	.665	0.19
Fp2	0.95 (0.38)	0.91(0.40)	0.32	43	.607	0.269
F3	1.08 (0.39)	1.03 (0.49)	0.435	43	.976	0.001
F4	1.07 (0.38)	1.02 (0.40)	0.434	43	.889	0.02
C3	1.18 (0.38)	0.99 (0.39)	1.633	43	.674	0.180
C4	1.27 (0.36)	1.10 (0.41)	1.48	43	.377	0.799
F7	0.90 (0.33)	0.78 (0.46)	1.021	43	.12	2.521
F8	0.89 (0.32)	0.80 (0.38)	0.794	43	.304	1.083
T3	0.90 (0.34)	0.66 (0.35)	2.218	43	.976	0.001
T4	0.90 (0.36)	0.74 (0.39)	1.374	43	.633	0.231

Note: D = Depressives; C = Controls; nª= 27; nº = 18

Table 2

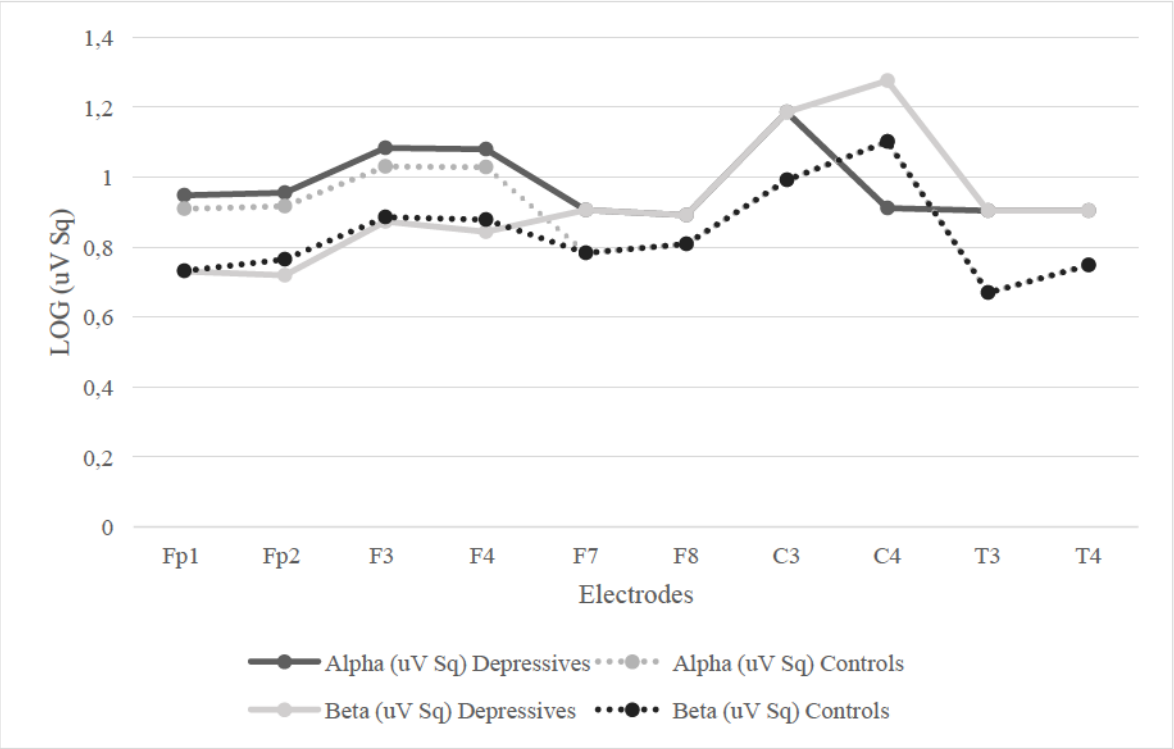
Beta absolute power normalized sample LOG (uV Sq) between depressive and control subjects, p(<0,05)

	Dª	Cº				
Electrodes	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1	0.72 (0.27)	0.73 (0.30)	-0.02	43	.685	0.167
Fp2	0.71 (0.26)	0.76 (0.27)	-0.557	43	.951	0.004
F3	0.87 (0.29)	0.88 (0.30)	-0.138	43	.756	0.098
F4	0.84 (0.27)	0.87 (0.30)	-0.388	43	.842	0.040
C3	0.92 (0.25)	0.87 (0.29)	0.519	43	.675	0.178
C4	0.99 (0.24)	0.94 (0.30)	0.581	43	.454	0.572
F7	0.74 (0.20)	0.72 (0.28)	0.181	43	.243	1.403
F8	0.71 (0.21)	0.70 (0.25)	0.098	43	.61	0.264
T3	0.74 (0.30)	0.78 (0.32)	-0.426	43	.854	0.034
T4	0.69 (0.28)	0.74 (0.27)	-0.599	43	.658	0.199

Note: D = Depressives; C = Controls; nª= 27; nº = 18

Figure 1

Comparison between depressives and controls for Alpha (8Hz – 12Hz) and Beta (12Hz – 25Hz) bands (uV Sq) measured in LOG (uV Sq)



2. EEG asymmetry in Alpha and Beta bands

The figures (3 and 4) stand for elucidating different distribution patterns of asymmetry in both alpha and beta bands for the experimental group (Figure 3) and the control group (Figure 4). We can verify in F8-F7, more alpha power in F7 than in F8 trough the negative value of logarithmic differences of absolute power (table 3). Yet, in F4-F3, the alpha absolute power is slightly superior in F4 of the same pair. Regarding, the pair C4-C3, the alpha absolute power is superior in C4 than in C3.

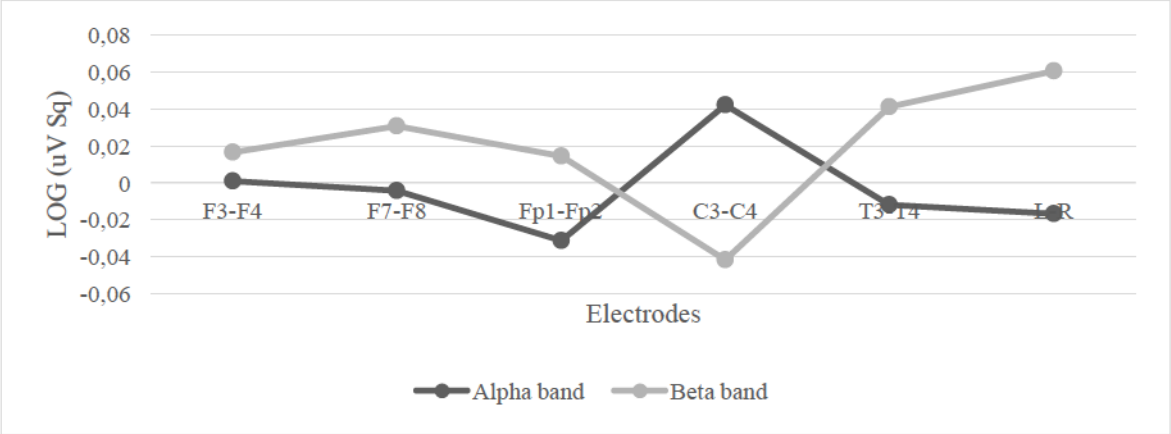
In beta band the absolute power is superior in F3 than in F4. In F7-F8, the absolute power is superior in F7 than in F8. For Fp1-Fp2, the absolute power is superior in Fp1. Regarding C3-C4, the absolute power is superior in C4, verified trough the negative value of logarithmic differences of absolute power (table 4).

Concerning Fp2-Fp1, the absolute power is superior in Fp1 for both alpha and beta bands, verified trough the negative values in alpha band and positive values in beta band.

As for Left-Right Hemispheres a superior absolute power for beta and alpha bands is found in Left Hemispheres.

Figure 3

Physiological asymmetry and inversion of asymmetry between homologous pairs of electrodes in alpha(8-Hz-12Hz) & beta(12Hz-25Hz) bands in the experimental group, measured in (LOG(uV)Sq)



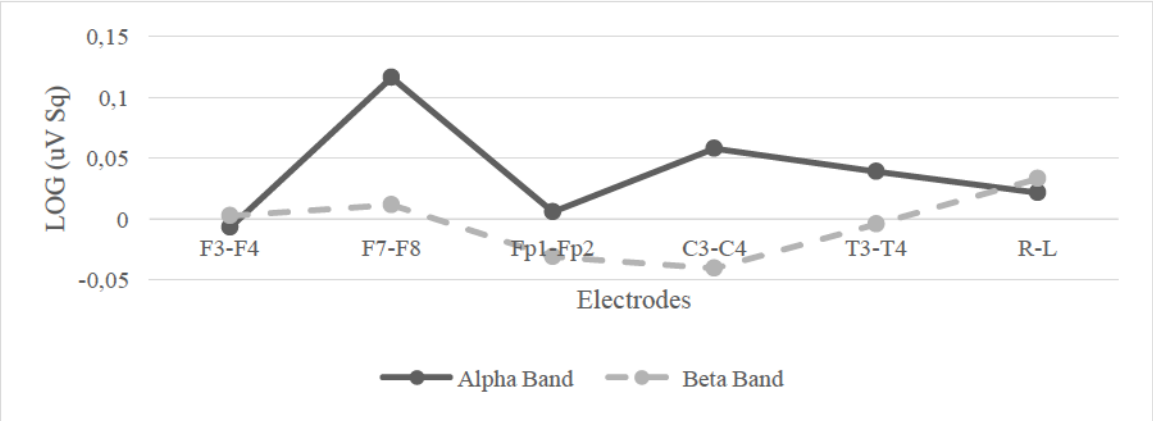
Note: Values in vertical axis correspond to converted raw scores (uV Sq) trough LOG equation; R-L (Right-Left Hemisphere (F4+F8)-(F3+F7) for alpha asymmetry calculation, (F3+F7)-(F4+F8) for beta asymmetry calculation

Concerning the controls (Figure 4; Table 3) in alpha band, for F4-F3, no differences in absolute power between electrodes were found. For the F8-F7 pair, the absolute power is superior in F8 verified through the positive value logarithmic differences of absolute power. For Fp2-Fp1 the absolute power is slightly superior in Fp2. As for C4-C3, the absolute power is superior in C4. For T4-T3 a superior absolute power is found for T4. As for Left-Right Hemispheres we found a superior absolute power in right hemisphere (absolute power superior in F4+F8 than in F3+F7).

Observing the beta band, for F3-F4, the absolute power is superior in F3 than in F4. For the pair F7-F8 a superior absolute power is found for F7. For Fp1-Fp2 we found a superior absolute power in Fp2 than in Fp1. The same is found for the pair C3-C4, revealing a superior absolute power in C4. In T3-T4 the absolute power is superior in T4. As for Left-Right Hemispheres we found a superior absolute power in left hemisphere (absolute power superior in F3+F7 than in F4+F8).

Figure 4

Physiological asymmetry and inversion of asymmetry between homologous pairs of electrodes in alpha(8Hz-12Hz) and beta(12Hz-25Hz) bands in the control group, measured in (LOG(uV)Sq)



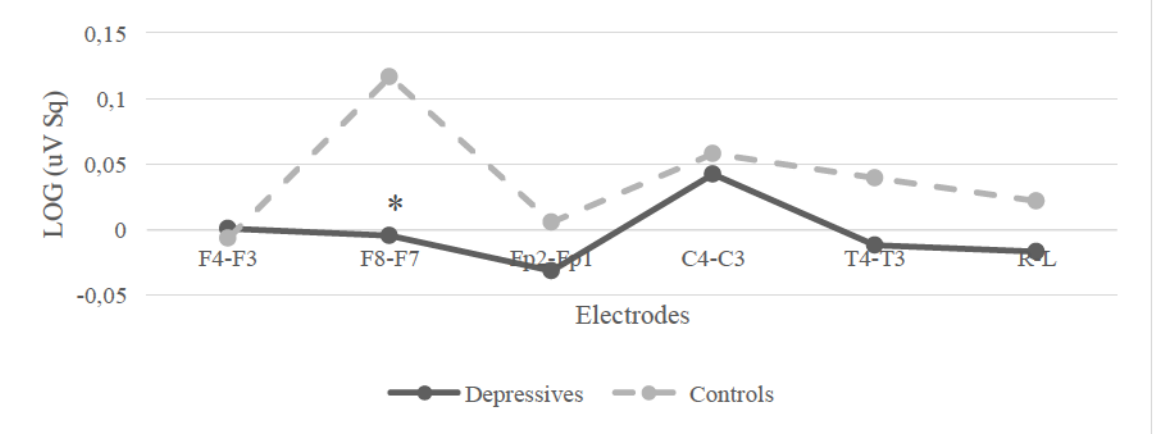
Note: Values in vertical axis correspond to converted raw scores (uV Sq) trough LOG equation; R-L (Right-Left Hemisphere (F4+F8)-(F3+F7) for alpha asymmetry calculation, (F3+F7)-(F4+F8) for beta asymmetry calculation

When comparing alpha band between the experimental group and the control group to find differences between intergroup interhemispheric pairs of electrodes (Figure 5) significate results were found only for F8-F7 ($F=5.325$; $p<0.05$; d.f=43), suggesting a superior alpha absolute power in F7 than in F8. We can verify for left-right hemispheres a superior absolute power in left hemisphere (F3+F7) than in right hemisphere (F4+F8).

Regarding the comparison between both groups concerning beta band (12Hz-25Hz) (Figure 6; Table 4), no significant differences were found.

Figure 5

Physiological asymmetry and inversion of asymmetry between homologous pairs of electrodes in alpha(8Hz-12Hz) band between the two groups, measured in (LOG(uV)Sq)



Note: Values in vertical axis correspond to converted raw scores (uV Sq) trough LOG equation; R-L (Right-Left Hemisphere (F4+F8)-(F3+F7) for alpha asymmetry calculation, (F3+F7)-(F4+F8) for beta asymmetry calculation; * = $p<0,05$

Table 3

Statistical analysis in alpha band (8Hz-12Hz) between depressive subjects and controls, measured in LOG Absolute power(LOG(uV)Sq)

	Dª	Cº				
Homologous pairs	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
F4-F3	0.0007 (0.07)	-0.006 (0.23)	-0.557	43	.117	2.560
F8-F7	-0.004 (0.10)	0.116 (0.47)	0.519	43	.026	5.325
Fp2-Fp1	-0.031 (0.17)	0.005 (0.03)	-0.02	43	.20	1.692
C4-C3	0.042 (0.05)	0.057 (0.07)	-0.138	43	.486	0.494
T4-T3	-0.011 (0.17)	0.039 (0.07)	0.581	43	.531	0.398
(F4+F8)-(F3+F7)	-0.016 (0.18)	0.021 (0.59)	-0.388	43	.804	0.062

Note: D = Depressives; C = Controls; nª= 27; nº = 18

Table 4

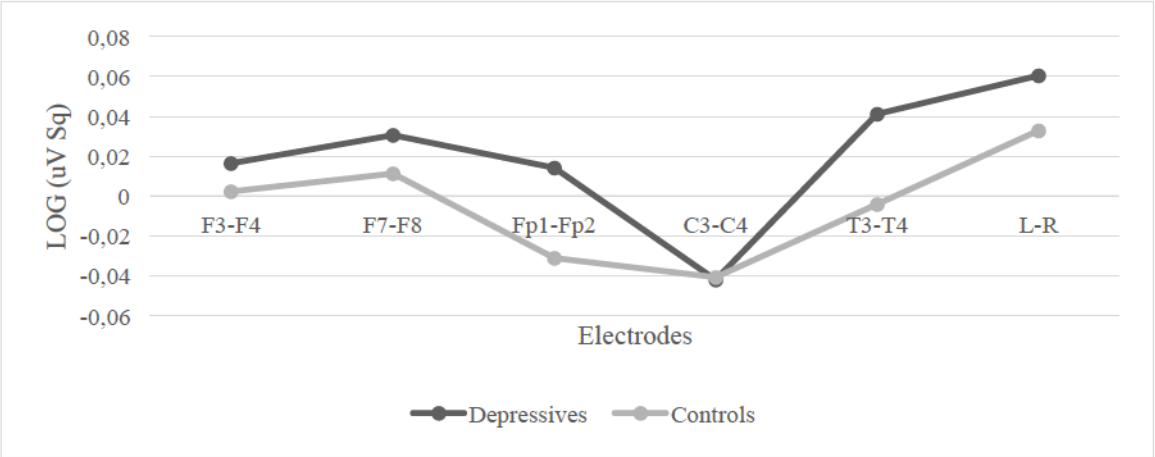
Statistical analysis in Beta band (12Hz-25Hz) between depressive subjects and controls, measured in LOG Absolute power(LOG(uV)Sq)

	Dª	Cº				
Homologous pairs	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
F3-F4	0.016 (0.05)	-0.002 (0.02)	0.993	43	.059	3.76
F7-F8	-0.029 (0.13)	-0.011 (0.11)	0.499	43	.891	0.019
Fp1-Fp2	0.014 (0.05)	-0.031 (0.15)	1.372	43	.195	1.732
C3-C4	-0.041 (0.04)	-0.040 (0.04)	-0.089	43	.847	0.038
T3-T4	0.042 (0.23)	-0.004 (0.16)	0.714	43	.389	0.758
(F3+F7) - (F4+F8)	0.060 (0.2)	0.032 (0.17)	0.464	43	.437	0.615

Note: D = Depressives; C = Controls; nª= 27; nº = 18

Figure 6

Physiological asymmetry and inversion of physiological asymmetry between homologous pairs of electrodes in beta(12Hz-25Hz) band between the two groups, measured in LOG Absolute power(LOG(uV)Sq)



Note: Values in vertical axis correspond to logarithmic difference calculated for each pair os electrodes; L-R (Left-Right Hemisphere (F3+F7)-(F4+F8); * = p<0,05

3. Inter-hemispherical Coherence analysis

An all band analysis was made for the homologous pairs Fp1-Fp2, F3-F4, C3-C4, F7-F8, T3-T4. For the delta coherence raw scores, as shown in table 5, a similar value of coherence in the temporal areas between groups, a slight decrease in coherence values in the prefrontal, a more accentuated decrease in the frontal and central areas can be seen, with statistically significant differences in F3-F4 (F=0.045; p<0.05; d.f=43), C3-C4 (F=9.334; p<0.05; d.f=43).

Table 5

Statistical analysis for coherence raw scores in delta band (1Hz-4Hz) between depressives and controls

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-Fp2	72.68 (19.55)	74.16 (18.21)	-0.256	43	.979	0.001
F3-F4	55.64 (22.77)	70.09 (12.73)	-2.444	43	.045	4.272
F7-F8	12.52 (12.73)	15.96 (11.07)	-0.934	43	.778	0.081
C3-C4	53.63 (23.02)	67.97 (10.50)	-2.471	43	.004	9.334
T3-T4	8.98 (11.53)	9.03 (7.72)	-0.017	43	.141	2.253

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

In the Theta band, a similar pattern to the delta coherence is found (Table 6). The midcenter, F3-F4 (F=4,179; $p<0.05$; d.f=43), central areas, C3-C4 (F=8,053; $p<0.05$; d.f=43) are found to be statistically significant. Also statistically significant, the temporal areas, T3-T4 (F=4,445; $p<0.05$, d.f=43) show a different pattern with an increase a in the theta coherence value in the depressive population relative to the control sample.

Table 6

Statistical analysis for coherence raw scores in theta band (4Hz-8Hz) between depressives and controls

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-Fp2	75.09 (16.89)	80.50 (8.68)	-1.249	43	.101	2.804
F3-F4	59.65 (20.24)	69.86 (10.26)	-1.972	43	.047	4.179
F7-F8	11.90 (12.85)	16.57 (7.96)	-1.372	43	.164	2.003
C3-C4	52.42 (17.01)	59.79 (9.06)	-1.681	43	.007	8.053
T3-T4	6.29 (7.38)	3.68 (3.96)	1.374	43	.041	4.445

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

Relative to the Alpha coherence (Table 7), depressives show a decrease in coherence raw score. In this analysis, significant differences are found in the frontal areas F3-F4 (F=5.083; $p<0.05$; d.f=43) and central areas C3-C4 (F=6.608; $p<0.01$; d.f=43). Despite no statistically significant results were found, the temporal region, similarly to the theta band also shows an increase in alpha coherence value, in T3-T4.

Table 7

Statistical analysis for coherence raw scores in Alpha band (8Hz-12Hz) between depressives and controls

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-Fp2	83.00 (17.46)	89.13 (7.25)	-1.405	43	.056	89.131
F3-F4	69.39 (22.35)	79.76 (9.74)	-1.849	43	.029	79.768
F7-F8	27.43 (23.03)	38.23 (22.28)	-1.561	43	.563	38.236
C3-C4	46.12 (21.48)	55.40 (13.49)	-1.628	43	.014	55.406
T3-T4	7.05 (7.04)	6.72 (5.74)	0.166	43	.283	6.727

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

Concerning Beta band coherence raw scores, no statistically differences were found (Table 8). Nevertheless, we can found as in the delta, theta and alfa bands a general pattern of a decrease of coherence values in depressive subjects, suggesting a weaker interconnection between areas of the brain. Also, in central areas, C3-C4, we can find that difference quite accentuated (Figure 9).

Table 8

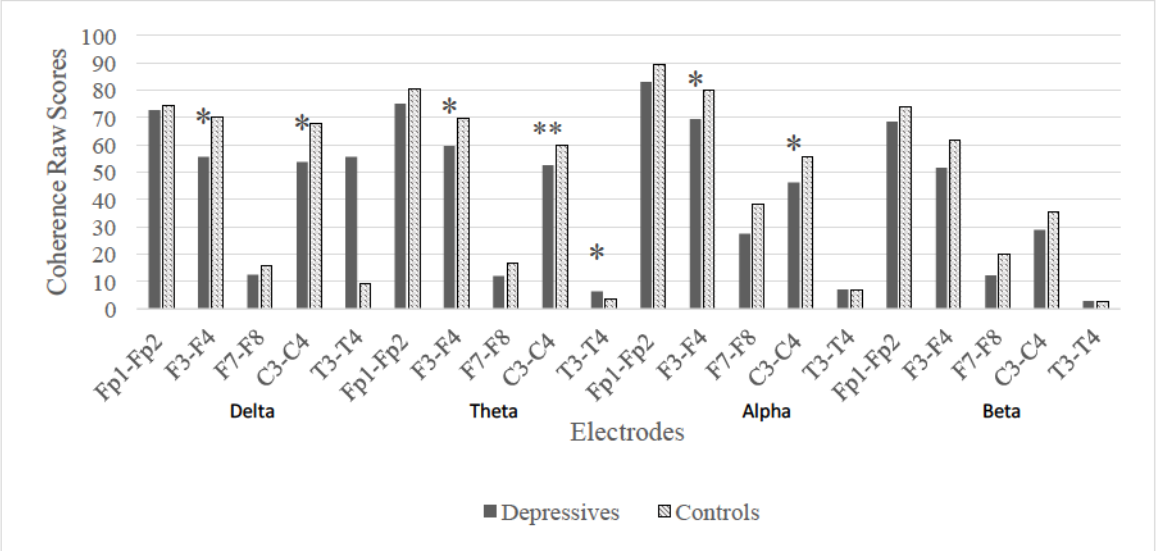
Statistical analysis for Coherence raw scores in Beta band (12Hz-25Hz) between depressives and controls

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-Fp2	68.49 (18.97)	73.7 (12.98)	-1.014	43	.104	2.765
F3-F4	51.51 (22.35)	61.62 (9.74)	-1.892	43	.377	0.796
F7-F8	12.32 (11.85)	19.76 (15.30)	-1.834	43	.381	0.784
C3-C4	28.96 (13.38)	67.97 (11.24)	-1.693	43	.237	1.44
T3-T4	2.75 (2.87)	2.76 (4.72)	-0.008	43	.252	1.349

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

Figure 7

Comprehensive graphic with homologous pairs in the four different bands by this order of presentation (Delta, Theta, Alfa and Beta) in both depressive and controls measured in raw scores (uV Sq).



*Note: The values on the vertical axis correspond to Coherence raw scores in a scale (0 – 100). Each band correspond to 5 homologous pairs of electrodes (Fp1-Fp2;F3-F4; C3-C4; F7-F8; T3-T4); * = p<0,05; ** = p<0,01*

4. Anteroposterior Coherence analysis

After measuring the inter-hemispherical coherences of frontal, central and temporal areas (Fp1-Fp2, F3-F4, C3-C4 and T3-T4), an analysis for the intra-hemispherical coherences raw scores was made for all bands and for each electrode aforementioned with his respective hemispherical posterior electrode (Fp1-P3, F3-P3, C3- P3, T3-P3, Fp2-P4, F4-P4, C4-P4 and T4-P4).

As we can see in table 9, statistically differences were found for delta band and for both hemispheres in the frontal areas, respectively F3-P3 ($F=5.041$; $p<0.05$; d.f=43), F4-P4 ($F=4.822$; $p<0.05$; d.f=43). For the prefrontal areas only significate differences were found for the left-hemisphere with Fp1-P3 ($F=5.475$; $p<0.05$; d.f=43). Except for Fp2-P4, all other pairs show a decrease in coherence values in the depressive patients comparing to the control group (Figure 8).

Table 9

Statistical analysis of Anteroposterior coherence raw scores between intrahemispheric pairs of electrodes in delta band (1Hz-4Hz) measured in (uV Sq).

	D[a]	C[o]				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-P3	12.49 (11.12)	12.96 (7.07)	-0.159	43	.024	5.475
Fp2-P4	14.32 (16.51)	10.53 (6.53)	0.924	43	.058	3.805
F3-P3	30.87 (17.47)	36.00 (11.34)	-1.098	43	.03	5.041
F4-P4	31.49 (16.75)	34.38 (11.16)	-0.643	43	.034	4.822
C3-P3	69.42 (12.77)	72.55 (8.74)	-0.905	43	.39	0.754
C4-P4	67.47 (15.43)	71.40 (8.77)	-0.976	43	.097	2.873
T3-P3	36.44 (15.23)	40.60 (12.44)	-0.962	43	.238	1.432
T4-P4	34.002 (14.40)	38.29 (10.78)	-1.077	43	.167	1.973

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; n^a= 27; n^o = 18

Concerning the anteroposterior coherence in theta band we can verify a similar pattern as seen in the anteroposterior delta band analysis (Table 10; Figure 9). No statistically differences were found, still, we can see a general tendency for a decrease in coherence in depressive patients relative to non-depressive subjects.

Table 10

Statistical analysis of Anteroposterior coherence raw scores between intrahemispheric pairs of electrodes in theta band (4Hz-8Hz) measured in (uV Sq).

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-P3	13.80 (9.99)	14.34 (8.14)	-0.192	43	.50	.463
Fp2-P4	16.15 (15.51)	14.05 (7.79)	0.53	43	.108	.695
F3-P3	32.30 (13.71)	33.02 (13.55)	-0.174	43	.992	0
F4-P4	30.94 (13.14)	31.30 (13.86)	-0.088	43	.982	.001
C3-P3	71.23 (8.36)	71.31 (9.24)	-0.032	43	.725	.126
C4-P4	68.62 (10.34)	68.69 (9.34)	-0.024	43	.626	.241
T3-P3	40.01 (12.83)	42.90 (13.96)	-0.716	43	.678	.174
T4-P4	34.74 (15.54)	39.66 (11.64)	-1.144	43	.253	.343

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

For alpha band we can verify a different tendency of the coherence values (Table 11). Comparing to controls (Figure 10) we can see in some pair of electrodes (Fp2-P4, C3-P3, C4-P4, T3-P3) an increase of alpha coherence in depressive subjects. Only the pair C4-P4 ($F=4.546$; $p<0.05$; d.f=43) show statistically significant differences, suggesting that the central-right part of the brain of depressives have a greater coherence than the controls.

Table 11

Statistical analysis of Anteroposterior coherence raw scores between intrahemispheric pairs of electrodes in alpha band (8Hz-12Hz) measured in (uV Sq).

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-P3	12.06 (10.47)	12.92 (10.28)	-0.274	43	.968	0.002
Fp2-P4	13.71 (18.04)	11.94 (11.73)	0.366	43	.751	0.102
F3-P3	18.72 (13.75)	19.76 (15.10)	-0.238	43	.66	0.196
F4-P4	18.07 (12.90)	18.38 (16.58)	-0.07	43	.262	1.291
C3-P3	59.13 (16.87)	58.67 (15.27)	0.093	43	.901	0.016
C4-P4	59.39 (17.62)	58.32 (12.32)	0.223	43	.039	4.546
T3-P3	36.62 (16.59)	35.92 (16.42)	0.637	43	.353	0.882
T4-P4	37.47 (18.60)	39.32 (15.75)	-0.346	43	.32	1.013

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

Concerning beta band, no statistically differences were found. A different pattern can be seen between depressives and healthy subjects. For central areas (C3-P3, C4-P4) and for temporal areas (T3-P3, T4-P4) bilaterally, we can see an increase in coherence in depressive subjects (Table 12; Figure 11). For prefrontal and frontal üpareas, we see the opposite except for right prefrontal hemisphere (Fp2-P4).

Table 12

Statistical analysis of Anteroposterior coherence raw scores between intrahemispheric pairs of electrodes in beta band (12Hz-25Hz) measured in (uV Sq).

	Dª	Cº				
H.P	*M (SD)*	*M (SD)*	*t*	df	*p*	*F*
Fp1-P3	5.98 (6.22)	6.98 (5.94)	-0.54	43	.504	0.455
Fp2-P4	8.35 (14.89)	7.29 (5.67)	0.285	43	.465	0.543
F3-P3	14.50 (8.80)	17.53 (8.22)	-1.16	43	.869	0.027
F4-P4	13.97 (7.81)	17.08 (8.74)	-1.243	43	.503	0.456
C3-P3	59.26 (8.92)	58.67 (9.73)	-0.081	43	.711	0.14
C4-P4	58.74 (9.31)	55.30 (10.53)	1.149	43	.403	0.714
T3-P3	32.20 (14.04)	29.29 (16.39)	0.637	43	.353	0.882
T4-P4	30.12 (12.37)	28.37 (10.73)	0.488	43	.575	0.32

Note: H.P = Homologous Pairs; D = Depressives; C = Controls; nª= 27; nº = 18

Discussion

The main objective of this study was to find a phenotype that could characterize depression. As second objective, this study focused in what it can be in the future a more precise lecture of the importance of other electroencephalography data analysis in understanding mood disorders. The results dissected before show us an "architectural plan" of what can be a more comprehensive analysis of mood disorders, such as depression. More than point out the most studied phenotype (frontal asymmetry) of the last years and sustain it as the main characterization of depression/anxiety, this study was regardless to point in just one direction. Albeit Davidson (Davidson, 1979) and other authors suggest that frontal asymmetry can be a phenotype to characterize depression, Kingery (Kingery, 2003) point out some limitations of the use of asymmetry as a "categorization" of mood disorders. Not only this author but Hagemann and Reid (Hagemann et al., 1999: Reid et al., 1998) made

studies in which have failed to replicate Davidson's model. More than ever, the comprehension of behaviour must take in account a whole and we are advancing trough complexity, which portray the structure of behaviour. For that reason, it was important to make an analysis which contemplates other electrophysiological data, capable of bringing a "fresh looking" of brain functioning and behaviour response, such as coherence scores.

The findings in this study reconcile with those found in literature concerning absolute power in alpha band and beta band. Despite the absence of significant results, the general pattern indicate us that depressive patients show a superior absolute power in alpha band in all studied sites (F3, F4, F7, F8, C3, C4, T3, T4, Fp1, Fp2) and for beta it's found superior absolute power in only C3, C4, F7 and F8, comparing to controls. This differences can be suggestive of a trend to alpha amplitude in the pre frontal, frontal, central and temporal region in depressive subjects compared to controls suggesting a less cortical activation (Davidson, Ekman, Saron, Senulis, & Friesen, 1990). However, the results obtained for beta band suggest that less cortical activation remains contradictory.

This may advocate that in depressive patients, the physiological alpha amplitude is apparently lost, although, concerning physiological beta asymmetry, the beta results suggest that higher beta amplitude is related to an increase of cortical activation and is typically associated with behavioural cognitive and emotional activation (Ray & Cole, 1985) Buchsbaum et al. (1986) has reported higher cerebral metabolism in affective disorders, including unipolar depression, showing higher anterior-posterior metabolism (greater relative frontal activation than controls). Also Knott, Mahoney, Kennedy and Evans (2000) found that beta absolute power was higher in depressives comparing to healthy subjects. Not least, there is an association between beta activity and regional cerebral blood flow (Nakamura et al., 1999). These findings were only partially replicated in our study.

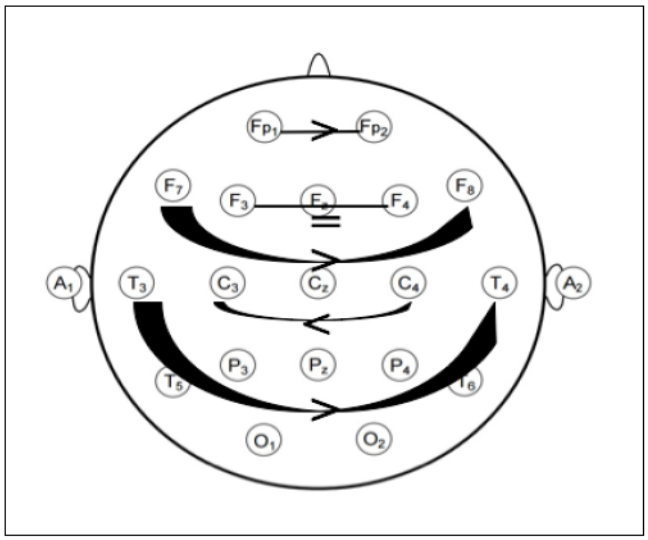
Since no significant differences were found for the absolute power, how both groups "behave", comparing the interhemispheric intragroup differences? To better understand this differences, it must be taken in account and explained the concept of physiological asymmetry. The physiological asymmetry is calculated as the logarithmic difference for each homologous pair of electrodes studied. This calculation is made differently for alpha and beta band (e.g. alpha band – (Fp2-Fp1/Fp2+Fp1); for beta band – (Fp1-Fp2/Fp1+Fp2)). Through this calculation, if a positive value is obtained in beta asymmetry calculation, for example for Fp1-Fp2, it means that the value is greater in left side, suggesting a superior beta amplitude in the left side Fp1>Fp2 that can be understudied as physiological asymmetry. If a negative value is obtained in alpha asymmetry calculation, it means that the

value is greater in left side, suggesting a superior alpha amplitude in the left side Fp1>Fp2, verifying an inversion of physiological asymmetry. If through the calculations we found a value near 0, it means that an inversion pattern isn't found but it suggests a loss of physiological asymmetry for that homologous pair.

Reminding the Davidson model, this study found statistical differences concerning physiological asymmetry. In fact, the values concerning midfrontal areas F4-F3 found an absence of physiological asymmetry and lateralfrontal F8-F7 was statistically significant, showing a slight inversion pattern, regarding alpha band, which is according with literature suggesting as phenotype for depression, since the increase of alpha exist in on left hemisphere and not in the right, leading to an activation of the right hemisphere which is responsible for negative emotional processes and withdrawal according to Davidson's model (Davidson et al., 1979). Greater relative right lateral frontal, but not midfrontal, EEG activity has been associated with higher negative emotionality in adults (Jacobs & Snyder, 1996), which is found in this study.

Figure 8

Interhemispheric alpha absolute power differences between homologous pairs of electrodes in depressive subjects



Note: The image represents the international 10-20 system. The arrows reflect not a tendency towards (e.g. from Fp1 to Fp2). The arrows reflect which electrode have a superior absolute power. In this case, Fp1 have superior absolute power than Fp2; For F4-F3 both electrodes have similar absolute power.

As we can see in Figure 8, the interhemispheric alpha absolute power differences between homologous pairs of electrodes in depressive subjects give us a comprehensive topographic view of that difference. We can observe that Fp1 have superior alpha absolute power than Fp2, F7 have a superior alpha absolute power than F8 and T3 have a superior

alpha absolute power than T4. As for midfrontal area, F4-F3, as said afore there's no difference concerning absolute power, suggesting a loss of physiological asymmetry. In this case, in the midcentral area, C4 have a superior alpha absolute power than C3, maintaining physiological asymmetry. We can see a predominance of alpha absolute power in the left-side, suggesting an inversion of physiological asymmetry.

As expected, the pattern found for group control is different from the one found for depressive subjects, showing a predominance of alpha absolute power in the right-side, which is in accordance with literature.

For beta band no statistically differences were found, still, the results found suggest a greater left lateral frontal asymmetry for both depressives and controls. Lopez-Duran (2011) suggest that lateral frontal asymmetry score may moderate the effects of exposure to stressful life events, like greater relative left lateral frontal activation. This study didn't lead hypothesis such as those found in the former study, yet, the same pattern is found for the same located sites. Other studies regarding midfrontal, but not lateralfrontal scores, suggest an association with emotion regulation and affective style, concerning the behavioural system of activation/inhibition (Coan & Allen, 2003), which is not in agreement with the pattern found in this study that lies on an absence of asymmetry F4-F3. Despite midfrontal areas aren't confirmed through Davidson model, this study can confirm lateralfrontal sites.

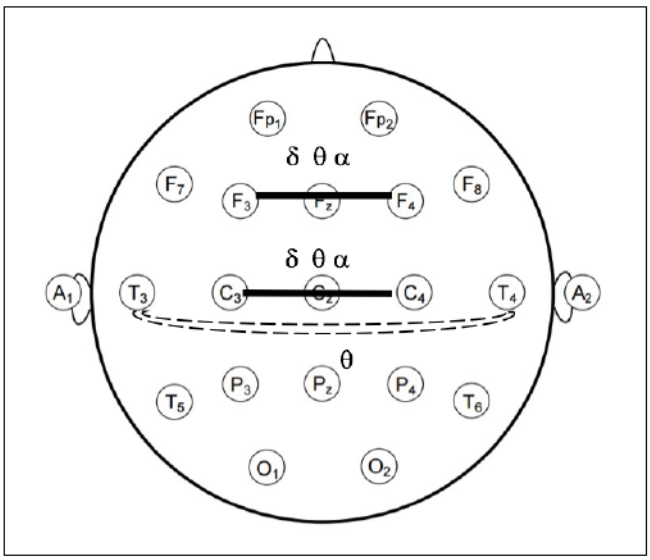
Although asymmetry patterns were studied, other objective of this study is deepen the investigation concerning other electrophysiological data that can ben carrier of additional and precise information for understanding mood disorders. Coherence scores may be helpful concerning the understanding of depression and brain functioning, as said afore. Coherence is the most common measure used to determine if different areas of the brain are generating signals that are significantly correlated (coherent) or not significantly correlated (not coherent) (Bowyer, 2016). The results found in this study suggest a general decrease in interhemispherical coherence scores in depressives in all studied bands, except for T3-T4 Delta. These findings are in accordance with the findings of Knott et al. (2000) who found the same pattern in depressive subjects.

Reminding the concept of coherence, it can indicate us which particular brain areas are working together, suggesting that high coherence between two electrodes can be interpreted as strong functional or anatomical connection between two brain areas. (Callaway & Harris, 1974; French & Beaumont, 1984). Nevertheless, we can look for the difference between depressives and controls and link the depressive symptoms with lower interhemispherical coherence scores on the first group. In fact, some studies found reduced

coherence in delta and theta bands (Lieber, 1988) which are in accordance with the findings in this study.

Figure 9

Interhemispheric coherence between homologous pairs in the different bands in depressive subjects



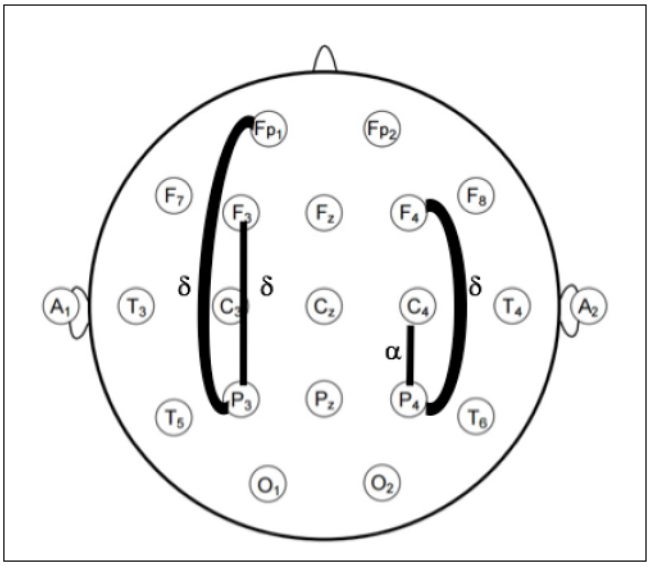
Note: The image represents the international 10-20 system. Each line represents the connection between sites. Only significant results obtain in statistical analysis were taken in account in the composition of this image. δ = Delta; θ = Theta; α = Alpha

In Figure 9, it is illustrated the statistical significant connections between interhemispheric homologous pairs in different bands.

In delta, theta and alpha bands we found a reduced coherence in midcentral areas (F3-F4 and C3-C4). As for T3-T4, it's found statistical significant connections only in theta band. being statistically significant midcentral areas in both bands (F3-F4; C3-C4). This may be suggestive of a less synchrony for mid frontal and central areas in depressives which can lead to a poorer communication between those brain regions. To better understand the importance of this results it must be taken in account not only what coherence measures but what is under that measurement. The communication between two electrodes (brain regions) are supported for networks of neurons (Bowyer, 2016). So, if the results found in depressives which are in accordance with other studies (Knott et al., 2000) suggest less connectivity comparing to controls it might be due to a "weaker" network connectivity between brain regions for depressives, which in this study is found for F3-F4, C3-C4 for delta, theta and alpha bands.

Figure 10

Anteroposterior coherence between pairs in the different bands in depressive subjects



Note: The image represents the international 10-20 system. Each line represents the connection between sites. Only significant results obtain in statistical analysis were taken in account in the composition of this image. δ = Delta; α = Alpha

Concerning anteroposterior intrahemispherical coherences this study found only significant results for for midfrontal areas for both hemispheres (F3-P3; F4-P4) and left hemisphere prefrontal area (Fp1-P3) concerning delta band, and right central area for alpha band (C4-P4), which is illustrated in figure 10. The view of anteroposterior connectivity is quite different of the interhemispherical view. In this study, as said above, the coherence scores in depressives showed to be lower than in controls. However, for anteroposterior coherence scores, only in all located sites except for Fp2-P4 show that depressives have hypocoherence comparing to controls. It is important to refer that regarding anteroposterior coherences there's very few studies who endorsed investigation in this field. Yet, we thought it could be essential focus in this connections to give us precisely what it could be a wider view of brain regions connections and their importance on depression. Since no differences were found despite the bands and sites referred before, an interpretation we may take from the results is that intrahemspherical connections have a different pattern from interhemispherical connections, showing variable coherence levels between groups, either greater or lower in almost all bands except for delta, as referred above. Hitherto, the findings in this study are interesting for the slow wave activity (SWA) regarding the frontal-posterior connections.

As for investigation between anteroposterior coherence values and mood disorders there's none literature found. A vector we may consider for this results is the important of

anteroposterior coherences in cognition. Hammar and Ardal (2009) found that depressive patients show cognitive impairment. Sauseng, Klimesch, Schabus, Doppelmayr, (2005) found that an increase in slow wave activity in long-range connectivity is associated with central executive demands. Nevertheless, "the involvement of a frontoparietal network in visuospatial working memory was found with different methods, the electroencephalogram" (Sauseng et al., 2004). In fact, what is found in depressive subjects in our study is suggestive of an hypochoerence in anteroposterior slow waves for, bilaterally, with greater expression in left side, showing only hypercoherence for C4-P4. This hypocoherence in frontoparietal connections are in accordance with the findings above mentioned, suggesting that anteroposterior hypocoherence may be linked to cognitive impairment, which is found in depressive subjects, specially concerning central executive demands.

Although, debating these results here can be very exploratory since literature is poor concerning anteroposterior connections in all bands, leaving up a suggestion of further investigation regarding anteroposterior coherences and depression

Conclusion

It is important to not take a risk step further considering this as a conclusion to anteroposterior coherence and mood disorders, as well the cognitive deficits associated and stated above. In advantage, it enlightens us to take that step further concerning investigation in this field.

No significant differences were found for absolute power in Alpha and Beta between depressive subjects and controls. Yet, F7-F8 confirmed to be an electrophysiological phenotype to characterize depression, showing an inversion of physiological asymmetry pattern. Concerning Coherences an hypocoherence is verified in the slow waves at interhemispheric homologous midcentral pairs (F3-F4/C3-C4). Also, for anteroposterior coherences a hypocoherence was found on delta and alpha bands, bilaterally, with greater expression in left-side.

Although, some limitations can be found in this study such as the number of subjects could have been an obstacle to this study, leaving up a suggestion of replicating these findings with a bigger sample. Also, the fact that the analysed data was made in resting state EEG, it could be important to make an EEG task-related recording. Though the sample was composed entirely by a diagnosis of major depressive disorder, it's heterogeneity must be

taken in account. Another limitation may lay on a severity symptom assessment and its relation with qEEG findings to give us a more detailed view. Not least important, methodological differences may lead to different outcomes.

We think that this approach can be suggestive for further investigations to better understand and develop knowledge in the relationship between mood disorders and qEEG profiles, within a holistic view regarding the macro and micro components characteristics of behaviour.

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