JECN

Journal of Epilepsy and Clinical Neurophysiology

ISSN 1676-2649

Volume 27 | Number 1 | Year 2021

ABSTRACTS PRESENTED AT THE 8TH BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (BRAINN-UNICAMP)

APRIL 4th - 6th 2022 - CAMPINAS, SP, BRAZIL

J Epilepsy Clin Neurophysiol 2021; 27(1): 1-37

www.jecn.org

JECN Journal of Epilepsy and Clinical Neurophysiology

Órgão Oficial da Liga Brasileira de Epilepsia

Indexada no LILACS – Literatura Latino-americana e do Caribe em Ciências da Saúde LILACS 25 years

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Ficha Catalográfica

Journal of Epilepsy and Clinical Neurophysiology (Revista de Epilepsia e Neurofisiologia Clínica) / Liga Brasileira de Epilepsia. – Vol. 26, n.1, jul 2020.

v.1, 1995 – JLBE: Jornal da Liga Brasileira de Epilepsia
v. 2 a 7 (n. 2, jun. 2001) Brazilian Journal of Epilepsy and Clinical Neurophysiology (Jornal Brasileiro de Epilepsia e Neurofisiologia Clínica)
Publicação trimestral.
ISSN 1676-2649

CDD: 616.8
CDU: 616.853(05)
616.8-092(05)
616.8-073(05)

Índice para Catálogo Sistemático:

Epilepsia – Periódicos – 616.853(05);
Neurofisiologia – Periódicos – 616.8-092(5);
Eletroencefalografia – Periódicos – 616.8-073(05);
Eletroneuromiologia – Periódicos – 616.8.073(05);
Neurologia – Fisiologia – Periódicos – 616.8-092(05).

Coordenação editorial, criação, diagramação, tradução e produção gráfica Atha Comunicação e Editora - E-mail: 1atha@uol.com.br

JECN Journal of Epilepsy and Clinical Neurophysiology

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A PIPELINE FOR AUTOMATED QUALITY ASSESSMENT OF MRSI SPECTRA BASED ON FUZZY ART NEURAL NETWORK AND K-MEANS

G. Dias[1], T. Abreu[1], S. Appenzeller[2], S. Dertkigil[3], L. Rittner[1]

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Introduction: Magnetic resonance spectroscopy imaging (MRSI) is a technique that enables the identification and quantification of metabolites from signals in the frequency domain. It has increasingly attracted the interest of neurologists, as it can support the diagnosis and treatment of diseases such as epilepsy, brain tumors and Alzheimer's [1]. However, MRSI often produces poor quality spectra that can induce quantification or interpretation errors that significantly impact the clinical use of spectroscopic data. Since manual spectral quality control is time-consuming and affected by human subjectivity, fast and reliable automated methods are of great interest to enable the application of MRSI in clinical routine. In this work, a pipeline was proposed for automated quality assessment of MRSI using Fuzzy ART artificial neural network [2] and K-Means. **Materials and Methods:** The dataset was composed of 106 MRSI acquisitions of the corpus callosum region from healthy volunteers and patients of the Clinical Hospital (HC - UNICAMP). Each acquisition comprised 208 spectra (13x16), totaling 22048 spectra to use in this study. The proposed pipeline starts with the Fuzzy ART due to its good performance, flexibility, speed, and the expectation that the MRSI spectrum can be interpreted as a time series. We obtain a cluster of signals with great variation using vigilance and learning rate parameters both equal to 0.7, 0.0001 as choice parameter and number of epochs equal to 6. From this cluster, a second step was performed using k-means. The number of clusters k was set to 15, since only high values of k generated clusters with significant distinctions. **Results:** Obtained clusters were qualitatively assessed (Fig.1, left). Quantitative comparisons with traditional metrics used to assess the quality of MRSI spectra were also conducted (Fig.1, right). Approximately, 93% of the spectra contemplated the SNR metric criteria, 85% for the FWHM, 100% for the CRLB and 81% considering the three criterias simultaneously. **Discussion/Conclusion**: The proposed model was able to find good quality patterns in the MRSI spectra. It is a fast, easily implementable model that is consistent with the traditional quality metrics used. In future work, other machine learning techniques will be explored with analysis on the spectra considered corrupted, whose artifacts could be corrected by using existing techniques.

References: [1] Nelson SJ, Mol Cancer Ther 2(5):497-507, 2003; [2] Carpenter GA et al., doi:10.1016/0893-6080(91)90056-B; [3] Pereira D et al., doi:10.1117/12.2582186.

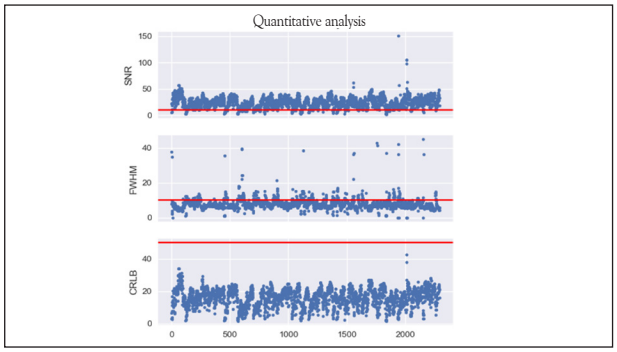

Figure 1. Left: Clustering obtained from the model for a multi-voxel spectral grid of a given patient. Spectra in black are interpreted as "bad" and those in blue as "good". Right: Quantitative analysis with typical threshold values for metrics indicated (SNR>10; FWHM<10; CRLB<50).

A TOOL FOR AUTOMATED COVID-19 AND LUNG SEGMENTATION USING COMPUTED TOMOGRAPHY IMAGES AND DEEP LEARNING

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Introduction: Recent research has shown that COVID-19 can cause neurological symptoms [1]. Many automated segmentation methods for COVID-19 infection using computed tomography (CT) imaging have been recently proposed. However, these methods are usually hard to reproduce and implement quickly in a medical research setting. In this abstract, we present an easy-to-use tool for that purpose. The tool can automatically segment chest CT images using our best deep neural network from our recently published method named CoEDet [2]. **Materials and Methods:** Our best CoEDet checkpoint was packaged into an inference reproducibility graphic interface using Python 3 and Tkinter. The tool can be installed with one command line using pip, supporting Windows and Ubuntu. The workflow for usage is simply selecting a folder containing CT images for a batch run, or a single CT image. The tool reports the progress with a progress bar and monitoring of computational resources (Fig. 2A), with the user indicating where to output the resulting volumetric mask. The output comprises of a volumetric mask (.nii.gz) for each input acquisition with labels 1 for the lung and 2 for consolidations and opacities, and a sheet (.csv) with lung occupation measurements. Additionally, the tool can provide a multi-view and 3D visualization of the results using ITKSnap (Fig. 2B). **Results:** The graphical tool is publicly available for inference, which takes around 10 seconds to segment a whole CT exam using a GPU or 15 minutes using a CPU. Detailed installation and usage instructions can be found at https://github.com/MICLab-Unicamp/coedet. **Discussion/Conclusion**: We develo-

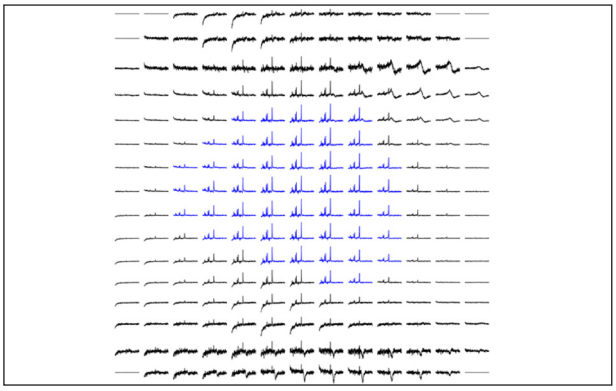

Figure 1.

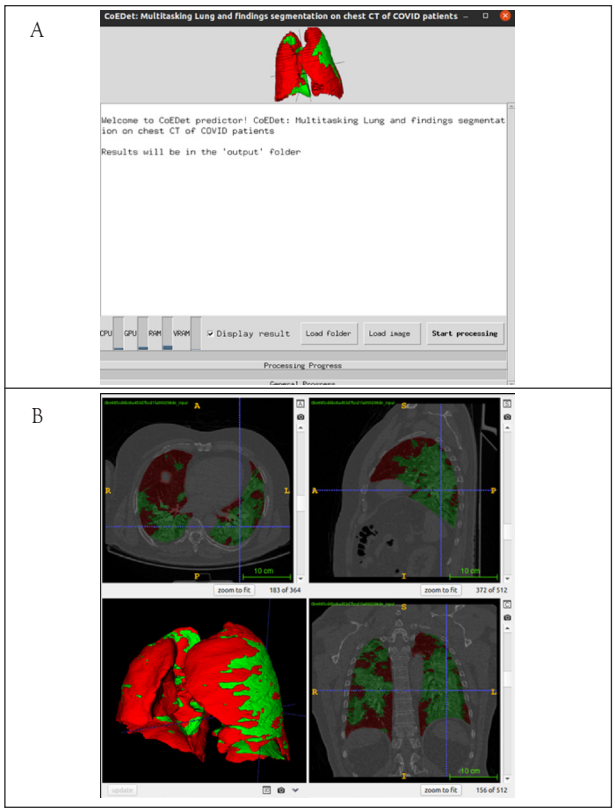

Figure 2. A - Visualization of the tool's user interface. B - Integrated visualization of the segmentation results, with lung in red and COVID-19 findings in green.

ped an automated lung and COVID-19 segmentation tool with a graphical interface and made it publicly available. We hope this tool can be of use for future medical research establishing links between lung impairment due to COVID-19 and other symptoms.

References: [1] Silva et al., doi.org/10.1016/j.jns.2021.119852; [2] Carmo et al., doi.org/10.1117/12.2606118.

AN IN-DEPTH LOOK AT CANDIDATE LOCI FOR MESIAL TEMPORAL LOBE EPILEPSY

P. H. M. Magalhães[1], E. M. Bruxel[1], M. C. P. Athie[1], Marina K.M. Alvim[2], R. Secolin[1], Clarissa L. Yasuda[2], F. Cendes[2], I. Lopes-Cendes[1]

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Introduction: Mesial temporal lobe epilepsy (MTLE) is the most common form of focal epilepsy in the adult population, and most patients are refractory to treatment with antiseizure drugs. MTLE is a genetically complex disorder for which the identification of predisposing genes is still elusive. Recent genomic association studies discovered a few regions that could harbor genetic variants predisposing to MTLE. Among these, there is the locus on the chromosome (ch) 2q24.3 [1,2,3]. Interestingly, the *SCN1A* gene and other genes from the *SCN* family are in this same location. Mutations in *SCN* genes, particularly *SCN1A*, have been extensively associated with monogenic epilepsy, especially in developmental and epileptic encephalopathies. Moreover, two other loci were previously linked to MTLE in a recent genome-wide association study: 3q25.31 and 6q22.31 [3]. It has been recognized that the genetic architecture of the population can influence genetic variants for complex disorders [4]. Thus, patients from different populations may have different combinations of predisposing variants. Therefore, this research aims to look deeper into these candidate loci in patients with MTLE using association analysis combined with the re-sequencing of the candidate region(s) identified in our cohort. **Materials and Methods:** Genome-Wide Human SNP Array 6.0 (Thermo Fisher, Waltham, Massachusetts, United States) was used to obtain SNP-array data from our cohort to better define the candidate regions for subsequent target re-sequencing. For this study, we analyzed only the SNPs located within the three candidate regions previously determined and located on chs 2q24.3, 3q25.31, and 6q22.31. The p-values obtained in the association study were adjusted for multiple comparisons. Subsequently, MiSeq target next-generation sequencing (Illumina, San Diego, California, USA) was used to sequence the candidate regions identified. Data were aligned using the Burrows-Wheeler Aligner algorithm. Variants will be detected by the Genome Analysis Toolkit and identified using the Variant Effect Predictor and ANNOVAR software. Sequencing data will be analyzed using burden tests. **Results:** The local association test performed in 472 patients with MTLE and 415 controls identified a significant association at ch 2q24.3 (p=0,03301). However, results on the two other candidate loci were less clear with suggestive signals but not reaching statistical significance. Target re-sequencing of this locus has been completed, and data is currently being processed and analyzed. **Discussion/Conclusion**: We found a significant genetic association for MTLE on ch 2q24.3 in our cohort of patients with MTLE. We also achieved a fine genetic mapping of the candidate region, which is currently being processed and analyzed to identify putative causative variants. Our study contributes to the ongoing worldwide efforts to unravel the genetics of complex epilepsies. **Supported by:** CAPES; FAPESP.

References: [1] Anney RJL et al., doi: 10.1016/S1474-4422(14)70171-1; [2] Kasperavičiute, D et al., doi: 10.1093/brain/awt233 [3] International League Against Epilepsy Consortium on Complex Epilepsies, DOI: 10.1038/s41467-018-07524-z [4] Martin, Alicia R et al., - DOI:10.1016/j.ajhg.2017.03.004

AN INVESTIGATION OF THE NEUROMUSCULAR FUNCTION IN LONG COVID

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Introduction: Part of individuals infected by SARS-CoV-2 develops long lasting effects which can include a wide range of symptoms; nonetheless, fatigue is one of the most common complaints [1]. The fatigue reported by COVID-19 patients is similar to the chronic fatigue syndrome (CFS), which has been reported in the literature as an aftereffect of other viral infections. CFS is poorly defined and understood, and its etiology is still unknown, but it is believed to involve multi-system alterations [2]. In this regard, it is yet to be clarified the neuromuscular determinants of COVID-19 long term effects, particularly the CSF. Here, we aim to identify changes in force generation and control, along with reaction tasks performed by patients infected by COVID-19 and controls. **Materials and Methods:** Participants had to perform an abduction force of the index finger of the dominant hand. The volunteers were divided into two groups: CONTROL group (nine women, 40±10 yrs) and COVID group (twelve women, 38±7 yrs, 5-30 weeks after COVID-19 diagnosis, most of them treated at home). The experimental protocol consisted of three stages: pre-fatigue, post-fatigue, and post-rest. At each stage, the maximum voluntary contraction (MVC) was estimated and three different tasks were performed: reaction time task (RT, at 20% MVC), trapezoidal force task (TRAP, at 20% MVC), and fatiguing contraction task (FT, at 40% MVC). Pre-fatigue stage consisted of 2xMVC, 1xRT, 2xTRAP, and 1xFT. Post-fatigue stage consisted of 1xMVC, directly after the previous FT task, 1xRT and 2xTRAP. After 5 min rest, the post-rest stage started and consisted of 1xMVC, 1xRT, 2xTRAP and 1xFT. An analysis of variance (ANOVA) was applied to MVC, RT, rate of force development (RFD) in RT data, standard deviation (STD) of the plateau in the TRAP task, mean-squared error (MSE) of ascending and descending phases of the TRAP task, and time to task failure (TTF) in FT task. Multiple comparisons were corrected with Bonferroni post-hoc test. The significance level was 0.05 for all statistical analysis. **Results:** MVC data showed significant differences between groups (p=0.001) and stages (p<0.001), and Bonferroni post-hoc test indicated differences between pre-fatigue and post-fatigue (p=0.001), and pre-fatigue and post-rest (p<0.001). COVID group produced less force (11.37±3.02 N) than the CONTROL group (16.49±2.58 N). A significant difference was found in STD data between stages (p=0.004), where effects between pre-fatigue and post-rest were shown in the Bonferroni post-hoc test (p=0.001). No significant difference was found in RT, RDF, TTF, and MSE data. In the TTF data, COVID group presented a shorter time (2.9±0.09 min) than the CONTROL group (3.8±0.09 min), also COVID group showed higher values of MSE in the ascending phase of the TRAP task (2.71±0.35 %MVC) than the CONTROL group (1.57±0.40 %MVC) and COVID group presented 39% higher STD (0,881±0,13 %MVC) than the

CONTROL group (0,632±0,13 %MVC). **Discussion/Conclusion**: COVID-19 participants presented a high degree of variability in their symptoms, thereby influencing the results presented here. Only MVC data showed a significant and consistent difference between groups, suggesting the COVID group had a lower capacity of force generation. TTF, STD, and MSE showed a difference between groups; but, no statistical difference was detected. These findings point to alterations in neuromuscular control after SARS-CoV-2 infection; however, a more homogeneous dataset from a large number of participants is needed to clarify the underlying mechanisms.

References: [1] LOPEZ-LEON et al., doi: 10.1038/s41598-021-95565-8; [2] POENARU et al., doi: 10.1177/20499361211009385.

AN OPTIMIZED DEEP LEARNING-BASED METHOD FOR CEREBELLUM SEGMENTATION

D. H. Shiraishi[1], G. Wertheimer[2], F. Reis[2], F. Cendes[1], M. C. França Jr[1], T. J. R. de Rezende[1]

[1]Department of Neurology, School of Medical Sciences, UNICAMP; [2]Department of Radiology, School of Medical Sciences, UNICAMP.

Introduction: Cerebellum segmentation is a challenging task as a consequence of intricately folded cortex tissue and proximity with the cerebral cortex. Additionally, we face an additional level of complexity when working with patients with conditions that reduce the cerebellar volume, which is a common finding of spinocerebellar ataxias (SCA) [1]. In order to measure the impact of modifier agents in studies for new therapies, sensitive variables are necessary. Different solutions have been proposed, such as SUIT [2], CERES [3], and ACAPULCO [4]. Although, we found accuracy and reproducibility issues, as well as a lack of cerebellar atrophy samples in some studies' training sets. Hence, we propose a deep learning-based model for cerebellum segmentation, addressing the known issues, and aiming to achieve a suitable method for longitudinal studies. **Materials and Methods:** In model development, we used T1-weighted MRI sequences acquired in a 3 T Philips Achieva (Philips Healthcare, Netherlands). This dataset is composed of approximately 1000 images of control subjects and 500 patients, all of them with molecular confirmation for hereditary ataxia. Also, the Kirby 21 dataset [5], composed of 21 healthy control subjects scanned twice, was selected to test-retest the models. In the deep learning domain, we chose the 3D U-net architecture [6] with a few modifications, which is a consolidated model for segmentation tasks in the medical imaging domain. Prior to further studies, a base segmentation model was trained on FreeSurfer [7] outputs for our dataset, controls only. This is a reasonable check to assess for potential suitability of the chosen model. Following activities will embrace a complete segmentation pipeline definition and training while working towards improving data quality. **Results:** Our initial U-net model was trained on Google Colab platform for nearly 12 hours and achieved 0.9755 for Dice score on the validation set. On the Kirby 21 test-retest dataset, our trained model achieved 0.639±0.422% on volume difference, a Dice of 0.991±0.002 and 0.998 for ICC (intraclass correlation coefficient). CERES and ACAPULCO scored 0.685±0.525%, 0.982±0.005, 0.998 and 1.060±1.704%, 0.697±0.160, 0.991 for volume difference, Dice and ICC, respectively. In Figure 1, we show two single slice output examples. **Discussion/Conclusion**: In conclusion, our first model demonstrates a feasible segmentation model, especially in terms of reproducibility, with minimal effort dedicated to architectural design. We focus on a data-centric approach, meaning that we value a high segmentation quality over the number of samples. So, it's planned a review in a subset of our dataset, correcting segmentation masks supervised by a specialist rater. Then, in the next phase of this project, we intend to develop a two-step sequential solution: one preliminary localization model, outputting a bounding box enclosing the cerebellum, and a second model for proper segmentation (Figure 2). For this last step, we are planning to apply the nnU-Net model, a state-of-the-art solution in medical segmentation. We will focus not only on the model but also on pre-processing steps such as normalization, registration, and orientation correction. Likewise, after the model inference, we plan to post-process the output refining the segmentation.

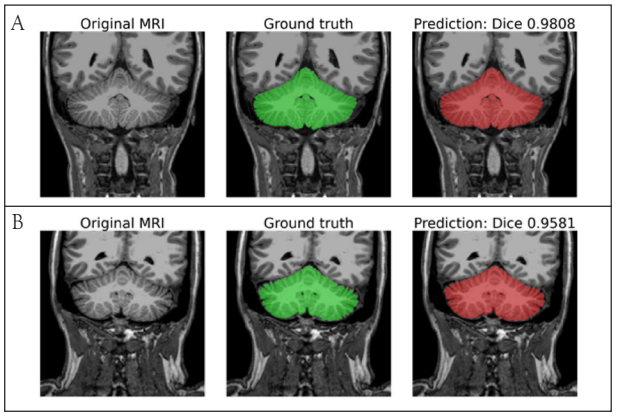

Figure 1. Examples of cerebellum segmentation on the test set. A - is the best segmentation prediction. B - is the lowest score.

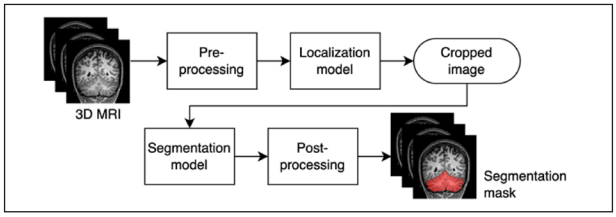

Figure 2. Segmentation pipeline architecture.

References: [1] Koeppen AH et al., doi:10.1097/NEN.0b013e31827e5762; [2] Diedrichsen J, doi:10.1016/j.neuroimage.2006.05.056; [3] Romero JE et al., doi:10.1016/j.neuroimage.2016.11.003; [4] Han S et al., doi:10.1016/j.neuroimage.2020.116819; [5] Landman BA et al., doi:10.1016/j.neuroimage.2010.11.047; [6] Ronneberger O et al., doi:10.1007/978-3-319-24574-4_28; [7] Available in https://surfer.nmr.mgh.harvard.edu/

ANALYSIS OF TISSUE EXPRESSION OF GLIAL MARKERS IN WHITE MATTER OF THE TEMPORAL ANTERIOR POLE OF PATIENTS WITH HIPPOCAMPAL SCLEROSIS

Vítor Henri Baldim[1], Bruna Cunha Zaidan[1], Marina Koutsodontis Machado Alvim[2], Enrico Ghizoni[2], Helder Tedeschi[2], Fernando Cendes[2], Fabio Rogerio[1]

[1]Pathology, FCM, UNICAMP; [2] Neurology, FCM, UNICAMP

Introduction: Epilepsy is the most common neurological disease [1]. MRI of patients with temporal lobe epilepsy (TLE) and hippocampal sclerosis (HS) revealed white matter (WM) alterations possibly associated with myelin and axonal damage [2,3]. Here, we investigated differences regarding tissue expression of glial markers in the white matter of the anterior temporal pole of patients with HS compared with specimens from individuals submitted to autopsy without history of neurological disease (control). **Materials and Methods:** Analysis of histological sections of specimens of epilepsy (HS; n = 15) and control (n = 10) groups was made by means of immunostaining for CNPase, GFAP and Iba-1 to evaluate oligodendrocyte, astrocyte and microglial populations, respectively. Also, myelin integrity was assessed by using Luxol Fast Blue special staining. Photodocumentation of microscopic fields (MFs) (40x) of the WM was followed by digital analysis with the ImageJ® software. A semiquantitative assessment of the stainings was performed with a digital processing technique (threshold) applied to each MF. Specifically, the image was initially transformed into grayscale. Then, the operator defined a cutoff point to convert the image into binary information (black/ white). The software divided the value of black pixels by the total pixels of the field, providing a value defined as "*mean*". Mann-Whitney test was used for statistical evaluation, the significance level $p<0.05$. **Results:** LFB staining and CNPase immunolabeling showed homogeneous distribution of myelin in the WM. Immunohistochemical investigation for GFAP showed astrocytic cytoplasmic processes, the same being observed regarding Iba1 and microglial cytoplasmatic processes. We found no qualitative or semiquantitative differences between the groups for each marker (Figure 1). **Discussion/Conclusion**: WM alterations have been reported in patients with chronic epilepsy [4,5]. Some patients with TLE and HS (32-68%) present blurring of the white and gray matter boundary in MRI. Garbelli et al. (2012) compared specimens of 32 patients with TLE and HS by electron microscopy and classified them as with or without blurring. The blurring group showed reduction in axonal number and density, less circular and more elongated axons [2]. Concha et al (2010) ultrastructurally studied 11 patients with epilepsy who underwent

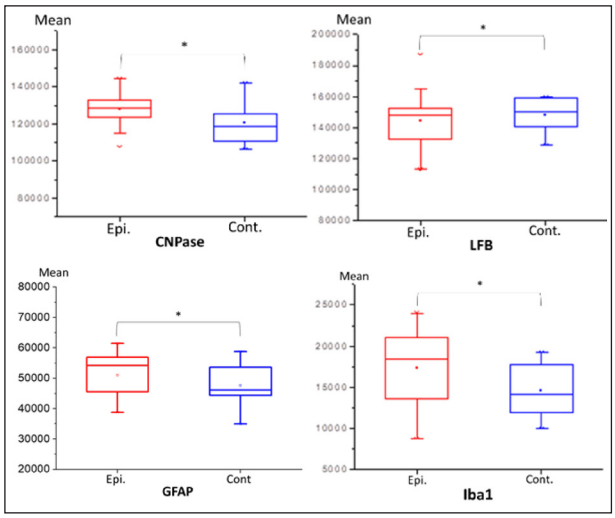

Figure 1. Semiquantitative analysis ("mean" values) of CNPase; LFB; GFAP; Iba 1 labeling of the WM. Epi: epilepsy (HS); Cont: controls. * $p<0.05$.

surgery, dividing them in two groups: TLE with mesial temporal sclerosis (MTS) and TLE without MTS. The first group showed a larger extra-axonal area, lower myelin fraction, fewer axons per field and lower axonal density [6]. In our study, we found no differences between epilepsy and control groups, however we used another technique (optic microscopy). The current protocol of digital analysis was successfully applied, and may be reproduced in other contexts of epilepsy.

References: [1] Steinhauser, C., et al.; Neuroscience, 323: 157–169, 2016; [2] Garbelli, R., et al.; *Brain*, 135(8): 2337-2349, 2012; [3] Eijsden, P.V., et al.; Epilepsia, 52(4): 841–845, 2011.; [4] Gross, D., et al.; Epilepsia, 47(8): 1360–1363, 2006.; [5] Knake S., et al.; Epileptic Disord., 11(3): 244-50, 2009.; [6] Concha, L., et al.; The Journal of Neuroscience, 30(3): 996–1002, 2010.

APPLYING A BRAIN BASED CLASSIFIER SYSTEM FOR DETECTION OF THE PSYCHOLOGICAL AND PHYSIOLOGICAL STRESS PRESENCE IN HUMANS

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Introduction: Suggestions for stress detection based on the biological signals analysis and classification have been proposed by some researchers [1], but the results pointed to identification of stress peaks, related to short term or acute stress only, and are useless for identification of the long term chronic stress, mainly characterized by the psychological and physical symptoms that the subjects have been experienced over the time. The objective of this work was to develop an intelligent classifier system, based on the use of an Artificial Neural Network (ANN), a brain based model, to detect the chronic stress presence in adult subjects. **Materials and Methods:** This project was approved by an ethics committee. A total of 120 volunteers were recruited and a consent term was signed by each participant. We verified the presence of psychological and physical symptoms of stress applying the ISSL (Lipp's Inventory of Stress Symptoms for Adults). For each individual we carried out the measurement of the systolic and diastolic blood pressure, the skin surface temperature and recorded the parameters of the heart rate variability in time and frequency domain, during five minutes, according to the short-time recording procedures [2]. All biological signals were recorded by using non-invasive sensors. After the stages of feature extraction and data normalization, the selected parameters of the physiological signals were used for training an ANN with MLP (Multi-Layer Perceptron) architecture, with 20 neurons in the input layer, 10 neurons in the hidden layer and 1 neuron in the output for the classification, indicating the presence or absence of stress. Next, the network's ability to detect the stress presence was tested via the classification with a non trained data set. Two experiments were conducted. At first, the ANN processed the information from all selected physiological signals. Then, there was the reduction in dimensionality of the search space through the use of the PCA (Principal Component Analysis) technique, with the application of the first 7 main components such as the network input signals. **Results:** For the ANN performance evaluation we elaborated the confusion matrix for the classification results and plotted the ROC curves for the two experiments. The system succeeds in classifying individuals with long-term stress with 80% accuracy, 80% sensitivity and 72% accuracy, using all the signs. And it succeeds with 79% accuracy, 75% sensitivity and 69% accuracy using the PCA technique. **Discussion/Conclusion**: The discrimination of the chronic stress presence by means of physiological variables analysis represents a challenge to establish plausible and predictable mathematic relations. A utilization of an intelligent classifier system based on an ANN offers a possible solution to this problem. We have trained a neural net and have got a feasible mathematical model for the chronic stress class identification, indicating that the ANN achieved an algebraic composition of synaptic weights capable of identifying correctly most of the individuals with chronic stress presence. A training set with more examples added could produce an increased accuracy index of performance. In conclusion, the present results indicate that the use of intelligent systems to classify biological signs and identify the chronic stress presence in humans could contributes to a more objective clinical analysis of the psychological and physical symptoms associated to stress presence, besides just the use of stress inventories. **Acknowledgments:** The authors thank Prof. Annie France Frère Slaets, Ph.D. who supervised this work, the Institutional Psychology Clinic for the support, the Laboratory of Signal Processing and Medical Imaging for providing technical resources and CAPES for the financial support.

References: [1] Sharma N et al., doi:10.1016/j.cmpb.2012.07.003. [2] Malik M et al., doi: 10.1161/01.CIR.93.5.1043.

BETA DOMINANT FREQUENCY FROM SUBTHALAMIC NUCLEUS LOCAL FIELD POTENTIAL ENCODES CANONICAL MOTOR SYMPTOMS IN PARKINSON'S DISEASE

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Introduction: Subthalamic nucleus local field potential (STN-LFP) beta (β) power defines an essential marker for Parkinson's disease (PD) rigidity and bradykinesia motor symptoms. In contrast, such an electrophysiological marker has not been convincingly related to the patient's tremor. Recently, parametric approaches for modeling the STN-LFP power spectral density (PSD) function unveiled an even stronger correlation structure between corrected β power and rigidity-bradykinesia [1,2]. Such parametric approach provided a valuable strategy for modeling and subtracting the LFP background behavior, highlighting the differential contribution of the synchronized neural activity through well-defined Gaussians functions, giving rise to the definition of the (corrected) dominant power (DP - the power of the most representative Gaussian in a LFP band) and its (corrected) dominant central frequency (DCF). This work shows that high β-DP, low β-DP and high β-DCF correlates, respectively, with rigidity, bradykinesia, and tremor, defining an electrophysiological space for PD canonical motor symptoms. **Materials and Methods:** 35 LFPs (13=bilateral, 9=unilateral) were recorded from the sensorimotor portion of the (STN) during 60s in rest condition during intra-operatory procedure for electrode implant aiming deep brain stimulation (DBS). Data were sampled at 24 kHz, notch filtered at 60 Hz, and downsampled to 1 kHz before z-scoring. PSD was evaluated through Welch method and LFP was decomposed into background () with superimposed Gaussians as described in [2]. DP and DCF were evaluated for the most representative Gaussian found in low β (13 - 22 Hz) and high β (22 - 35 Hz) sub-bands according to the functional division commonly employed. Tremor, rigidity, and bradykinesia clinical scores were evaluated according to the Unified Parkinson's Disease Rating Scale (UPDRS - items 20, 22, 23, respectively) before the surgery and in the absence of dopaminergic medication. The study was approved by the local Ethical Committee (CAAE: 62418316.9.2004.0066). **Results:** Table 1 shows significant correlations between high β-DP and low β-DP with rigidity and bradykinesia, respectively. More importantly, significant correlation was found between high β-DCF and tremor clinical scores.

Tabela 1. The most significant correlations found between clinical symptoms scores and features.

Symptom	Sub-band	Feature	Spearman	95% CI	p-value
Tremor	High β	DCF	-0.3513	[-0.6191 -0.01019]	0.0385*
Bradykinesia	Low β	DP	-0.3647	[-0.6285 -0.02557]	0.0312*
Rigidity	High β	DP	0.5781	[0.2940 0.7684]	0.0003***

Discussion and Conclusion: Our work defines a novel electrophysiological space for PD canonical motor symptoms. We have shown that the parametric approach for STN-LFP PSD provides a new set of biomarkers strongly associated with PD motor symptoms. These findings can contribute with the delineation of enhanced strategies for closed-loop DBS systems in future clinical studies.

References: [1] Martin et al., doi: 10.1038/s41531-018-0068-y; [2] Haller et al., doi: 10.1038/s41593-020-00744-x

BIOMETRY FROM FUNCTIONAL CONNECTIVITY EEG DATA USING SPACE-TIME RECURRENCES

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Introduction: The use of electroencephalography (EEG) data for biometrics purposes has been increasingly explored [1], with some studies having used features from functional connectivity (FC) measures obtained from methods such as coherence [2]. This study aimed to identify an individual from EEG data through FC from space-time recurrences. In previous work subject data were compared using the minimum Euclidean distance [3]. Here we used maximum correlation instead. **Materials and Methods:** EEG data from 11 subjects from the Physionet database were used [4]. Only the two resting-state acquisitions from each subject were used, the first with eyes open (R1) and the second with eyes closed (R2). Data were preprocessed using the EEGLab toolbox in MatLab, by first removing artifacts by eye and decomposing the data using ICA to map and remove movement/noise components. After that, we applied a tool called CleanLine for filtering the frequency of the power grid (60 Hz) and a basic notch filter to remove the alpha frequency (7-13 Hz), known to be strikingly different between open and closed eyes acquisitions [5]. Four 5 s epochs were selected from R1 (10-15; 20-25; 30-35 and 40-45 s) and one from R2 (10-15 s). Thereafter, the space-time recurrence method [6] was applied to compute FC matrices for each epoch using homemade MatLab code. The resulting matrices for R1 were averaged. To evaluate the similarity among the signals, the Pearson correlation coefficient was calculated between the mean R1 FC matrix and the R2 FC matrix of all subjects. **Results:** Figure 1 shows the Pearson coefficients between R1 and R2. The method was able to correctly identify an individual among other 10 with an accuracy of ~64%. **Discussion/Conclusion**: The 64% classification rate is above chance level; however, it is not yet satisfactory for biometrics purposes. Also, it would be necessary to implement this analysis for a larger group of individuals. Furthermore, the preprocessing methods could be improved, e.g, using a different method to filter noise components, to achieve more accurate results. Finally, future studies could include comparison methods other than Pearson correlation. **Acknowledgements:** CNPq/PIBIC and FAPESP (grant 2013/07759-3) for financial support.

	S01	S02	S03	S04	S05	S06	S07	S08	S09	S10	S11
S01	0.03	0.042	0.224	-0.041	0.277	0.036	0.011	-0.03	0.342	0.147	0.0062
S02	0.162	0.276	-0.034	0.064	0.075	0.113	0.205	-0.038	0.019	0.183	0.0621
S03	0.154	0.15	0.281	0.355	0.238	0.178	0.256	-0.032	0.141	0.286	0.0849
S04	0.124	0.126	0.141	0.404	0.004	0.004	0.212	-0.065	-0.027	0.198	0.0632
S05	0.032	0.059	0.037	-0.023	0.341	0.18	0.032	-0.012	0.469	0.127	-0.032
S06	-0.048	-0.044	-0.035	-0.05	0.22	0.241	-0.039	-0.017	0.5	0.077	-0.0405
S07	0.114	0.098	-0.012	0.197	0.112	0.079	0.223	-0.008	0.047	0.294	0.0006
S08	0.183	0.173	0.241	0.268	0.113	0.194	0.193	0.043	0.196	0.291	0.0345
S09	-0.04	-0.053	0.242	-0.012	0.11	0.073	-0.016	-0.013	0.775	0.026	-0.0091
S10	0.295	0.119	-0.023	0.197	0.069	0.173	0.147	-0.044	0.1	0.234	0.0497
S11	0.006	0.066	0.156	0.018	-0.025	0.038	-0.005	-0.027	0.008	0.073	0.6065

Figure 1. Figure 1 shows the Pearson coefficients between R1 and R2. The method was able to correctly identify an individual among other 10 with an accuracy of ~64%.

References: [1] Campisi P et al., doi: 10.1109/MC.2012.233. [2] La Rocca D et al., doi: 10.1109/TBME.2014.2317881. [3] Paulo MC et al., XXIX Congresso IC UNICAMP, 2021. [4] https://physionet.org/content/eegmmidb/1.0.0. [5] Berger H, doi: 10.1007/BF01797193. [6] Rodrigues PG et al., doi: 10.1007/s11517-019-01989-w.

CANNABIDIOL INDUCES CHANGES IN GENES ASSOCIATED WITH ENERGY METABOLISM, PROTEIN TRANSLATION, NEUROPLASTICITY, AND CHROMATIN CHANGES IN MICE VENTRAL CA1 NEURONS

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Introduction: Cannabidiol (CBD) is one of the most common cannabinoids found in *Cannabis sativa* flowers. CBD interacts indirectly with cannabinoid receptors and affects several non-cannabinoid targets. CBD has already been investigated as a therapeutic strategy showing anticonvulsant, neuroprotective, and antiepileptic benefits demonstrated in both animal and human models. To investigate the influence of CBD on the transcriptome we used RNAseq to assess gene expression of the ventral CA1 hippocampus area following intraperitoneal (i.p) administration of CBD for 1 or 7 days compared to controls. **Materials and Methods:** Adult C57BL/6JUnib mice (Animal Use Ethics Committee protocol 5367-1/2019) were divided into four groups: CR1 - 1 day administration of NaCl 0,15 M, i.p., CBD1 - 1 day treatment with CBD (100 mg/kg, i.p.), CR7 - 7 days administration of NaCl 0,15 M, i.p., and CBD7 - 7 days treatment with CBD (100 mg/kg, i.p.). CBD (99.6% pure, no other cannabinoid, BSPG-Pharm, Sandwich, UK) was freshly prepared and used. Animals were euthanized 24 hours after the last injection, and their brains were processed for laser microdissection with a Zeiss PALM LCM. Total RNA was isolated from each sample's ventral CA1 pyramidal layer, and libraries were produced for RNA-seq on the Illumina Hiseq platform. The STAR Aligner/DESeq2 pipeline was used to align, quantify, and compare sequences. The clusterProfiler R-package was used to examine GO terms. **Results:** We obtained the following differentially expressed genes results (adjusted p<0,05): 299 (CBD1xCR1) and 1936 (CBD7xCR7). While PCA for CBD1xCR1 samples overlap, PCA for CBD7xCR7 samples shows an evident clustering. CBD7xCR7's GO analysis evidenced 76 terms significantly enriched (p.adjust <0.05). Downregulated genes list provided top enriched terms like: '*mitochondrion organization*', '*cytoplasmic translation*', '*oxidative phosphorylation*' and '*ribosome biogenesis*'. Furthermore, GO analysis for upregulated genes in CBD7xCR7 shows the following most enriched biological terms: '*covalent chromatin modification*', '*regulation of cell morphogenesis involved in differentiation*', and '*synapse organization*'. **Discussion:** We found evident segregation of the transcriptomic profile from CBD administration frequencies. The enrichment analysis of one-day CBD administration was only associated with the ubiquitin processes. On the other hand, 7 days of CBD administration indicates a decrease of electron transport chain and ribosome biogenesis transcripts, while chromatin modifications and synapse organization transcripts were found increased. Enriched terms of transcriptome changes indicates that CBD may influence protein turnover after only one i.p. administration in ventral CA1. Furthermore, continuous CBD administration for seven days seems to induce reduction of metabolism, translation and increase in synaptic plasticity. These observed changes, and the lack of hypoxia and cell death markers, suggest that 7 days of CBD induce a cellular profile compatible with reduced energy consumption by this cell population. **Conclusion:** The present dataset contributes to a deeper understanding of the CBD effects on gene expression in ventral CA1 of healthy mice and provides evidence that CBD induces an extensive change in neuroplasticity and chromatin regulation genes. Furthermore, CBD induces a marked reduction of protein translation machinery and energy metabolism genes in ventral CA1 neurons.

CEREBROSPINAL FLUID SIGNATURE OF CYTOTOXIC T CELLS AND NEW WHITE MATTER LESIONS IN POST-COVID: CASE REPORT

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Introduction: Neurological/neurovascular abnormalities suggestive of central nervous system (CNS)-autoimmunity have been reported in post-COVID

patients. Here we describe a patient whose brain magnetic resonance imaging (MRI) showed new demyelinating white matter lesions after a moderate SARS-CoV-2 infection. However, immunological mechanisms eventually involved in CNS-damage during post-COVID have not yet been well elucidated. **Materials and Methods:** We have followed this patient since 2021. She underwent multimodal assessment with a neurological examination (by a skilled neurologist), magnetic resonance imaging (MRI), and blood and cerebrospinal fluid collection. We applied a comprehensive battery composed of mini-mental state examination, logical memory subset, Rey-Osterrieth complex figure, digit span test (WAIS-III), five-digit test, color trail test, nine-hole peg test, semantic and phonemic verbal fluency test, Beck depression inventory (BDI-II), Beck anxiety inventory (BAI). Moreover, we investigated T subsets in the peripheral blood (PBMCs) and CSF using several markers for flow cytometry analyses (CD3, CD4, CD8, CD20, CD25, CD27, CD28, CD38, CD45RA, CD49d, CD56, CD57, CD94, CD150, CD195, CD215, IRF4, RORγT, T-bet and GzmB). **Results:** We have followed this patient since 2020. She presented an acute COVID-19 in November 2020, which evolved with dyspnea and supplementary oxygen necessity. After 2 months, she persisted with "weakness and pain" in the legs (unable to walk since the infection). During physical examination she exhibited a functional pattern, with a normal neurological exam. Her neuropsychological evaluation was unremarkable, except for the presence of anxiety and depressive symptoms. Since her sister has multiple sclerosis, she performed a brain MRI for investigating the disease in 2019. No brain abnormalities were found that time. New MRI was performed. New 3T MRI revealed white matter lesions (some suggestive of microvascular lesions) and some ovoid lesions suggestive of demyelinating disease (**Figure 1A-D**). The neuropsychological evaluation revealed severe dysexecutive syndrome (motor and cognitive dysfunction) with anxiety and depressive symptoms. Our flow cytometry analyses from CSF and PBMCs demonstrated that expression of serine-protease granzyme-B (GzmB), evidencing cytotoxic behavior, in T cells is related to several effector markers (*CD27*$^{-}$, *CD195*$^{-}$, *CD49d*$^{+}$, *CD56*$^{+}$, *CD94*$^{+}$, *CD215*$^{+}$) including those suggestive of senescent/exhausted phenotype (*CD57*$^{+}$, *CD28*$^{-}$) (**Figure 1E-G**). Considering these markers, classical CD8^{+}GmB^{+} T and non-classical CD4^{+}GmB^{+} T cytotoxic subsets exhibit a distinctive signature compared to non-cytotoxic CD8^{+}GzmB^{-} and CD4^{+}GzmB^{-} T counterparts, in both compartments, respectively (**Figure 1H**). **Discussion/Conclusion**: Dysfunctional behavior of CD8^{+} T lymphocytes is observed in patients with severe COVID-19 [1–3]. On the other hand, individuals with mild disease course exhibit increased percentage of circulating CD8+GzmB+ in the peripheral blood [4]. Our findings suggest that effector T subsets expressing GzmB, and exhibiting senescent/exhausted-like (*CD57*$^{+}$, *CD28*$^{-}$) features may persist, in the CSF and peripheral blood, even a few months after symptomatic COVID-19 recovery. As well-known during neuroinflammatory conditions [5], sustained cytotoxic behavior derived from effector T subsets may be associated with triggering/worsening immune-mediated neurological/neurovascular manifestations in post-COVID [6,7].

References: [1] Zheng M,et al., doi:10.1038/s41423-020-0402-2; [2] Diao B, et al., doi:10.3389/fimmu.2020.00827; [3] De Biasi S, et al., doi:10.1038/s41467-020-17292-4; [4] Westmeier J, et al., doi:10.1128/mBio.02243-20; [5] van Nierop GP, et al., doi:10.1007/s00401-017-1744-4; [6] Kremer S, et al., doi:10.1212/WNL.0000000000010112; [7] Palao M, et al., doi:10.1016/j.msard.2020.102377.

CHARACTERIZATION OF THE GUT MICROBIOME IN PATIENTS WITH DIFFERENT FORMS OF EPILEPSY AND AUTOIMMUNE ENCEPHALITIS

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Introduction: Over time, man and microorganisms have co-evolved simultaneously to integrate a complex ecosystem [1]. Studies in animal models have shown that the enteric microbiota plays a pivotal role in host physiology and acts as a key mediator in the central nervous system [2, 3, 4]. Such bidirectional signaling known as the gut-brain axis is achieved through metabolic, neuroendocrine, and neuroimmune pathways [5, 6, 7]. Epilepsy and autoimmune encephalitis (AE) are heterogeneous diseases that affect all ages and contribute to the global economic burden [8]. The main objective of this work is to characterize the composition of the intestinal microbiome in individuals with different forms of epilepsy and AE using an amplicon sequencing approach [9, 10]. **Materials and Methods:** A total of 115 regular users of the Hospital das Clínicas at the University of Campinas (HC-UNICAMP) were enrolled in this study between 2019 and 2021. They were divided into three groups: forty-three (43) with mesial temporal lobe epilepsy, fourteen (14) patients with genetic generalized epilepsy (GGE), and twelve (12) with AE. Additionally, forty-six (46) healthy individuals were enrolled in the control group. Fecal sampling was done by participants using a sterile tube (OMNIgene-GUT OM-200®) at home. Total nucleic acids were extracted from frozen stool samples using the QIAamp POWERFECAL PRO DNA KIT (Qiagen®). DNA integrity, purity, and concentration were assessed. According to the manufacturer's instructions, genomic libraries were constructed from the V3 and V4 hypervariable regions of the 16s rRNA gene marker. Obtained reads were analyzed using Galaxy Australia (version 21.01). Alfa and beta diversity were measured to compare intra- and inter-subject variability. **Results:** A total of 4,406,303 reads were obtained in the four groups. Sequences were grouped into operational taxonomic units according to a similarity threshold of 97%. The taxonomy profile revealed a predominance of *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, and *Proteobacteria* at the phylum level. In addition, rare enterotypes including *Synergistetes* and *Euryarchaeota* were also detected. For the alfa diversity indices, there were no differences in both community diversity and species evenness across groups: Chao1 (p-value: 0.88979), Shannon (p-value: 0.85438), and Simpson (p-value: 0.88666). Beta diversity profiling at the species level revealed different microbiome compositions among all groups (p-value < 0.014). At the genus level, the univariate analysis demonstrated that important genera such as *Akkermansia*, *Faecalibacterium*, and *Enterobacteriaceae_unclassified* were enriched according to the groups GGE (p-value: 7.2606e-4), control (p-value: 0.023497), and AE (p-value: 0.32941) respectively. **Discussion/Conclusion**: The genus *Akkermansia* is generally known for maintaining the integrity of the intestinal barrier through mucin and local serotonin production in mice. Its overgrowth could promote excessive mucin degradation leading to an increase of epithelial permeability that, in turn, could affect the gut brain-axis signaling pathways as seen in the patients with GGE. *Enterobacteriaceae* genus was also found enriched in AE group. Members of this genus can contribute to inflammation processes triggered by bacterial metabolites or cell wall components. For example, it has been reported that lipopolysaccharide can modulate Toll-Like receptor 4 signaling which is related to neuroinflammation, a cardinal sign in AE patients. Finally, we observed a predominance of *Faecalibacterium* genus among individuals from control group. This butyrate-producing bacteria has been associated to a widespread benefits for host health involving energy metabolism, histone deacetylases inhibition and anti-inflammatory cytokines upregulation. An increase in the relative abundance of this genus in the control group may indicate a microbial signature of healthy individuals. In conclusion, this study reveals that patients with epilepsy exhibit a substantial alteration in fecal microbiota composition and specific microbial markers might mediate seizure occurrence.

Supported by: CEPID-BRAINN, FAPESP.

References: [1] Sampson TR et al., doi: 10.1016/j.chom.2015.04.011; [2] Fung TC et al., doi: 10.1038/nn.4476; [3] Turnbaugh PJ et al., Nature. 449(7164):804-10, 2007; [4] Qingqing Feng et al., doi: 10.3389/fmicb.2018.00151; [5] Chen X et al., doi: 10.1007/s13238-013-3017-x; [6] Collins SM et al., doi: 10.1053/j.gastro.2009.01.075; [7] Tremlett H et al., doi: 10.1002/ana.24901; [8] Devinsky O et al., doi: 10.1038/nrdp.2018.24; [9] Oulas A et al., doi: 10.4137/BBI.S12462; [10] Human Microbiome Project Consortium doi: 10.1038/nature11209.

CIRCULATING NUCLEIC ACIDS AS A POTENTIAL NON-INVASIVE BIOMARKER FOR PREDICTING PHARMACORESISTANT IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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Introduction: Around 30-40% of patients with mesial temporal lobe epilepsy (MTLE) will not respond to treatment with anti-seizure medication (ASM). Furthermore, lack of seizure control is one of the risk factors for sudden unexpected death in epilepsy (SUDEP). To date, there are no predictive biomarkers to assist neurologists in identifying which patients with MTLE will be pharmacoresistant. Identifying resistance to treatment with ASM is necessary for timelining plan-

ning of alternative treatments, such as epilepsy surgery. Circulating nucleic acids, such as cell-free DNA (cfDNA) and cell-free RNA (cfRNA), have been used as biomarkers in liquid biopsies in several diseases, especially cancer. Thus, our objective is to evaluate if circulating nucleic acids could be used as biomarkers of pharmacoresistance in patients with MTLE. **Materials and Methods:** In this study, we included 149 patients with MTLE and 80 controls, all over 18 years. All patients were diagnosed with MTLE, according to the International League Against Epilepsy (ILAE) criteria. Patients with MTLE were considered responsive (n=48) if seizure-free for at least twelve months and refractory (n=101) when they had seizures after two years of optimal treatment with ASM. We analyzed cfDNA and cf-microRNAs levels in the plasma by digital droplet PCR (ddPCR) using *Taqman* probes, a precise and sensitive technique. We measured cfDNA levels of mitochondrial (mt-cfDNA) and nuclear (nu-cfDNA). In addition, we quantified cf-microRNAs in a subset of 21 individuals, seven controls, seven patients with responsive MTLE, and seven patients with refractory MTLE. Statistical tests were performed by Kruskal-Wallis with correction for multiple comparisons using the Dunn's or the FDR test. **Results:** We found that the nu-cfDNA copy number is significantly higher in the refractory group than responsive MTLE (p.adjust = 0.002) and controls (p.adjust = 0.032). On the other hand, mt-cfDNA could not differentiate responsive from refractory patients (p.adjust = 0.71), but was also higher in patients when compared to controls (p.adjust = 0.009). Furthermore, when performing a three-way comparison, we found higher mt-cfDNA levels in the refractory group only (p.adjust = 0.011). In addition, we identified 20 candidate cf-microRNAs based on RNAseq results previously obtained and quantified these in the subset of 21 samples. Of these, two cf-miRNAs, miR-139-5p and miR-let7-c-5p, could differentiate patients with refractory MTLE from controls (p.adjust = 0.037 and 0.022, respectively). Furthermore, two cf-microRNAs, miR-636 and miR-627-5p, were differentially expressed in patients with refractory MTLE compared to responsive MTLE (p.adjust = 0.042 and 0.017, respectively). **Conclusion**: We identified that plasma levels of mt-cfDNA and nu-cfDNA can discriminate patients with MTLE from controls. But, most importantly, it can also differentiate patients with refractory from responsive MTLE (p.adjust < 0.05). Furthermore, we identified at least four cf-miRNAs as potential biomarkers for refractory MTLE. **Supported by**: FASPES and CEPID-BRAINN

CLASS ASSOCIATION RULES FOR PHARMACORESPONSE IN MRI AND CLINICAL DATA

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Introduction: Class Association Rule mining (CARM) [1] is a well-known data mining approach used to extract the relationship between a set of variables *X*, and a class label *c*. A class association rule has the form $X \rightarrow c$ and can be read as IF *X* then class label *c*. In this work, CARM is used to extract the association between magnetic resonance imaging (MRI), clinical data, and the antiseizure antiepileptic drug (ASD) response of patients with temporal lobe epilepsy (TLE), the most common form of epilepsy in adulthood, often related with pharmacoresistance. It is reasonable to expect that ASDs influence MRI evaluation. However, the great number of ASDs taken makes this evaluation a challenging task and only a few studies have addressed this question with only some medications [2]. Thus, the aim of the study was to evaluate the relationship between MRI data, ASDs, and pharmacoresponse in TLE. The antecedent part of the rules is restricted to *closed patterns* [3], which guarantees that all possible variables are present in a rule. The CARM algorithm is based on the In-Close5 [4], a computationally efficient bicluster algorithm. **Materials and Methods:** This study involved MRI of temporal lobe epilepsy (TLE) and clinical data of 127 patients (52 ASD-responsive and 75 ASD-resistant). The parameters used in the CARM algorithm were: minimum support = 10 and minimum confidence = 90%. The data set includes structural and metabolic MRI features (ipsi- and contralateral hippocampal volume [Hvol] and total n-acetylaspartate, myo-inositol, total glutamate, and total glycerophoscoline [GPCt] ratios to total creatine) and clinical features (hippocampal atrophy side -SideHA-, diagnostic of major depression, ASD-regimen, and use of antidepressant medication). The ASDs were grouped into 5 classes according to their main mechanism of action: 1. gamma-aminobutiric acid (GABA) enhancement, 2. rapid inactivation, and 3. slow inactivation of voltage-gated Na+ channels, 4. antiglutamatergic, and 5. modulation of synaptic protein SV2A. The MRI features were binarized by the increase (↑) or decrease (↓) value considering the changes of 2 standard deviations based on the z-scores of MRI data from 50 control individuals. **Results:** We found 14 rules and 11 of them grouping patients taking ASDs in at least one type of mechanism of action along with MRI changes and clinical features(Table 1). For example, the first rule (Table 1) grouped left-sided TLE patients using GABA-EN medication in polytherapy with increased levels of myo-inositol in the ipsilateral hippocampus. **Conclusion**: Using CARM we could find MRI changes related to clinical data and types of ASDs that discriminate pharmacoresistant patients with 90% accuracy or more. These findings might help to better understand pharmacoresistance in TLE. **Supported** by grants from Fapesp and CNPq.

Tabela 1. Class Association Rules mined and selected by the presence of ASD classes, and the related confidence and support values.

#	Rule Antecedent (*X*)	*c*	Conf.	Supp.
1	{SideHA = **Left**, Regimen = **Polyth.**, GABA-EN_use = **yes**, ipsilNS = ↑ }	AED-resistant	90.9%	11
2	{Depression = **yes**, Regimen = **Polyth.**, RVGNa+_use = **yes**, Ipsi_Hvol = ↓ }	AED-resistant	100%	10
3	{Depression = **yes**, Regimen = **Polyth.**, GABA-EN_use = **yes**, Ipsi_Hvol = ↓ }	AED-resistant	100%	10
4	{Regimen = **Polyth.**, RVGNa+_use = **yes**, GABA-EN_use = **yes**, ipsilNS = ↑, Ipsi_Hvol = ↓ }	AED-resistant	100%	10
5	{Regimen = **Polyth**, RVGNa+_use = **yes**, GABA-EN_use = **yes**, ipsiNAAt = ↓}	AED-resistant	100%	10
6	{Regimen = **Polyth**, GABA-EN_use = **yes**, ipsilNS = ↑}	AED-resistant	90%	20
7	{Regimen = **Polyth**, GABA-EN_use = **yes**, ipsilNS = ↑, Ipsi_Hvol = ↓}	AED-resistant	100%	11
8	{RVGNa+_use = **yes**, ipsilNS = ↑, Ipsi_Hvol = ↓}	AED-resistant	100%	11
9	{RVGNa+_use = **yes**, ipsiNAAt = ↓}	AED-resistant	100%	12
10	{GABA-EN_use = yes, ipsilNS = ↑, Ipsi_Hvol = ↓}	AED-resistant	91.7%	12
11	{GABA-EN_use = **yes**, ipsiNAAt = ↓}	AED-resistant	100%	11

Legend: SideHA:side of hippocampal atrophy; GABA-EN: gamma-aminobutiric acid enhancement; RVGNa+ rapid inactivation of voltage-gated Na+ channels; ipsilns: ipsilateral myo-inositol.

References: [1]Ventura, S et al., doi:10.1007/ 978-3-319-98140-6; [2] Petroff et al., doi: 10.1053/seiz.1999.0267; [3] Andrews, S., CLA 2018, pp. 255–266; [4] Zaki, M. J. et al, doi: 10.1109/TKDE.2005.60.

CLINICAL PREDICTORS OF POSITIVE GENETIC INVESTIGATION IN DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES

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Introduction: Developmental and epileptic encephalopathies (DEE) are characterized by frequent epileptiform activity and seizures, associated with developmental, cognitive, and behavioral impairments [1-2]. The improvement of genetic tests optimized the etiology diagnosis, and, presently, a genetic factor is identified in approximately 40% of children with DEE [3]. As the landscape of DEEs expands, tests should be directed to increase the diagnostic yield. Therefore, the present study aims to investigate the clinical predictors of positive genetic investigation in DEE. **Materials and Methods:** This study included 66 patients diagnosed with DEE followed in the Clinical Hospital of University of Campinas (UNICAMP). All patients were submitted to Sanger sequencing of *SCN1A*, Chromosomal Microarray Analysis (CMA), and Whole Exome Sequencing (WES). The association of clinical variables with a positive genetic test was investigated using univariate analysis, followed by multinomial logistic regression analysis. Written informed consent was obtained from all patients, and the Research Ethics Committee approved the study. **Results:** Sanger sequencing of *SCN1A*, CMA and WES allowed genetic diagnosis in 34 (51.1%) patients with DEE in our sample. Positive genetic test was associated with female sex (OR 3.0, CI 95% 1.06 – 8.53, $p = 0.03$), first febrile seizure (OR 19.2, CI 95% 2.22 – 157.97, $p < 0.01$) and focal seizures (OR 3.6, CI 95% 1.2 – 10.04, p

= 0.01). Negative genetic test was associated with generalized discharges in the electroencephalogram (OR 0.4, CI 95% 0.13 – 0.98, $p = 0.04$), and the electroclinical diagnosis of epilepsy with myoclonic-atonic seizures (OR 0.1, CI 95% 0.01 – 0.48, $p < 0.01$) and Lennox-Gastaut syndrome (OR 0.2, CI 95% 0.04 – 0.64, $p < 0.01$). In multivariate analysis epilepsy with myoclonic-atonic seizures ($p = 0.02$) and Lennox-Gastaut Syndrome ($p = 0.03$) were independently associated with a negative genetic test in DEE. **Discussion/Conclusion**: The present study showed that female sex, first febrile seizure and the occurrence of focal seizures increased the chances of a positive genetic test in DEE. In contrast, generalized discharges on the EEG and the electroclinical diagnosis of epilepsy with myoclonic-atonic seizures and Lennox-Gastaut Syndrome decreased the chances of a positive genetic test in this group. Data about predictors of genotype-phenotype correlation are warranted since prioritizing comprehensive genetic testing for DEE investigation could reduce costs, and improve genetic counseling [3-4]. Further studies with larger samples are needed.

References: [1] Berg AT et al., doi:10.1111/j.15281167.2010.02522.x; [2] Scheffer IE et al., doi:10.1016/j.ejpn.2019.12.023; [3] Berg AT et al., doi:10.1001/jamapediatrics.2017; [4] Palmer EE et al., doi:10.1007/s13311-021-01133-3.

COMPARISON OF AUTOMATIC AND MANUAL LACUNA SEGMENTATION IN PATIENTS WITH EXTRATEMPORAL EPILEPSY – A PILOT STUDY

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Introduction: Epilepsy is a debilitating condition characterized by recurrent, unprovoked seizures, affecting 0.5-1% of the world population [1]. Resective surgery of the epileptogenic zone is the treatment of choice in focal epilepsies refractory to antiepileptic drugs. Nevertheless, the varied rates of good surgery outcome elicit uncertainties on the definition of the target regions to be removed [2]. A previous study from our group has already validated the use of an automatic tool to perform the lacuna segmentation in the temporal lobe. In this pilot study, we investigated the validation of the automatic segmentation performed by the ResectVol in extra-temporal epilepsy cases. **Materials and Methods:** Eighteen extratemporal epilepsy patients (37.9 ± 14.1 years old; 13 women) underwent a 3.0 T MRI scan (Philips Achieva) at Unicamp's Clinical Hospital. The anatomical postoperative T1 images were visually inspected for artifacts and then, the resective lacuna was manually segmented using MRIcron (version 1.0.20190902). Moreover, we used the ResectVol program [3] to perform automatic segmentation of the surgical gap in patients with extratemporal epilepsy. This tool requires the pre- and postoperative images as inputs to carry out the segmentation. To assess its performance in extra-temporal regions, we compared the automatic to the manual segmentation using the Dice coefficient (DC). **Results:** We found a median DC of 0.65 (range: 0.22 - 0.84) (**Figure 1**). Furthermore, there were four patients who had a DC value of zero (not considered in the median calculation), indicating no overlap between the manual and the automatic segmentation. **Discussion:** Using the manual segmentation as the gold standard, we noticed that the lacuna size in the four unsuccessful cases (DC = 0) ranges from 160.17 to 3647 mm^3, which is significantly smaller (Wilcoxon rank sum p = .0034) than the volume in the other cases (volume range: 1289 - 32990 mm^3). During the image analysis, ResectVol subtracts the post-operative from the pre-operative image and selects the largest cluster as the most probable lacuna candidate. In these small-lacuna cases, the algorithm may have misclassified a larger spurious cluster as the final lacuna, instead of the correct smaller one. **Conclusion:** The DC calculated for extratemporal lacunas is smaller than result obtained for the temporal cases (DC = 0.77). Although more subjects must be included to allow for a more precise and representative DC, ResectVol could include a visual check of lacuna candidates, so that users could impart a priori knowledge to help selecting the correct lacuna cluster.

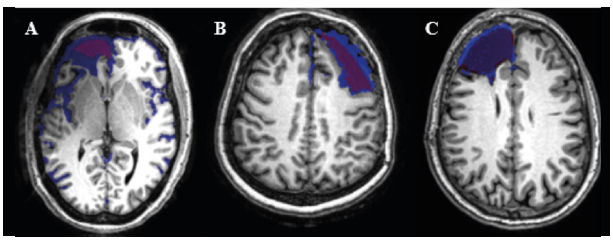

Figure 1. Minimum (A), median (B), and maximum (C) Dice values. Manual segmentation in red; automatic, in blue.

References: [1] Thijs RD et al., doi.org/10.1016/S0140-6736(18)32596-0 [2] Jehi L et al., Anticancer Res 35(5):2881-6, 2015 [3] Casseb RF et al., doi.org/10.1002/EPI4.12546

CRITICAL MOTOR-DEPENDENT SYNAPTIC BALANCE MODULATION IN THE SUBTHALAMIC NUCLEUS: A NEW FEATURE FOR ADAPTIVE DEEP BRAIN STIMULATION

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Introduction: The power spectrum density (PSD) of local field potential (LFP) provides valuable electrophysiological information at the micro and meso neuronal scales. Recent works have shown that the decay present in LFP PSD is a result of intricate interactions between fast synaptic glutamatergic excitatory currents and slow inhibitory synaptic GABAergic activity [1]. Indeed, the decay (α-parameter) given by in PSD can exhibit critical task-dependent modulation, establishing a synaptic-based framework for explaining the fine frequency tuning at the LFP level within neuronal loops. While some studies have shown that spectral decay can be modulated under psychiatric disorders (e.g., epilepsy, schizophrenia, and autism), no such evidence has been detected for movement disorders [2]. The present study aims to show that decay of subthalamic nucleus (STN) LFP can be modulated by movement activity in Parkinson's disease (PD) patients. **Materials and Methods:** STN-LFPs were recorded (24 kHz) during surgery for DBS electrodes implanted in 24 patients for 60s (totaling 35 LFP recordings, 13 bilateral and 9 unilateral) in rest and active arm flexion movement. Recordings were notch filtered and z-score normalized before PSD evaluation through the Welch method. Spectral decay (α) was estimated in the log (PSD) *vs.* log (f) using spectral windows of 8 Hz width in steps of 1 Hz through the beta band spectrum (13-30 Hz). The p-values for decay (α-parameter) comparison between rest and movement conditions across the spectrum were obtained by permutation tests and corrected by multiple comparisons. **Results:** STN-LFPs for the PD population show a clear power-law behavior along the beta spectrum in which the motor-dependent shape at the beta band (Figure 1A). The differences between rest and movement decays are observed for central frequencies (CF) from 24 to 28 Hz (Figure 1B). The CF at 26 Hz (i.e., 22 – 30 Hz band) best discriminates motor activity ($p<0.0001$, N=35, Figure 1C). **Discussion/Conclusion**: Our work suggests a critical movement-dependent

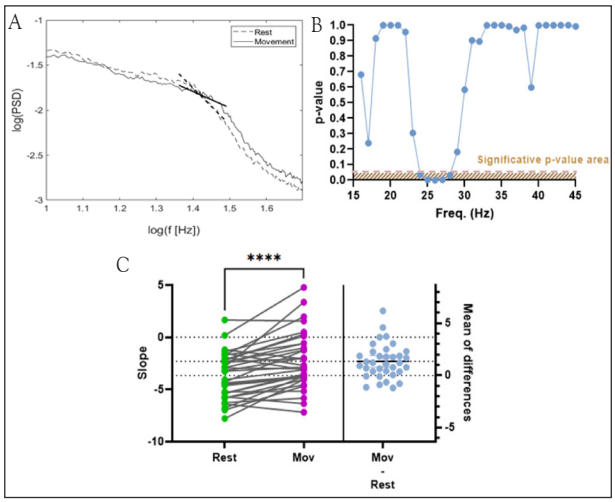

Figure 1. A – log (PDSm) vs. log (f) plots of STN-LFP under rest (dashed line) and movement for the PD population, where PSDm denotes the mean of PSD. B – Corrected p-values for α-parameter across CF concerning rest vs. movement comparison. C- α-parameter values for rest and movement conditions (left) and the difference between them (right).

decay modulation within the beta band for PD patients on STN-LFP, the main target for treating PD motor symptoms. This synaptic-based feature can outline a new characteristic for investigating the PD pathophysiology underlying the cortico-basal-thalamic loop and a crucial marker to define adaptive deep brain stimulation strategies.

References: [1] Gao R, Peterson EJ, Voytek B. doi: 10.1016/j.neuroimage.2017.06.078. [2] Uhlhaas PJ, doi: 10.1038/nrn2774.

CROSS OVER CLINICAL TRIAL USING MANDALAS DAS EMOÇÕES® METHOD FOR MENTAL HEALTH SUPPORT OF HEALTHCARE WORKERS

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Introduction: Though literature describes the impacts of Covid-19 in mental health of healthcare workers (HCWs), there is a scanty intervention studies with emotional support projects aimed at this audience [1]. Thereby, we conducted a crossover clinical trial (Rebec: RBR-5c8pz5r), approved by Ethics Committee of School of Medical Sciences (Unicamp), carried out between November 2020 and September 2021, aiming to analyze the effects of an emotional management activity program as mental health support to HCWs. **Materials and Methods:** The sample was divided into two groups: A, which underwent the intervention twice, and B, which underwent only once. The intervention, completely digital, consisted of a six weeks program of emotional management activities, inspired by Traditional Chinese Medicine (Mandalas das Emoções® Method). The exercises provided a reflection about the emotional responses to the pandemic daily life and sensitized to emotional management. As assessments, we applied the Patient Health Questionnaire-9 (PHQ-9) and the Medical Outcomes Short-Form Health Survey (SF-36). Data analysis was performed by the program IBM SPSS Statistics 22 (descriptive statistics and ANOVA for repeated measures with Sidak post hoc). **Results:** The sample consisted of 53 HCWs (23 in group A and 30 in group B), mostly nurses (33,96%), and one male participant. Most of them worked on the front line (58.49%). For the PHQ-9, both groups showed statistical differences between initial and final scores [A: $Z(2.38, 52.42) = 6.590$; $p < 0.05$], [B: $Z(1.72, 49.78) = 6.900$; $p < 0.05$]. In the period soon after the intervention, despite a trend of improvement in scores throughout the program for both groups, there were no significative differences. For the SF-36, group A showed a statistical improvement in the scores of the domains "Limitations due to emotional problems" [$Z(3, 66) = 4.007$; $p < 0.05$] and "Energy/fatigue" [$Z(3, 66) = 5.987$; $p < 0,05$] right after the first time of intervention and when comparing the beginning and the end of the study. Group B showed statistical differences right after the intervention for the domains "Energy/fatigue" [$Z(2.173; 63.027) = 8.907$; $p < 0.05$] and "Pain" [$Z(2,391; 69.342) = 11.628$; $p < 0.05$]. These aspects and "Emotional well-being" [$Z(2.083; 60.405) = 7.688$; $p < 0.05$] also showed improvement in scores comparing measures at start and end of the study. **Discussion/Conclusion**: This clinical trial demonstrated the positive impact of Mandalas das Emoções® Method in aspects related to mental health of HCWs. Our findings align with a study [2] in which 68% of the intervention group reported, after a five-minutes intervention of Mandalas das Emoções®, body and mind changes mainly related to relaxation and well-being. Thus, this approach showed potential as a rapid, high range and low-cost intervention that, because of its self-applicable character, contributes to emotional management and coping of short and long-term mental health difficulties unleashed by pandemic.

References: [1] Zaçe et al. Journal of Psychiatric Research 136:319–333, 2021. [2] Spagnol GS. Thesis (Doctorate), 2020.

DEVELOPMENT OF VIRTUAL REALITY SCENARIOS ATTACHED TO A MOTOR IMAGERY-BASED BCI FOR REHABILITATION OF LOWER AND UPPER LIMBS

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Introduction: The development of Virtual Reality (VR) scenarios for rehabilitation purposes has grown with the advances of technology [1]. VR facilitates the execution of the patient's body movements, acts on the sensorial systems, improves cognition, and dynamic and static balance, and enables training the rhythm of patients with ambulation difficulties [2]. On the other hand, Brain-Computer Interfaces (BCI) constitute a direct communication channel between the brain and a computer [3], allowing analysis of brain activity and neural responses to certain stimuli and tasks. Notably, the decoding of signals related to motor imagery (MI) is useful in VR scenarios for motor rehabilitation. VR environments have been shown capable of intensifying neural activity during MI [4] and assisting recovery [5]. Thus, the integration of VR environments with BCIs has the potential to create helpful supplementary tools for rehabilitation therapies. **Materials and Methods:** Electroencephalography signals obtained from 10 subjects (mean age 25±4, 70% males) during MI were used. Signals were first pre-processed to reduce noise and remove possible artifacts. Features were generated using Common Spatial Patterns filters and the average power over the frequency bands related to MI. These were input to a Support Vector Machine classifier and the response is sent to the application. The VR application was designed with support from a neurorehabilitation specialist, in Unity. The available hardware and software were adapted to attend three therapy conditions: necessary movements; daily activities; and parameters such as speed susceptible to changes to better attend the patient's treatment. **Results:** Figure 1 shows the VR environment, where the user walks in first person perspective, with their velocity controlled by the BCI. **Discussion/Conclusion**: The integration between the BCI and the VR environment was functional and practical, being easily adapted to different Unity scenarios. Throughout the offline tests, the accuracy rates stayed around (60±11)%. The next steps are notably the improvement of the BCI's accuracy and proceeding with tests on healthy subjects to validate the implementation. **Acknowledgements:** FAPESP (grants 2020/16800-0, 2020/11184-9, 2013/07559-3).

Figure 1. VR environment BCI-controlled.

References: [1] Burdea GC, Methods Inf Med 2003;42(5):519-23. [2] Darekar et al., doi: 10.1186/s12984-015-0035-3. [3] Graimann B et al., doi: 10.1007/978-3-642-02091-9. [4] Sollfrank T et al., doi: 10.3389/fnhum.2015.00463. [5] Vourvopoulos A et al., doi: 10.3389/fnhum.2019.00244.

EFFECTS OF PHARMACORESPONSE ON IN-VIVO NEURONAL DAMAGE IN MTLE PATIENTS: A LONGITUDINAL STUDY

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Introduction: Mesial temporal lobe epilepsy (MTLE) is an heterogenous disease which frequently presents with pharmacoresistance. Changes in metabolites measured by proton magnetic resonance spectroscopy (1H-MRS), such as reduction in hippocampal N-acetylaspartate (NAA) levels, a marker of neuronal dysfunction, have been regarded as sensitive to the effects of pharmacoresponse and presence of hippocampal sclerosis (HS) in MTLE [2]. Progression of structural damage, such as HS, has been reported even in patients with good seizure control [1]. However, whether there is also progression of metabolic damage remains an open question and could help clarify how neuronal dysfunction behaves in the long run for MTLE. We aimed to longitudinally investigate metabolic changes, measured by NAA levels, in patients with MTLE with or without adequate seizure control, using 1H-MRS, a non-invasive method capable of quantifying in vivo metabolic changes. **Materials and Methods:** We measured ipsi- and contralateral hippocampal NAA ratios to creatinine (NAA/Cr) using single-voxel 1H-MRS from 161 individuals, namely: 66 pharmacoresponsive MTLE patients, 95 pharmacoresistant patients and six healthy controls. We selected up to four 1H-MRS per individual (scan-1 to 4). The mean time interval between scan-1 and scan-2 was 2.1±1.8 years, between scan-2 and scan-3 was

2.1±1.4 years, and between scan-3 and scan-4 the time interval was 1.8±0.9 years. We performed generalized estimated equation models with an identity link function, including pharmacoresponse and time as main effects, and a pharmacoresponse-by-time interaction term, covarying for age at each scan. P<0.05 was set as significant. The best model fit was evaluated using Quasi Likelihood Independence Model Criterion (QIC) scores. **Results:** We found that there were significant effects of time (p=0.039), pharmacoresponse (p=0.024) but no pharmacoresponse*time (p=0.082) interaction on ipsilateral NAA/Cr, as follows: ipsilateral NAA/Cr was reduced in pharmacoresistant patients when compared to pharmacoresponsive patients (p=0.043) and controls (p=0.004). Ipsilateral NAA/Cr was also decreased over time, reducing from scan-1 to scan-3 (p=0.006) and scan-4 (p=0.051); also reducing between scan-2 and scan-3 (p=0.00) and scan-4 (p=0.012). However, there was only a significant effect of time on contralateral NAA/Cr (p=0.037) with no significant effects of pharmacoresponse (p=0.12) nor interaction (p=0.2). Contralateral NAA/Cr decreased from scan-1 to scan-2 (p=0.034). **Discussion/Conclusion**: Our data suggest unilateral effects of pharmacoresponse and bilateral effects of time in NAA/Cr in MTLE patients.

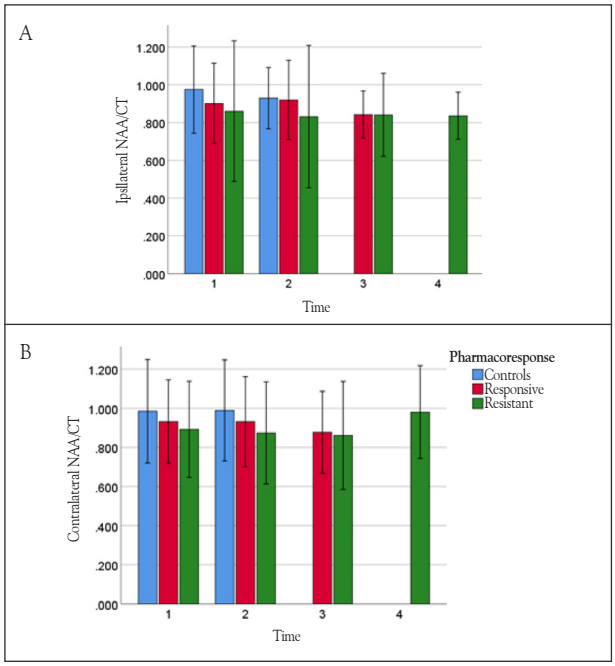

Figure 1. Graphs showing lower ipsilateral (A) and contralateral (B) NAA/Cr levels over time according to pharmacoresponse.

References: [1] Alvim MKM et al., doi: 10.1111/epi.13334; [2] Pimentel-Silva LR et al., doi: 10.1111/epi.16509

EVALUATION OF THE EFFECTIVENESS OF AN EDUCATIONAL INSTAGRAM FOR HEALTH PROMOTION FOR YOUNG ADULTS

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We believe that there is a gap in health information in the population and that it is important to expand the means of communication to promote healthy habits and motivate changes in behavior among young people. This work aims to evaluate an intervention using the social network Instagram to promote health, improvement in quality of life, physical and mental well-being, and healthy habits of followers, particularly the young population. We created an Instagram page and invited the followers to complete an initial online questionnaire to assess the profile of the public that followed Instagram and its habits at the beginning of the study. After an interval of 6 months, this questionnaire was reapplied together with an opinion questionnaire about the page. The work was approved by the research ethics committee. For categorical variables, comparisons were made using the chi-square test; to compare continuous variables between two groups, the Students' t-test was used, considering that the distribution was normal. For binary logistic regression, the frequency of reading posts in two categories was considered as a dependent variable: nothing/little and a lot/too much and as independent variables sex, age, education, scores of questionnaires 1 and 2. P values were considered significant at 0.05. Answered the initial questionnaire 86 participants and the analysis of the sociodemographic profile showed that 68 (79%) participants were female, 62 (72%) were between 18 and 30 years old, 62 (72%) considered themselves white, 13 (15%) considered themselves multiracial and 8 (9%) considered themselves black. Regarding education, 29 (32%) had completed high school and 57 (66%) had completed higher education; 20 (23%) participants claimed to have some chronic disease. Thirty-four participants answered the final questionnaire. The mean score of the initial questionnaire was 19.3 (± 3.8; n=86) and the mean score of the final questionnaire was similar, 19.7 (± 3.7; n=34). No participant achieved an improvement in scores of 33% or more, however, when comparing participants who followed the Instagram page and read the content a few times (n=22) with those who read it often or always (n=12), the participants with the best scores in the initial questionnaire accessed and read little of the content on the page, and the participants with the worst scores were those who followed and read the content more. After 6 months, there was no significant difference between the scores when comparing the two groups. Binary logistic regression analysis comparing those who read little with those who read a lot of content, adjusting for sociodemographic variables, showed a negative association with the scores of the first questionnaire, suggesting that participants with worse scores read more content (Questionnaire score 1.OR= 0 .45, p=0.006, 95%CI[-1.33 – -0.22]), while those with better health habits showed little interest in this type of information and did not change their habits significantly. In addition, there was a positive association with the scores of the second questionnaire, suggesting that frequently following the Instagram page was associated with a significant improvement in the participants' habits (Questionnaire score 2, OR=1.69, p=0.05; CI95 %[0.00 - 1.06]). It was possible to observe that the Educational Instagram page had good acceptability among the public. The participants had a high level of education, had good health habits, performed some physical activity, had moderate consumption of alcoholic beverages and a significant portion had not used illicit substances in the last 12 months. The prevalence of chronic diseases was below the national average for adults. Fast-food consumption was frequent, demonstrating that the greatest difficulty was food control.

References: [1] KAMEL BOULOS, M. N et al, doi: 10.3390/fi8030037; [2] O´REILLY, doi: 10.1080/09638237.2020.1714007; [3] PINTO, P, doi: 10.29397/reciis.v13i4.1634; [4] PEREIRA, E. F, et al, doi: 10.1590/S1807-55092012000200007.

EXAGGERATED ALPHA RHYTHM FROM SUBTHALAMIC NUCLEUS DISCRIMINATES FREEZERS FROM NON-FREEZERS PARKINSON'S DISEASE PATIENTS: A POSSIBLE FEATURE FOR CLOSED-LOOP DEEP BRAIN STIMULATION

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Introduction: Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder. Freezing of gait (FOG), a disabling motor symptom, affects around 50% of advanced PD patients, impacting on mobility and quality of life. Its unpredictable occurrence outlines a significant relevance in PD treatment and the understanding of the electrophysiological phenomena underlying cortical and subcortical remains scarce. Altered alpha and beta oscillations during FOG were yet reported considering different movements, not even during at rest. Elucidating the structures and electrophysiological biomarkers in FOG should open new strategies of neuromodulation of this severe PD symptom. This works aims to characterize the spectral composition of the subthalamic nucleus (STN) in FOG group compared to those without freezing (n-FOG) during movement and rest. **Materials and Methods:** We studied 23 PD patients, being 14 with FOG (FOG group) and 9 without FOG (n-FOG), according to the clinical FOG questionnaire applied. Subthalamic nucleus local field potentials (STN-LFP) recordings were performed during deep brain stimulation (DBS) from the STN sensorimotor portion for 60 seconds both at rest and movement

conditions (active flexion of the elbow). The 37 STN-LFP recordings were exported and processed in Matlab 2018b – downsampled at 1 kHz, notch filtered at 60 Hz, bandpass filtered (2–200 Hz) and z-scored normalized. These preprocessing routines preserved the main LFP sub-bands: theta (4–8 Hz), alpha (8–15 Hz), low beta (15–25 Hz), high beta (25–35 Hz) and gamma (35–200 Hz). The spectral composition of FOG and n-FOG patients were performed through Welch periodograms considering power spectral density estimation. Sixty seconds of the STN-LFP for each patient were Hamming windowed (4 seconds) with 50% of overlap followed by a square of the magnitude estimates of the discrete Fourier transform, whereas considering all windows (spectral resolution of 0.25 Hz). Additionally, the temporal dynamics of alpha activity (alpha bursts) was assessed through the Continuous Wavelet Transform of LFP time-series, considering suprathreshold (75th percentile) LFP amplitudes envelope. Bandpower and alpha bursts comparisons between FOG and n-FOG groups were computed by two-way analysis of variance (ANOVA), considering phenotype and movement/rest conditions as factors. Post-hoc tests were performed only if preceded by significant main effect and multiple comparisons were corrected by Bonferroni method. The correlation coefficients (r) between bandpower and FOG scores were performed through Pearson's coefficient method. **Results:** ANOVA showed significant main effect [$F(1,35)=7.23$; $p=0.01$] for alpha activity between FOG and n-FOG. Accordingly, FOG patients had higher alpha activity relative to n-FOG patients both at rest ($p=0.03$) and movement conditions ($p=0.03$). Only FOG patients had higher alpha bandpower during rest relative to movement ($p=0.05$). Alpha bandpower and FOG scores had a direct and significant correlation ($r=0.31$; $p=0.05$) at rest. ANOVA showed significant main effect [$F(1,35)= 3.88$; $p=0.04$] on alpha bursts, with significantly higher duration in FOG patients ($p=0.01$). **Discussion/Conclusion**: Our results suggest higher alpha bandpower of STN-LFP in FOG PD compared to n-FOG group, and such bandpower positively correlated with FOG scores. We also noticed longer alpha bursts duration in FOG patients, revealing important temporal behavior differences between FOG and n-FOG. Exaggerated alpha activity might be linked to a deficit in attention and executive circuit underpinning FOG manifestation. These findings may contribute to new electrophysiological biomarkers for the FOG phenomenon, and suggest a new feedback variable of control of this symptom by closed-loop DBS.

FATIGUE, SOMNOLENCE AND DEPRESSION PERSIST AFTER SIX MONTHS IN RECOVERED INDIVIDUAL AFTER THE ACUTE COVID-19

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Introduction: COVID-19 is currently a high prevalent disease and neuropsychiatric symptoms may persist after the acute infection. A growing frequency of depression / anxiety symptoms, fatigue and sleep disturbances in the post-infection context have been observed. This association is probably not restricted to severe acute infection cases. There is an urgent need for comprehension of these interaction. **Materials and Methods:** We included 1183 consecutive cases of post-Covid infection (79% women; median age 41 [12-77]) who answered the second interview of our online survey (median interval of 191 days [50-503] after the infection). We used the Hamilton Anxiety and Depression Scale (HADS) to evaluate the intensity of anxiety (HADS-A) and depression (HADS-B) symptoms, the Chalder Fatigue Scale (CFS) to measure the severity of fatigue and the Epworth Sleepiness Scale (ESS) to assess daytime sleepiness. Individuals also answered the PHQ-9 (Patient Health Questionnaire-9). Patients were separated according to the type of treatment (home [1046, median 41 years], ward [87, median 45.5 years] or ICU [50, median 48.5 years]). We used SPSS26 for statistical analysis with Mann-Whitney tests to compare continuous variables among groups and Spearman tests for correlations. **Results:** Anxiety symptoms (HADS-A) were more severe in ICU patients (median score 12 [0-19]) compared to the home group (median score 9 [0-21]; $p=0.012$). Similarly, the severity of physical fatigue (CFS-fatigue) was higher in the patients treated in ICU (median score 16 [2-21] compared to home treatment (median score 13 [0-21]; $p=0.004$). However, the severity of depression symptoms ($p=0.1$), PHQ-9 scores ($p=0.06$), mental fatigue scores ($p=0.06$) and daytime sleepiness scores ($p=0.6$) were similar among the three groups. Overall, there were positive correlations between sleepiness and both mental ($r=0.33$, $p<0.001$) and physical fatigue ($r=0.44$, $p<0.001$). The PHQ-9 scores positively correlated with sleepiness ($r=0.36$, $p<0.001$), with mental fatigue ($r=0.63$, $p<0.001$) and with physical fatigue ($r=0.73$, $p<0.001$). Interestingly, these correlations were present for the three groups, even after splitting according to treatment. **Discussion/Conclusion**: We confirmed persistent symptoms of fatigue, daytime sleepiness, anxiety and depression symptoms in a large group of recovered individuals after six months from the acute infection. It was surprising that patients with mild infection presented equivalent intensity of symptoms of mental fatigue, somnolence and depression, compared to those who required hospitalization. Neuroimaging studies of large groups are required to clarify the neural substrates for the neuropsychiatric symptoms.

FULLY AUTOMATED TOOL FOR CONSCIOUSNESS CLASSIFICATION USING EEG

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Introduction: The electroencephalography (EEG) is a technique that measures big scale neural oscillations on the brain based on voltage variations captured by different electrodes, useful to investigate and monitor neurological diseases but also able to inform about the consciousness stages. The human alert stage results in the detection of beta waves (12-35 Hz); as the patient relaxes and reduces anxiety, the EEG detects alpha waves (7-12 Hz), followed by the sleepiness stages, divided in theta waves (4-8 Hz) and delta waves (0.5-4 Hz) [1]. A wavelet transform is an analysis tool dedicated to attributes that vary over different scales, such as time and frequency. The continuous wavelet transform (CWT), covers the time-frequency plane with variable window sizes [2]. An algorithm was developed aiming to identify the stages of consciousness based on the frequency bands potential variation associated with sleepiness and awakeness through EEG data. **Materials and Methods:** EEG data (30 minutes, 21 channels) were obtained with a Nihon Kohden Neurofax Electroencephalograph from 40 subjects. Briefly, the algorithm developed using Matlab, separates the EEG data into two frequency bands through CWT. The first, called awake band (9 to 12 Hz) and the second, to the sleep/sleepiness stages (4 and 7 Hz). The relation between frequency bands average magnitude was estimated, which allows it to define periods indicative of either to an awake or sleep/sleepiness stages, in epochs defined as 30 seconds. Finally, we compared the obtained result with the clinical hypnograms handed by the neurophysiologists. For validation purposes, an image is given as a result (Figure) indicating the concordance between the hypnogram and the algorithm results. The tool sensibility, specificity and accuracy were estimated. **Results:** The comparison between the hypnogram and the algorithm returned a sensitivity of 78%, specificity of 91% and accuracy of 86%. The sensitivity returns the probability of the algorithm to be in equivalence with the hypnogram (true positive rate). The specificity gives the probability of the algorithm to result in a different conclusion to the hypnogram (true negative rate). The accuracy is the overall probability that the consciousness stage was correctly assessed. **Discussion/Conclusion**: The algorithm developed shows good equivalence with the clinical reports. These results encourage the application of the algorithm to fast and automatically evaluate the consciousness stages of patients undergoing EEG exams, providing important information for big data studies. In addition, the resultant temporal series associated with sleep and awake ratios provides the notion of progression/transition between stages and can be further investigated with functional MRI data.

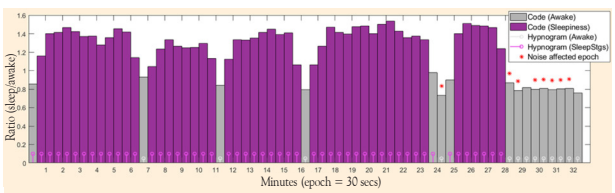

Figure 1. Grey bars representing the moments in which the algorithm points towards awakeness and purple bars, representing sleep/sleepiness; circular indicators pointing to the results provided by the neurologist, white indicating awakeness and the purple indicating sleep/sleepiness.

References: [1] Abhang PA, doi:10.1016/B978-0-12-804490-2.00002-6; [2] Akansu AN et al., doi: 10.1016/B978-012047141-6/50006-9

GENETIC CHARACTERIZATION OF A LARGE COHORT OF PATIENTS WITH DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES FROM LATIN AMERICA

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Introduction: Developmental and epileptic encephalopathies (DEE) are a group of severe epilepsies, usually resistant to drug treatment, and associated with delayed neuropsychomotor and cognitive development. With the advancement of molecular studies in recent years, new mutations associated with DEE have been described. However, a significant number of patients remain without identified causative genetic variants. **Materials and Methods:** First, we performed whole-exome sequencing (WES) and chromosomal microarray analysis (CMA) to determine the molecular diagnostic yield in 242 patients from several different countries in Latin America, assuming a monogenic model of inheritance. Second, we used the group of patients in whom a monogenic cause for the disease could not be found to test for a polygenic effect, i.e., mutations of a minor individual but with a cumulative effect, occurring in several genes of common or different pathways that may converge to a larger final effect on the phenotype. For the polygenic analysis, we used two methods, logistic regression (LR) and SKAT-O. **Results:** WES allowed the genetic diagnosis in 36.3% of 234 patients, while CMA achieved the diagnosis in 6.3% of 239 patients. In the LR analysis using common variants (n=142 patients), we found one SNP (rs9374755) possible associated with the disease. Using SKAT-O analysis in the same group of patients, we identified significant association with a set of ultra-rare variants present in ten genes: *LAMC3, PTPN23, TBCD, FASN, RELN, CREBBP, ASPM, SPTAN1, RYR3,* and *HERC.* **Discussion/Conclusion**: Using both WES and CMA, it was possible to confirm the genetic diagnoses of 41.3% of the patients with DEE studied. WES alone achieved a higher diagnostic yield than CMA alone (36.3% x 6.3%); however, using both methods increased the proportion of patients with positive findings. Furthermore, the polygenic analyses identified an association with a common SNP and ultra-rare variants in 10 candidate genes for epilepsy, thus indicating that a polygenic inheritance could also be present in patients with DEE. Noteworthy, this is the first large and comprehensive genetic study of patients with DEE in Latin America.

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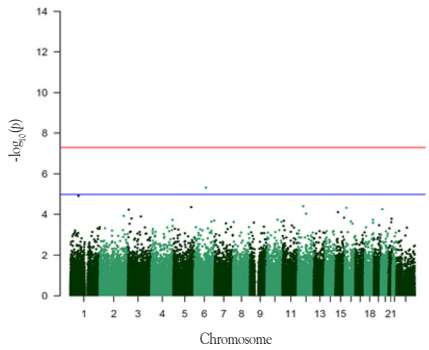

B

Gene	p-value	SNPs number
ASPM	0.045517718	15
CREBBP	0.032086627	16
FASN	0.009504475	29
HERC1	0.053036286	21
LAMC3	0.001417445	27
PTPN23	0.004014821	18
RELN	0.017928247	16
RYR3	0.047068168	27
SPTAN1	0.045613193	10
TBCD	0.006100143	26

Figure 1. A- Manhattan Plot using logistic regression and common variants; B- Gene identified by SKAT-O analysis showing their p-values and the number of variants. Exclusive genes in gray (when compared with the whole dataset).

GENOMIC DISTRIBUTION OF DNA METHYLATION IN MESIAL TEMPORAL LOBE EPILEPSY

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Introduction: The modulation of gene expression by epigenetic modifications may be related to disease mechanism. DNA methylation is one epigenetic modification which can be analyzed using high throughput sequence methods to determine the distribution of DNA methylation in the entire genome, the so called methylome. Mesial temporal lobe epilepsy (MTLE) associated with hippocampal sclerosis (HS) is one of the most frequent and severe types of epilepsy [1], and it may be related to abnormal DNA methylation profile [2, 3]. In this work, we aim to evaluate the methylome in brain tissue samples from patients with MTLE+HS compared to control tissue obtained from autopsy. **Materials and Methods:** We used whole-genome bisulfite sequencing to analyze DNA from 11 brain samples obtained by epilepsy surgery from patients with medically refractory MTLE+HS, as well as from four autopsy controls (hippocampus and dentate gyrus). Samples from patients were divided into two groups: i) patients with less than 20 years of disease duration (G1 - n = 5); and ii) patients with more than 20 years of disease duration (G2 - n = 6). Methylome was performed in an Illumina® platform, and differentially methylated regions (DMRs) were identified after bioinformatics and statistical analyses. We conducted two comparisons: first, all patients (G1+G2) x autopsy controls, followed by the comparison between the two patient groups (G1x G2). Furthermore, we catalog the putative genes related to the regions with different levels of DNA methylation levels identified. **Results:** We observed thousands of DMRs in the two comparisons. DMRs did not show a homogeneous distribution throughout the different genomic portions evaluated (Figure 1), and an overall hypermethylation profile was prevalent in patients. DMRs were observed in more than one genomic portion, depending on their length. Introns and promoters had increased DMRs related to both methylation status (hyper and hypo) (Figure 1). 6,371 catalog genes were related to the DMRs from G1 x Controls; 5,548 in G2 x Control; and 4,088 in G1 x G2. **Discussion/Conclusion**: We found a thousands of DMRs in patients with MTLE+HS compared to controls. These were related to thousands of candidate genes potentially involved in the mechanisms underlying MTLE+HS. Our work highlights the importance of study the methylome in a complex disease such as MTLE+HS, since epigenetic regulatory elements may play numerous roles in a biological system, affecting multiple molecular layers and networks.

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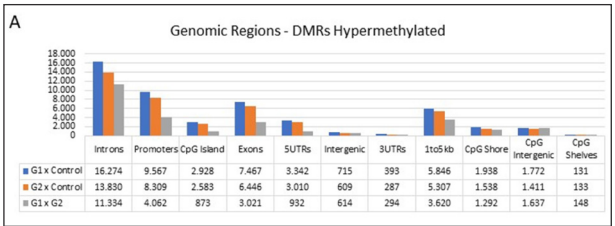

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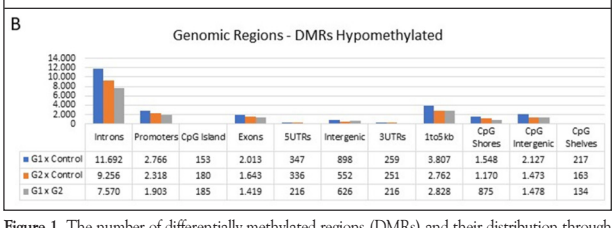

Figure 1. The number of differentially methylated regions (DMRs) and their distribution through the genome. (A) DMRs hypermethylated; (B) DMRs hypomethylated.

References: [1] Wieser, H.G. et al., DOI: 10.1111/j.0013-9580.2004.09004.x; [2] Long et al., DOI: 10.1038/srep43810; [3] Xiao et al., DOI: 10.1111/cns.13394.

GRAY MATTER ATROPHY ASSOCIATED WITH ANXIETY AND DEPRESSION AFTER MILD COVID-19 INFECTION

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Introduction: Despite emerging reports exploring persistent neuropsychiatric symptoms after acute SARS-CoV-2 infection, there is a lack of evaluation of mildly affected patients and neural correlation for their impairments. Therefore, we investigate gray matter changes in mildly infected patients according to the presence of symptoms of anxiety and depression. **Materials and Methods:** We analyzed 254 patients (non-hospitalized) with confirmed COVID-19 diagnosis (177 women, median age of 41 years (range 18-78), median interval between diagnosis and visit of 82 days [range 13-367]) and compared to a group of 148 healthy controls (100 woman; median age of 35 years [range 17 – 68]), paired by sex (p=0.7). Individuals answered the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) to quantify symptoms' severity. Patients were split in asymptomatic-group (152, ASYMPT-group; no symptoms of anxiety or depression) and concurrent-symptomatic (102, CONCUR-group; BAI>10 and BDI>13). All individuals underwent 3T MRI. We used CAT12 TOOLBOX/MATLAB2019/SPM12 to perform voxel-based morphometry and analyze grey matter volume (GMV) changes. We covariated the analyses for sex, age and intracranial volume (ICV) and compared groups with Bonferroni correction to adjust for multiple comparisons. **Results:** While the CONCUR-group presented higher scores (median BDI=21 and BAI=24 score), the ASYMPTO-group (median BDI=5 and BAI=4) and the controls (median BDI=4, BAI=3) resented lower scores. After adjusting the GMV analyses for sex, age and ICV, only the CONCUR--GROUP presented GM reduction in the left cingulum (86 voxels) and inferior frontal lobe (91 voxels), p<0.005. No GM changes were detected in the ASYMPT-group. **Discussion/Conclusion**: We observed persistent neuropsychiatric symptoms (consistent with long-COVID), associated with GM atrophy in the CONCUR-group. These findings suggest that structural changes may occur even after mild SARS-CoV-2 infection. Early treatment may prevent persistent suffering and improve quality of life.

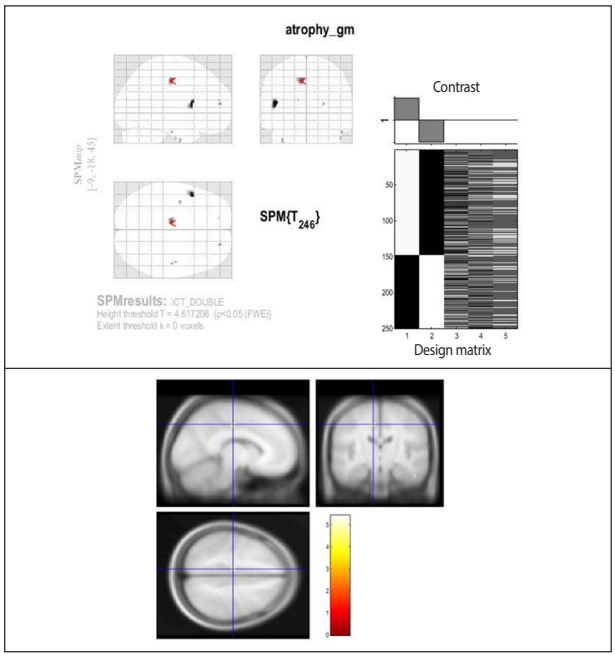

Figure 1. VBM analyses show GM atrophy in the left cingulum and inferior frontal lobe.

HISTOPATHOLOGICAL EVALUATION OF WHITE MATTER GLIA AND CORRELATION WITH MRI FINDINGS FROM EPILEPSY PATIENTS SURGICALLY TREATED IN A BRAZILIAN INSTITUTION

Ingrid Carolina da Silva Cardoso[1], Bruna Cunha Zaidan[1], Brunno Machado de Campos[2], Luciana Ramalho Pimentel da Silva[2], Vanessa C. Mendes Coelho[2], Marina Koutsodontis Machado Alvim[2], Clarissa Lin Yasuda[2], Enrico Ghizoni[2], Helder Tedeschi[2], Fernando Cendes[2], Fabio Rogerio[1].

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Introduction: Epilepsy is a common neurological disease [1]. Almost 30% of patients are pharmacoresistant and become candidates for surgery, hippocampal sclerosis (HS) and focal cortical dysplasia (FCD) being the most frequent neuropathological findings [2]. Here, we performed histological analyses of the white matter (WM) of specimens from individuals surgically treated due to hypothesis of HS or FCD, focusing on astrocytic and microglial populations [3]. We also obtained preoperatory WM MRI data from the same brain regions. Our aim was to correlate histopathological findings with neuroimaging data from Brazilian patients. **Materials and Methods:** Analysis of histological sections of specimens of epilepsy (n=21) and control (autopsied patients without history of neurological disease; n=20) groups was made by means of immunostaining for GFAP and Iba-1 to evaluate astrocyte and microglial populations, respectively. All sections were scanned (Aperio Scanscope CS2 #23CS100) and digital photos of the WM were analyzed (ImageJ® software). Using the Threshold tool, each image was transformed into grayscale with a defined cutoff point to convert the photo into binary information (black/white). The software calculated the value of black pixels and the total pixels of the field, providing a ratio defined as '*Mean*'. We examined MRIs (3T Philips Achieva) from the frontal, temporal, and occipital lobes from patients (n=21) and compared with matched controls, following a routine protocol [4]. T2-weighted multiecho MRIs were evaluated with in-house software. T2 signals were computed from five echoes in regions of interest (ROI) in the WM. DWI and T1-weighted images were evaluated using the ExploreDTI software [5]. From each ROI, we obtained the mean values of the following parameters: fractional anisotropy (FA), mean, axial, and radial diffusion. For statistical evaluation, Mann-Whitney test, Spearman test and Wilcoxon test were used at a significance level of p<0.05. **Results:** We found significant increases in '*Mean*' values of Iba-1 and GFAP immunostainings from epilepsy patient samples compared to controls (p<0.001). Also, we found significant increase in T2 signal from patients compared to controls (p<0.001), as well as when comparing the ipsilateral to the contralateral areas (p=0.028) of the same patient. DWI analysis presented a significant FA decrease particularly in the temporal pole of patients with HS compared to controls (p=0.042) and to the contralateral area (p=0.028). There was no significant correlation between immunostaining (Iba-1 and GFAP) and any of the parameters evaluated on MRIs. **Discussion/Conclusion**: Increased Iba-1 expression corresponds to microglial activation, whose biological role in seizures depends on the stage of the disease: inhibitory or stimulatory for acute or chronic epilepsy, respectively [6]. Similarly, increased GFAP expression (gliosis) may play a role in inhibiting or promoting seizures, as well as in synaptic communications [7]. Moreover, microglia and astrocyte interaction may induce chronic co-activation [3]. T2 hyperintense signal is associated with greater amount of free water in the tissues, which occurs in the case of gliosis. Decrease in AF could correspond to a decrease in axonal integrity. Our observations are original for Brazilian individuals with epilepsy and agree with previous studies from other institutions [8]. **Funding:** FAPESP (2013/07559-3, 2019/08259-0, 2020/12651-0) and FAEPEX Unicamp (2037/19).

References: [1] Steinhauser C et al.; doi: 10.1016/j.neuroscience.2014.12.047; [2] Blumcke I et al., doi: 10.1056/NEJMoa1703784; [3] Kinoshita S et al., doi: 10.4103/1673-5374.300976.; [4] Kubota BY et al., doi: 10.1016/j.yebeh.2015.04.001; [5] Lebel C et al., doi: 10.1016/j.neuroimage.2007.12.053; [6] Eyo UB et al., doi: 10.1523/JNEUROSCI.0416-14.2014.;[7] Ortinski PI et al., doi: 10.1038/nn.2535.; [8] Concha L et al., doi: 10.1523/JNEUROSCI.1619-09.2010.

IDENTIFICATION OF INDIVIDUALS FROM EEG DATA USING SYNCHRONIZATION BY MOTIFS FOR FUNCTIONAL CONNECTIVITY

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Introduction: In this study, from data obtained from electroencephalography (EEG) of 11 subjects, we analyzed the ability of this diagnostic exam to differentiate individuals, according to their brain traces, searching for a biometric signal related to the subject's functional connectivity (FC). In order to calculate the FC of each individual, we used the technique of synchronization by motifs [1]. To compare individuals, Pearson correlation was used, differently from previous work [2]. **Materials and Methods:** EEG data from 64 electrodes were obtained from the Physionet online database (https://physionet.org/content/eegmmidb/1.0.0./). Eleven subjects were analyzed using two 1-min long resting-state acquisitions (eyes open – A1 – and closed – A2). To remove artefacts from the signals, using EEGLAB/MATLAB, they were visually cleaned, followed

by ICA to remove movement components. Subsequently, the CleanLine tool was used to remove the electrical frequency (60 Hz), followed by the removal of the alpha band (7-13 Hz), which could lead to divergencies between closed and open eyes signals [3]. Finally, the Common Average Referencing (CAR) method was applied to remove common artefacts to all electrodes. Four 1 s epochs were extracted from A1 and one 1 s epoch from A2. Next, the motifs method using 3 points (Figure A), implemented in MATLAB by the author, was used to compute FC for these epochs. A1 FC matrices were averaged. Pearson correlation was then computed between all A1 and A2 matrices. If the highest correlation value was for A1 and A2 of the same individual, it was possible to identify the person. **Results:** Figure B shows the results for the 11 subjects. About 64% of the individuals were identified correctly, marked in green. **Discussion/Conclusion**: The 64% hit rate was not very satisfying for biometrics purposes. For better results, we can consider taking a larger interval from the signal, such as 5 or 10 seconds, and analyze more subjects beyond the 11 in this study. **Acknowledgements:** CNPq/PIBIC and FAPESP (grant 2013/07759-3) for financial support.

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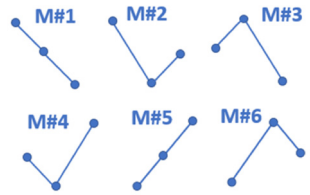

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A1/A2	S072	S073	S074	S075	S076	S077	S078	S079	S080	S081	S082
S072	0,7833	0,6957	0,7350	0,6726	0,6638	0,5020	0,6588	0,6590	0,7196	0,7331	0,7616
S073	0,7958	0,8511	0,7456	0,6856	0,7045	0,6092	0,7006	0,7149	0,7275	0,8147	0,7209
S074	0,8126	0,7750	0,8144	0,7659	0,7104	0,5390	0,7327	0,7705	0,7864	0,8289	0,7568
S075	0,7966	0,6909	0,6951	0,7911	0,6424	0,5854	0,6691	0,7053	0,7325	0,8139	0,7442
S076	0,7394	0,7877	0,8051	0,6604	0,9264	0,4636	0,8563	0,7471	0,8192	0,6695	0,7659
S077	0,7621	0,6846	0,6963	0,7020	0,6836	0,5549	0,6832	0,7097	0,0000	0,7577	0,7261
S078	0,7465	0,7103	0,7308	0,6868	0,6866	0,4409	0,7473	0,6972	0,7113	0,7300	0,7175
S079	0,7597	0,7471	0,7232	0,6972	0,7019	0,5293	0,7321	0,7636	0,7174	0,7681	0,7390
S080	0,7587	0,7247	0,7882	0,7348	0,7592	0,5199	0,8182	0,7400	0,8654	0,7363	0,7695
S081	0,7559	0,7555	0,7545	0,6893	0,7148	0,5416	0,7539	0,7501	0,7606	0,8318	0,7628
S082	0,7509	0,6927	0,7407	0,7156	0,7096	0,5134	0,7273	0,6826	0,7676	0,7102	0,8210

Figure 1. A - Three-point motifs used in this work. B - Correlation coefficients between the two acquisitions of the 11 subjects.

References: [1] Rosário et al., doi: 10.1016/j.physa.2015.07.018. [2] Davanço MAV et al., XXIX Congresso IC UNICAMP. 2021. [3] Berger H, doi: 10.1007/BF01797193.

INDIVIDUAL CHARACTERIZATION OF EPILEPSY PATIENTS USING FUNCTIONAL CONNECTIVITY

B. M. Carlos[1,2], B. M. Campos[3], M. K. M. Alvim[3], F. Cendes[2,3], G. Castellano[1,2]

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Introduction: Epilepsy is one of the most common neurological diseases and it is in many cases a condition resistant to drugs, imposing the necessity of brain surgery. The electroencephalogram (EEG) exam is a powerful tool to detect a diverse range of physiological manifestations, including epileptic activity. Studies have shown that the brain networks' organization of epilepsy patients, which can be accessed through connectivity measures in EEG, presents irregular behavior when compared to healthy subjects [1]. It has also been shown that functional connectivity could be used to assess diagnosis and individual characteristics [2]. In this study, we aim to find relevant features from EEG signals of epilepsy patients with the intention to better understand the relationship between brain network organization and epilepsy. To reach our purpose, we performed functional connectivity measures (coherence) and tested how different sets of features performed in a biometry classification, even for patients with similar diagnostics. **Materials and Methods:** Signals from 30 epilepsy patients (mean age 39 years, 16 females) with different etiologies and diagnostics were selected from previous EEG exams collected in the Laboratory of Neuroimaging, at UNICAMP. The acquisition was in resting-state condition during magnetic resonance sessions, with a compatible 64-electrode brain cap (including one electrocardiogram electrode). We extracted 300 s of signals from two trials (600 s total) of the same session for every patient, segmented into epochs of 10 s, and labeled each trial as train or test dataset. Magnitude-squared and imaginary coherence (COH and ICOH, respectively) were calculated for each epoch in the frequency bands delta, theta, alpha, beta, gamma (30–70 Hz), and 1–70 Hz. We performed the classification using both a Support Vector Machine (SVM) with linear kernel and a Linear Discriminant Analysis (LDA) and evaluated the accuracies using the interactions between different sets of frequency bands and spatial regions, divided in frontal, temporal, parietal, central, and occipital. **Results:** We first performed the classification using all 63 electrodes and divided our classifiers by frequency band. As a result, accuracies over 56% and 69% were obtained using ICOH with SVM and LDA, respectively. For COH, we achieved accuracies over 68% with SVM and 82% with LDA. The best results were 93% (COH, LDA) for beta band, 92% (ICOH, LDA) and 87% (COH, LDA) for 1–70 Hz, 87% (ICOH, LDA) for gamma, and 86% (COH, LDA) for theta. According to these first results, we then implemented the classification for each pair of spatial regions in the beta band with COH and LDA. The most relevant accuracies were 86% for the interactions inside the parietal region (pp) and 91% considering all the pairs containing the parietal region. **Discussion/Conclusion**: In summary, we found that the most relevant features for personal identification ("EEG fingerprints") might come mostly from the beta band and from the interaction of the parietal lobe with the other regions. Moreover, the subtype of epileptic syndrome did not seem to interfere in the classification patterns. The significant alterations in parietal connectivity of some patients [3] could support the idea that individual aspects of the disease are contained in this area, and a similar study with healthy subjects can be useful to enhance our results. Work supported by FAPESP (grants 2020/16571-0, 2017-25795-7 and 2013-07559-3)

References: [1] Stam CJ, doi: 10.1038/nrn3801. [2] Nentwich M *et al.*, doi: 10.1016/j.neuroimage.2020.117001. [3] Burianová H *et al.*, doi: 10.1016/j.eplepsyres.2017.09.001.

INFLUENCE OF DEPRESSIVE DISORDERS ON POSTURE AND BODY IMAGE: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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Introduction: The present study aimed to compare postural and self-image changes in patients with depression. Depression has become a recurring theme in the health area in recent decades. In its diagnosis, the following are taken into account: psychic and physiological symptoms and behavioral evidence. Clinical observation of depression suggests a distinct and recognizable behavior, notable of sad facial expression, frowning forehead, hunched shoulders and lack of spontaneous body movements. **Materials and Methods:** The present work complied with the norms regulated by the research department, CAAE (Certificate of Presentation for Ethical Appreciation) 15057219.5.0000.0106. Ten female subjects, aged between ±20 and ±60 years, were included. Four questionnaires were used: Socio Demographic form, "My body image - AMIC", "Body Shape Questionnaire - BSQ" and "Posture Assessment Instrument – IAP". **Results:** It can be concluded that individuals with depressive disorders have important postural changes, these findings are supported by the current literature, however other studies should be carried out in order to elucidate other variables of this possible clinical correlation. **Discussion/Conclusion**: Regarding body image, the average BSQ score ranged from 75.82 ± 35.30 to 90.03 ± 38.46, thus classifying the sample in the absence of distortion or mild

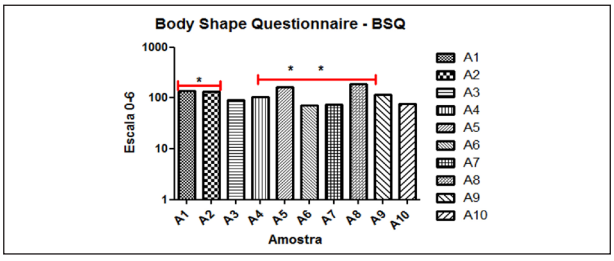

Figure 1. Body Shape Questionnaire – BSQ.

Table 1. Distribution in points - BSQ.

Sample	Punctuation	Classification
A1	186	Severe distortion
A2	166	Severe distortion
A3	140	Moderate distortion
A4	132	Moderate distortion
A5	115	Moderate distortion
A6	106	Light distortion
A7	92	Light distortion
A8	78	Absence of distortion
A9	74	Absence of distortion
A10	72	Absence of distortion

distortion, however, it is pointed out in the present study, that there was no statistically significant difference between the results (p = 0.4373). It can be concluded that individuals with depressive disorders have important postural changes, these findings are supported by the current literature, however other studies should be carried out in order to elucidate other variables of this possible clinical correlation.

INTRAVOXEL INCOHERENT MOTION OPTIMIZATION OF B-VALUES ACQUISITION FOR DIFFERENT FITTING ALGORITHMS

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Introduction: This study proposed to compare different fitting algorithms for IntraVoxel Incoherent Motion (IVIM) in b-value sampling reduction. Choosing the best distribution of b-values is an essential objective of the studies in IVIM imaging [1]. The optimization of the b-value sample has been studied since the optimal sampling can reduce the number of b-values to estimate the IVIM maps better and turn the acquisition protocol faster. **Materials and Methods:** We simulated an IVIM signal with 15 b-values (0, 4, 8, 16, 30, 60, 120, 250, 500, 1000, 1200, 1400, 1600, 1800, 2000 s/mm^2) consisting of a N = 10000 signal (Figure A). As ground truth, we used the values of D, D*, and f as 0.00081 mm^2/s, 0.022 mm^2/s, and 0.2 [2]. We added a normal deviation of 0.25 in the signal to create noise. For analysis, we used the mean of the three RRMSE, selecting the best b-value subset to continue the reduction process. The codes were written in Python using the libraries Dipy and Numpy (https://github.com/inbrainlab/IVIMReduction). **Results:** We found that the mean value of pseudo-diffusion D* is privileged by reducing the number of b-values. Fitting the original data with Dipy non-linear least-squares algorithm, the average values for D, D* and f were (0.8±0.2)x10^{-3} mm^2/s, (30±120)x10^{-3} mm^2/s, and 0.15±0.30. Applying the algorithm for reduction of 5 b-values, we got the reduced b-value scheme of 10 b-values (0, 4, 8, 16, 120, 500, 1000, 1200, 1800, 2000 s/mm^2) and D, D* and f of (0.8±0.2)x10^{-3} mm^2/s, (24±140)x10^{-3} mm^2/s and 0.15±0.30. **Discussion/Conclusion**: The Dipy fitting algorithm better estimates the mean value of pseudo-diffusion, which is privileged by reducing the number of b-values but with a great standard deviation. Our next steps are to analyze other fitting methods to compare the consistency and deeply study the impacts of a b-value reduction for multiple fittings methods.

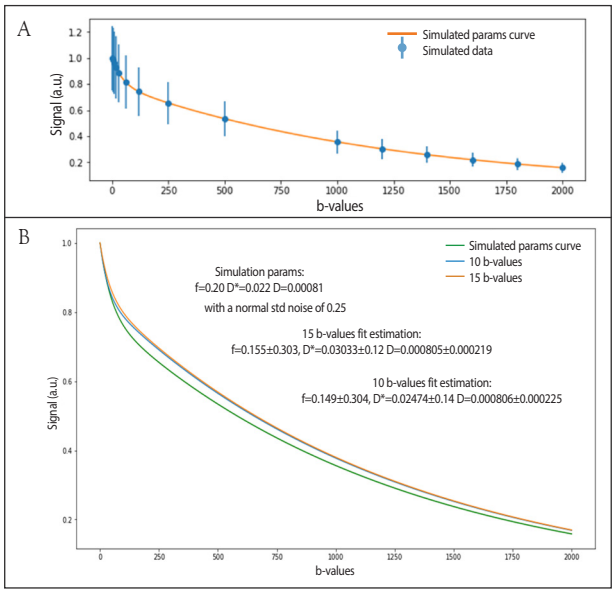

Figure 1. A - The distribution of simulated data. B - Fitting results from different b-value samples.

References: [1] Malagi, A. V. et al., doi:10.1007/s10334-019-00764-0; [2] Chabert, S et al., doi:10.2463/mrms.mp.2019-0061.

INVESTIGATION OF THE EFFECT OF MYGALIN IN MICE WITH HALOPERIDOL-INDUCED CATALEPSY

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Introduction: Catalepsy is understood as the inability to initiate voluntary movements [1]. It is characterized by having degrees of muscle stiffness and low flexibility, resulting in immobility [1]. The aim of the present study was to investigate the effect of mygalin injection on the duration of haloperiodol-induced catalepsy. **Materials and Methods:** Male Swiss mice were used. Catalepsy was induced by intraperitoneal administration of haloperiodol, an antipsychotic at a dose of 0.5 mg/kg diluted in saline, a volume of 1 ml/kg was injected [2], the animals in the control group received injection of the vehicle. To assess the effects of Migalin on catalepsy, mice received (0.48, n= 9; 0.048, n= 6; and 0.0048m, n= 6/Haloperidol group) or vehicle solution (n= 12; vehicle group /Haloperidol) Mygalin was administered intraperitoneally 10 minutes after haloperidol. Kalepsy was evaluated by means of the bar test [3] at the following moments after the administration of haloperiodol 15, 30, 60, 90 and 120 minutes. **Results:** We found that after the intraperitoneal injection of haloperiodol the animals showed catalepsy behavior in the following evaluation times 15, 30, 60 and 90 minutes ($p < 0,05$). A catalepsia foi realmente atenuada seguida de injeção de Migalin 0,48 mM ($p < 0,05$) aos 15, 30, 90 e 120 minutos; e Haloperidol/Migalina 0,048 mM, $p<0,05$ em 15 minutos comparado com Haloperidol/grupo veículo (Figure.1A-E). Although Migalin was not effective at a lower dose of 0.0048 mM ($p>0.05$). **Discussion/Conclusion**: In conclusion, the present study suggests that mygalin attenuates holoperidol-induced catalepsy.

References: [1] Waku I El al ., doi: 10.1111/ejn.15222; [2] Sanberg PR ., Nature 284 (5755): 472-473, 1980; [3] Abdel-Salam OM ., EXCLI journal 11: 45, 2012.

INVESTIGATION OF TRANSCRIPTOME ALTERATIONS (RNASEQ) IN NEURONAL POPULATION OF VENTRAL HIPPOCAMPUS IN SOCIAL DEFEAT STRESS SUSCEPTIBLE AND RESILIENT MICE

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Introduction: Depression is a very common and recurrent mental disorder nowadays, impairing the daily life and well-being of the individual. Induction of depressive behavior through social stress is already well established in the literature, highlighting the social defeat stress model (EDS), using social interaction to analyze depressive behavior. In this model, the social interaction test is used to analyze social avoidance, and not all mice that are submitted to this protocol develop a behavior of social avoidance, being called resilient. The ventral hippocampus is one of the most studied structures in depression, due to its neuroplasticity and relation with the limbic system. In addition, the ventral hippocampal cell layers show different functions when related to behavior. Ventral CA1 inactivation increases avoidance of conflict cue behavior, while CA3 inactivation increases approach behavior to conflict cue. Furthermore, neurogenesis confers resilience to chronic stress by inhibiting granular cells of ventral dentate gyrus. Litterature shows different results depending on the specific hippocampal cell layer, making their separation very important. **Materials and Methods:** In the present study it was applied the EDS protocol with modifications by Pagliusi and Sartori 2019. Briefly, 12 week old C57/BL6 mice were subjected to 10 minutes aggression sessions with 6 month old aggressor Swiss mice for 10 days. One day after the last aggression session, the

social interaction test was applied to separate depressive from resilient groups, analyzing the social avoidance behavior. One day after social interaction, mice were euthanized and the brains were collected, fresh-frozen in isopentane and stored at -80 biofreezer for downstream analysis. **Results:** With the modified EDS protocol and social interaction analysis of 30 male C57 mice, we could classify 7 animals as resilient with social interaction ratio (SIR = time in seconds spent at interaction zone without SWISS target – time spent at interaction zone with SWISS target) average 3.02 and 11 animals presenting social avoidance depressive like behavior with SIR = 1,03, besides the 10 animals belonging to the control group, where EDS protocol was not applied with SIR = 2.32. **Discussion/Conclusion**: The application of the optimized EDS protocol was successful, and we could observe and classify the mice as presenting either depressive-like behavior or resilient behavior. This is an ongoing study and the material collected from such animals will be submitted to transcriptome analysis of Laser Capture Microdissection (LCM) of CA1, CA3 and Dentate Gyrus of each group (control, depressive-like and resilient).

References: [1] Golden, Sam A., Herbert E. Covington, Olivier Berton, and Scott J. Russo. 2011. "A Standardize Protocol for Repeated Social Defeat Stress in Mice." *Nature Protocols* 6 (8): 1183–91. [2] Pagliusi, Marco Oreste F., Jr, and Cesar R. Sartori. 2019. "Social Defeat Stress (SDS) in Mice: Using Swiss Mice as Resident." *Bio-Protocol* 9 (6): e3197.

IS THERE A RELATIONSHIP BETWEEN COVID-19 VACCINATION AND GUILLAIN-BARRÉ SYNDROME?

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Introduction: In July 2021, the COVID-19 subcommittee of the WHO Global Advisory Committee had a virtual meeting to discuss rare reports of Guillain-Barré Syndrome (GBS) development after COVID-19 vaccination with vaccines from Janssen and AstraZeneca [1]. GBS is a is an inflammatory auto-immune polyneuropathy, mostly being secondary to a viral or bacterial infection, rare condition that affects the nerves compromising mainly the feet, hands, and limbs, causing symptoms such as numbness, weakness, and pain. Around 70% of the cases occur after a viral or bacterial infection leading to an immune response that affects peripheral nerves [3]. Thus, the purpose of this research was to identify a possible relationship between COVID-19 vaccines and GBS. **Materials and Methods:** We performed a PUBMED search between May and August 2021, using the following mesh terms and combinations: COVID-19 vaccines and Guillain-Barré syndrome, vaccines and Guillain-Barré Syndrome, SARS-COV-2 and Guillain-Barré syndrome. Inclusion criteria were: case studies, research articles, articles published between 2020 and 2021. Exclusion criteria were: incomplete manuscripts, reviews, manuscripts in languages other than English and Portuguese. **Results:** 46 manuscripts were found, 35 were excluded according to exclusion criteria and 11 articles were selected. **Discussion/Conclusion**: The most effective way to control contagious diseases is vaccination of a large percentage of the population to guarantee community immunity. In all studies used in this review, patients had some GBS symptoms after an interval of 10-14 days of vaccination with the Pfizer-Biontech or AstraZeneca vaccines. None of the patients have had COVID-19 before vaccination. Several case reports observed a possible causal association between COVID-19 and GBS [4], raising the hypothesis of a possible relation between COVID-19 vaccines and the development of GBS. Considering the mechanism of these vaccines and the fact that, to our knowledge, there is no relationship between GBS and vaccines using attenuated or inactive viruses or protein vaccines, one can hypothesize that the AstraZeneca and the Pfizer-Biontech vaccines might influence the development of GBS. However, it is extremely necessary to mention that those were rare events and the safety provided by the vaccines has more benefits than side effects. Also, based on the literature research performed here, it is not possible to conclude that GBS is caused by those vaccines. Regarding the COVID-19 vaccines, so far, none contain immunogenic material previously proven to cause GBS. The risk of autoimmune disorders such as GBS after vaccination has been investigated for years and based on previous findings it should not be considered a reason to stop vaccination programs as the relationship between vaccination and those diseases may be trivial and not causal.

Referências: [1] World Health Organization, 2021; [2] PORTARIA Nº 1.171, DE 19 DE NOVEMBRO DE 2015; [3] ANSARI, B. *et al*. doi: 10.4103/abr.abr_50_17. PMID: 29930927; [4] Montalvan, V., et al., doi: 10.1016/j.clineuro.2020.105921.

MAIN EMOTIONS PERCEIVED BY BRAZILIAN HEALTHCARE WORKERS DURING THE COVID-19 PANDEMIC: A CROSS-SECTIONAL STUDY

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Introduction: Declared as a global pandemic in March 2020, Coronavirus disease (Covid-19) presents high rates of infection and mortality, and also imposes a biopsychosocial burden to healthcare workers (HCWs) [1,2]. The scenario full of stressors has had severe impacts on the mental health of those on the frontline of health services. Studies show worsening psychological health of HCWs during the outbreak [3], with high prevalences of symptoms of depression and anxiety [4, 5, 6]. Thus, the aim of this study is to provide an overview of the main emotions perceived by brazilian HCWs during the fight against the Covid-19. **Materials and Methods:** We performed a cross-sectional study as the first step of a clinical trial (Rebec: RBR-5c8pz5r), approved by Ethics Committe of School of Medical Sciences (Unicamp). We applied a survey between November 2020 and June 2021, with the open question "What is the main emotion you feel/felt during the pandemic?" and performed a descriptive analysis. **Results:** The sample consisted of 80 brazilian HCWs, mostly women (93.25%), nurses (38.75%) and working on the front line (63.75%). A total of 23 emotions were cited; the most frequent was *fear* (23.8%), followed by *anxiety* (17.5%) and *sadness* (10%). We collected the replies at three different times during the pandemic: November 2020, April and June 2021, and the pattern of responses showed slight differences when comparing groups. For the first group (Nov. 2020, n = 35), *fear* was the most frequent response (30.6%), followed by *sadness* (11.1%) and *anxiety* (8.3%). The second (Apr. 2021, n=18), presented *fear* and *anxiety* as the most frequent emotions (each with 27.8%), followed by *insecurity* and *anguish* (each with 11.1%). The third group (Jun. 2021, n = 26) reported *anxiety* (23.1%), followed by *fear* and *sadness* (each with 11.5%). **Discussion/Conclusion**: This study presents an overview of the main emotions perceived by brazilian HCWs during three diferente times of the pandemic. A meta-review [7] about the wordwide overall mental health situation of this audience identified anxiety, depression and stress as the most prevalent mental health problems reported/assessed. In opposition to our findings, the emotion *fear* was not identified in the majority of the studies. Furthermore, it was possible to verify changings in the pattern of responses over time, what may be related to application of strategies for overcoming mental health difficulties – although there was also a increase in rates of anxiety. Therefore, continued emotional and psychological support, as recomended by World Psychiatric Association [8], is essencial to mitigate the long term impact of pandemic in mental health of HCWs.

References: [1] Shmerling RH. What's it like to be a healthcare worker in a pandemic?, 2020. [2] Fottrell Q. Nurses are wearing garbage bags as they battle coronavirus: 'It's like something out of the Twlight Zone, 2020. [3] Bettinsoli et al. Appl Psychol Health Well Being 12(4):1054-1073, 2020. [4] ALGhasab et al. Medicine 100:15, 2021. [5] Peng et al. Front Public Health 5;9:603273, 2021. [6] Pappa et al. Brain, Behavior, and Immunity 88:901–907, 2020. [7] Chutiyami et al. Front. Psychiatry, 12, 2022. [8] Stewart DE, Appelbaum PS. World Psychiatry 19:406, 2020.

MOTOR SKILLS DYSFUNCTION AND FATIGUE PERSIST AFTER MILD INFECTION BY SARS-COV 2

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Introduction: Although neuropsychiatric manifestations have been reported after COVID-19, little is known about fine motor difficulties, especially after mild infection. Here we evaluated fine motor impairment after COVID-19 (along with fatigue, depression, anxiety and somnolence), and compare to a control group. **Materials and Methods:** We Applied the 9-Hole peg test and the "Box and blocks" test to evaluate dexterity and fine motor skills and the Tower of Hanoi test (with 3 and 4 pieces) for executive function. Individuals also answered the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Chalder fatigue questionnaire (CFQ) and the Epworth sleepiness Scale (ESS). We used SPSS26 with Mann-Whitney U-test (to compare variables between groups) and partial correlations to correlate the continuous variables. **Results:** We evaluated 49 subjects recovered from mild infection by COVID-19 (median of 4 months after diagnosis) (37 women; median of

39 years, (range 16-64)) and 73 healthy controls (50 women; median 35 years (range 14-63) without COVID-19, balanced for sex (p=0.4) and age (p=0.1). The COVID.

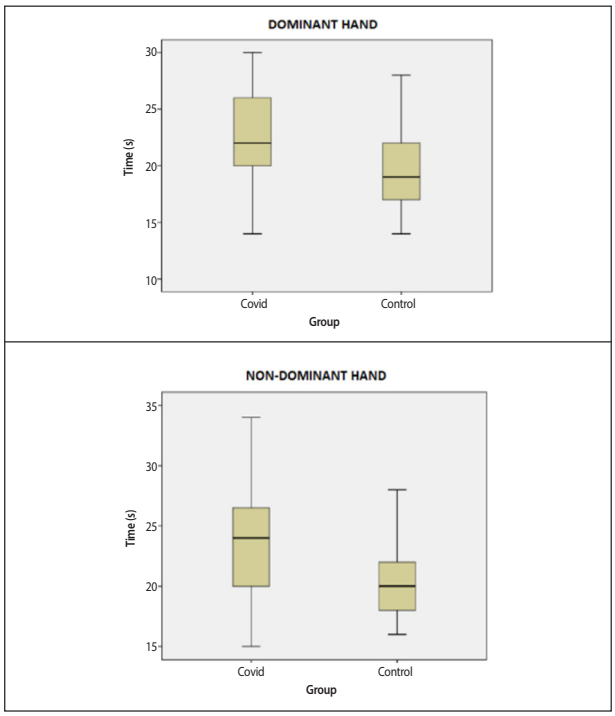

Figure 1. COVID group performs slower than controls on Nine Hole Peg Test.

MULTIOMICS ANALYSIS IN THE PLASMA OF PATIENTS IN CHRONIC PHASE OF ISCHEMIC STROKE: INSIGHTS INTO MOLECULAR MECHANISMS LEADING TO RECOVERY

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Introduction: Ischemic stroke (IS) is a complex and multifactorial disease affecting almost 1/3 of elderly patients. The acute stage of IS, when the tissue lesion occurs, is characterized by inflammatory and hypoxic conditions, whereas, in the chronic phase, there is neural repair and plasticity [1]. Recent studies of patients with IS in the acute phase have identified putative biomarkers of the acute lesion [2]; however, reports in the chronic stage of IS have been limited. Because the recovery mechanisms taking place in the chronic phase of IS may be relevant for determining the long term outcome and the risk of recurrence, we evaluated the expression of non-coding RNAs (ncRNAs) and metabolites in plasma samples of patients in the chronic phase of IS. **Materials and Methods:** We obtained plasma samples from 10 patients with chronic IS for exosomal small RNA sequencing and 20 patients for metabolomics analysis and compared them with samples from controls (n=10 for ncRNA and n=20 for metabolomics). Samples from patients were collected at least six months from the acute episode of a stroke at the Neurovascular Clinic of the University of Campinas (UNICAMP) hospital. Informed consent was obtained from all subjects ascertained, and the project was approved by the research ethics committee of UNICAMP. For ncRNAs, we initially purified exosomes using mirCure Exosome Serum/Plasma kit (Qiagen Inc), followed by a total RNA extraction using the miRNeasy Serum/Plasma Advanced Kit (Qiagen, Inc). The small RNA library and sequencing were performed using Qiaseq miRNA Seq kit (Qiagen, Inc) and NextSeq 500 equipment through 75 single end cycles (Illumina, Inc). Sequencing data were analyzed by DESEq 2 software.

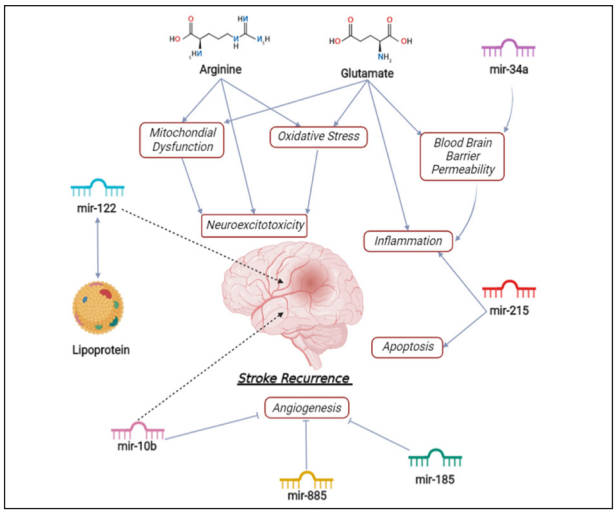

Figure 1. Mechanisms affected by the ncRNAs and metabolites found to be altered in patients with chronic IS. Created in Biorender.com.

We performed a proton nuclear magnetic resonance (H^1-NMR) from total plasma for the metabolomics analysis. Using CPMG spectra, we normalized and identified metabolite peaks. Data analysis and metabolite identification were performed using MetaboAnalyst software (https://www.metaboanalyst.ca/) and Human Metabolome Database (HMDB). Results from patients were compared to controls to identify differences in the two groups, patients x controls. **Results:** We identified 28 microRNAs, and 61 tRNAs fragments differentially expressed in patients. Among these there, we found the upregulation of mir-122, mir-34a, mir-185, mir-885, tRNA-Phe, and tRNA-Leu; and the downregulation of mir-215, mir-10b, tRNA-Gly, and tRNA-Val. These ncRNAs have been previously described as regulating angiogenic, inflammatory, and neurological damage processes. Furthermore, we found increased amounts of arginine, valine, and glutamate and decreased creatinine, lipoproteins, and glucose in patients. These molecules affect pathways related to amino acid and carbohydrate metabolisms, biosynthesis of tRNAs and regulation of gene expression, energetic metabolism, and excitotoxicity processes. **Discussion/Conclusion**: Based on the differential profile of ncRNAs and metabolites found, we identified abnormal mechanisms occurring in the chronic stage of IS, such as abnormal oxidative stress, excitotoxicity, and blood-brain barrier permeability [3, 4]. Also, we observed the abnormal expression of mir-10b and mir-122, which have been putatively linked to increased risk of recurrent stroke and the risk of secondary cardiovascular events [5, 6].

References: [1] Dobkin BH and Carmichael ST, doi:10.1177/1545968315604400; [2] Ekkert A et al, doi: 10.3390/genes13010048; [3] Wang X et al, doi: 10.3389/fneur.2019.01425; [4] Ren X et al, doi: 10.1016/j.neuint.2018.10.019; [5] Jiang H et al, doi: 10.1038/s41598-019-54542-y; [6] Badacz R et al, doi: 10.3390/biomedicines9081055.

MVDR AND CAR FILTERS COMBINED WITH SVM AND CNN CLASSIFIERS: PRELIMINARY STUDIES ON A BCI-SSVEP

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Introduction: A Brain-Computer Interface based on Steady-State Visually Evoked Potential (BCI-SSVEP) allows establishing direct communication between the brain and computer devices. Its working principle is formulated on the analysis of brain signals to identify the visual stimulus on which a volunteer is focused. We investigated the impact on the performance of a BCI-SSVEP by applying three filtering techniques – no filter, Common Average Reference (CAR) and the Minimum Variance Distortionless Response (MVDR) –, and two classifiers – Support Vector Machine (SVM) and Convolutional Neural Network (CNN). **Materials and Methods:** In this study, electroencephalography (EEG) signals from a public database [1] were employed. We considered EEG signals acquired by 16 electrodes [2] from Subject 34. Signals were sampled at 250 Hz comprising six repetitions for each frequency. The BCI-SSVEP was

projected to discriminate four visual stimuli flickering at frequencies: 8, 10, 12 and 15 Hz. The pre-processing involved the segmentation of the EEG signal in five windows of 1 s each and the filtering with one of three options: no filter, CAR and MVDR [2]. The MVDR was designed with order 5 and the signals from the 16 electrodes were combined two by two. For all cases of filtering, the magnitudes of the Fast Fourier Transform (FFT) at the evoked frequencies were extracted as features. To discriminate the four classes of stimuli, two classifiers were evaluated: SVM with linear kernel and CNN structured as shown in Fig. 1. The combination of techniques regarding filtering and classification steps resulted in six distinct scenarios of evaluation, as indicated in Tab. 1. **Results:** Table 1 presents the average performance and standard deviation of the BCI--SSVEP considering 10-cross-fold-validation for the six scenarios analyzed. **Discussion/Conclusion**: In all analyzed scenarios, the BCI-SSVEP achieved an adequate performance (higher than 85%) for the discrimination of the four visual stimuli. The best scenario involves the combination of the MVDR filtering, feature extraction via FFT and the CNN classifier, which reached a high average accuracy (almost 100%) and low standard deviation. More tests will be conducted with other volunteers to verify the scope of operation of the MVDR filter and further improve the BCI-SSVEP system. **Acknowledgments:** The authors thank FAPEMIG and UFOP for the financial support.

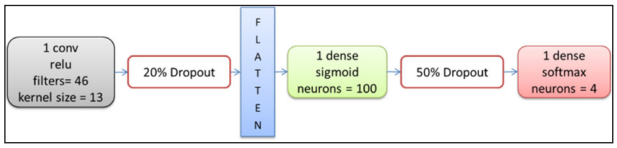

Figure 1. CNN topology.

Table 1. Average accuracy of BCI-SSVEP for the six scenarios.

	SVM	CNN
MVDR	94.69 ± 3.92	99.66 ± 0.99
CAR	92.62 ± 5.71	93.66 ± 1.79
No Filter	88.87 ± 5.32	90.99 ± 2.13

Reference: [1] WANG, Y. et al. A benchmark dataset for SSVEP-based brain–computer interfaces. IEEE Trans. on Neural Systems and Rehabilitation Eng., 2016. [2] VARGAS, G. V. et al. Analysis of the spatiotemporal MVDR filter applied to BCI-SSVEP and a filter bank extension. Biomedical Signal Processing and Control, 2022.

NEUROIMAGING ANALYSES OF THE HIPPOCAMPUS IN SYSTEMIC SCLEROSIS: A LONGITUDINAL VOLUMETRIC AND METABOLIC CHANGES STUDY

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Introduction: Systemic sclerosis (SSc) is a multisystem disease characterized by functional and structural abnormalities of small blood vessels, fibrosis of the skin, internal organs and central nervous system involvements [1]. The hippocampus is located in the medial temporal at both sides of the brainstem and its can be divided into subfields: cornu ammonis (CA)1; CA2/3; CA4/dentategyrus (DG); strata radiatum/lacunosum/moleculare (SR/SL/SM) and the subiculum [2]. MR-based techniques are widely used for analyzing metabolic and volumetric changes the hippocampus. Our objective is to investigate longitudinally volumetric and metabolic changes in SSc using magnetic resonance spectroscopic imaging (MRSI) and magnetic resonance imaging (MRI). **Materials and Methods:** We included 37 SSc patients (mean age of 50.86) and 37 healthy controls (mean age of 49.23). ^{1}H-MRSI was performed over the bilateral hippocampus (Fig. 1A) and signals from N-acetyl-containing compounds (NAA), choline (Cho) and creatine (Cr). An automatic volumetry of the hippocampus subfields volumes (Fig. 1B) was performed by the volBrain online software [3]. The selection of the spectra of interest were done using a MRSI toolbox developed in-house [4]. After 48 months, MRI and ^{1}H-MRSI acquisitions were repeated in 26 SSc patients and 26 healthy controls. **Results:** We found a significant reduction in NAA/Cr ratios in SSc patients when compared to controls (p = 0.035), associated with cognitive impairment, presence of migraine, use of prednisone and methotrexate. Follow-up study showed an increase in Cho/Cr ratios (p = 0.011), when compared to patient's baseline values. In addition, we observed a significant reduction in the hippocampus in SSc patients when compared to healthy controls (Table 1) associated with Raynaud's phenomenon, insomnia complaints and current use of losartan, diltiazem and bromopride. **Discussion/Conclusion**: In this study showed evidence of axonal dysfunction and hippocampal subfield atrophy in SSc patients associated with mild cognitive impairment, clinical, laboratory and treatment features. Therefore, the metabolites NAA, Cr and Cho and volumetry analysis may be are useful tools in studies of the hippocampus in systemic sclerosis.

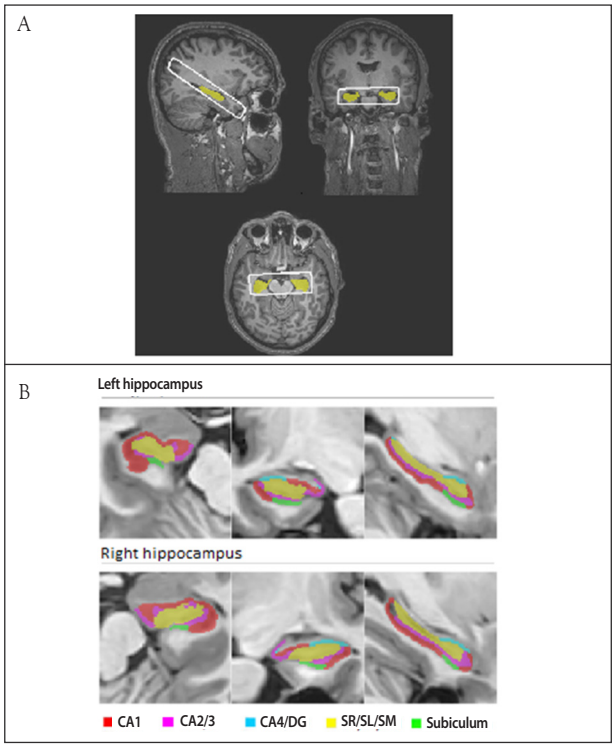

Figure 1. Hippocampal analysis using different MR-based techniques: (A) Magnetic resonance spectroscopic imaging (MRSI) and (B) Magnetic resonance imaging (MRI).

Table 1. Comparison of hippocampal subfields volumes among the SSc patients and healthy controls.

Volumes (cm^3)	37 SSc	37 HC	p value
Total hippocampi	4.78	5.01	0.033*
Total CA1	1.59	1.78	0.139
Total CA2/3	0.30	0.33	0.139
Total CA4/DG	1.23	1.30	0.001*
Total SR-SL-SM	0.94	1.01	0.071
Total Subiculum	0.53	0.59	0.071
	37 SSc (initial)	**26 SSc (follow-up)**	**p value**
Total hippocampi	4.78	4.50	0.027*
Total CA1	1.59	1.58	< 0.001*
Total CA2/3	0.31	0.30	0.256
Total CA4/DG	1.23	1.22	0.806
Total SR-SL-SM	0.94	0.89	0.131
Total Subiculum	0.53	0.51	0.014*

References: [1] Amaral, TN et al., doi:10.1016/j.semarthrit.2013.05.002 [2] Schultz, C et al., doi: 10.1159/000360925. [3] Manjón, JV et al., doi:10.3389/fninf.2016.00030. [4] Pereira, D et al., doi: 10.1117/12.2582186

NEUROSCIENCES: THE MOST PUBLISHED SUBJECTS OVER THE YEARS

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Introduction: This study aims to present the evolution of publications in recent years related to Neurosciences. Observing the approximate number of articles in

the literature is extremely important to elucidate trends within the field of Neurochemistry, Neurophysics, Neurobiology and Neuropsychology, as well as areas that deserve more attention, given the relatively small number of publications. **Materials and Methods:** The searches were divided into three main searches: Psychoactive Substances (Ayahuasca, Ecstasy, DMT, Cocaine, LSD, Opium and Heroin), Physiological diseases (Alzheimer's Disease, Parkinson's Disease, Epilepsy, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Ataxia, Guillain-Barré Syndrome, Bells's Palsy and Migraine) and Psychological Diseases (Anxiety, Depression, Bipolar Disorder, Schizophrenia, Personality Disorder, Anorexia, Bulimia, Insomnia and Narcolepsy). The searches were performed on PubMed. There are articles dating back to 1897 and the searches ended on January 25, 2022. The keywords used were the exact name of each subject of interest. The results were compiled, treated and organized year by year, in order to have the temporal evolution of each research area, with the respective subjects sought, as well as the total over time, that is, from the first article published within the researched subject. **Results:** We noticed that, among the three large research groups, psychological diseases had the highest percentage of articles over the years, with 57%. In second place, physiological diseases, with 39% and, finally, psychoactive substances, with 5%. The percentage presented here is based on the total number of publications searched in this search. Depression is the subject with the highest number of publications among all those surveyed (25.75%), followed by Anxiety (16.82%). Among the Physiological Diseases, the largest amount falls on Alzheimer's Disease (11.73%), followed by Parkinson's Disease (8.07%). In the field of Psychoactive Substances, Cocaine leads the search (2.59%), followed by Heroin (1.03%). **Discussion/Conclusion**: Finally, we see that Depression has shown itself as a leader in Neuroscience publications. Other fields, such as Psychoactive Substances, may need more research, especially Ayahuasca and DMT, which, according to the literature, presents itself as a strong ally in the fight against depression. Paying greater attention to this field can bring more answers to questions not so well answered by Neurosciences.

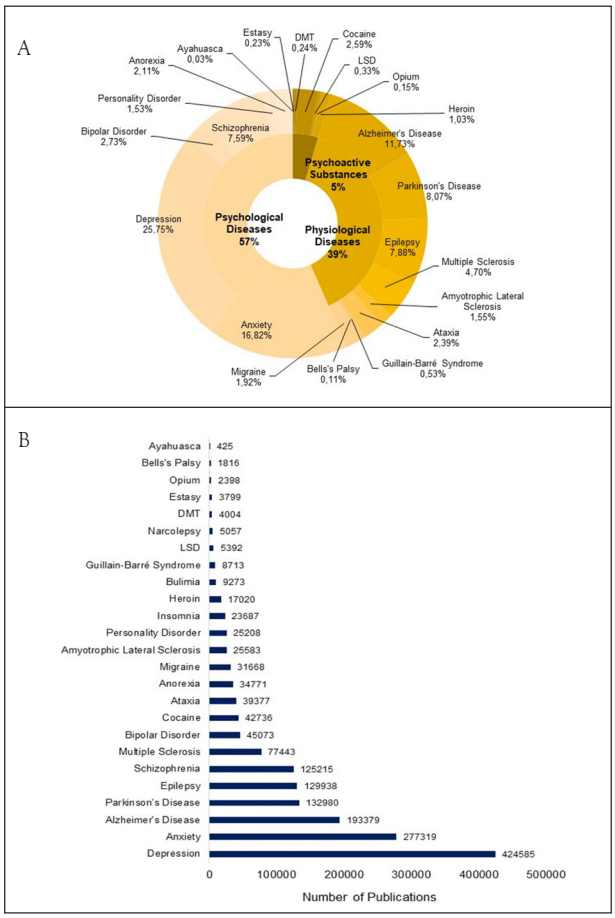

Figure 1. Percentage and absolute number of publications in Neurosciences. A - Percentage of the total number of publications. B Absolute numbers of publications over the years.

PERFORMANCE IN COGNITIVE FLEXIBILITY AND INHIBITORY CONTROL AND ITS ASSOCIATION WITH BEHAVIOR AND MENTAL HEALTH IN ADOLESCENT MOTHERS

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Introduction: Executive functions are cognitive processes that enable the regulation of cognition, emotion, and behavior. Among these processes are two important functions: cognitive flexibility and inhibitory control [1]. In adolescence, these capabilities are still underdeveloped because the neural networks in areas where these functions are predominant are not yet fully matured [2]. Studies show that these skills can predict health, prosperity, and crime in adolescence and adulthood [3]. The natural vulnerability of this period, when added to the experience of motherhood, can represent a challenge. One study showed lower performance in executive functions in adolescents mothers compared to adult women, which can negatively impact the interaction between the young mother and her children [4]. We aim to evaluate cognitive flexibility and inhibitory control in adolescent mothers and the association of these functions with behavioral and mental health. **Materials and Methods:** The following assessment instruments were used: for depressive symptoms, the PHQ-9; for cognitive flexibility and inhibitory control, five-digit test (FDT); for substance use, CRAFFT. A sociodemographic questionnaire was also applied, where one of the information collected was whether the pregnancy was planned. For comparative data analysis, young mothers were divided into two subgroups: comparing mothers who performed >-2SD and ≤-2SD in cognitive flexibility and inhibitory control. Young mothers with performance ≤-2SD were considered to have severe impairments. We used the chi-square test to compare the association between the data and the Student's t-test to compare two groups with continuous variables. **Results:** We evaluated 28 adolescent mothers aged between 14 and 19 years (17.2±1.3); 18 did not plan pregnancy (72%), and 16 (74%) referred to use psychoactive substances. The mean depressive symptoms score was 9.2 (±6.6) suggesting mild depression. Ten (35%) adolescent mothers performed ≤-2SD in cognitive flexibility, 90% of them also had severe impairment in inhibitory control (χ^2 test, p=0.002), and 100% did not plan their pregnancy (χ^2 test, p=0.019). There was no association between cognitive flexibility impairment and depressive symptoms or substance use. Fourteen (50%) adolescent mothers performed ≤-2SD in inhibitory control. There was no association between inhibitory control impairment and planning the pregnancy or substance use. The mean score for depressive symptoms in adolescent mothers with severe inhibitory control impairment was 6.6 ± 4.5, while in the adolescent mothers with inhibitory control >-2 SD was 11.7 ± 4.5, (Student's t-test p=0.055), suggesting that adolescent mothers with better inhibitory control may be more susceptible to depression, but the sample is not powerful enough to confirm it. **Discussion/Conclusion**: Executive functions impairment was associated with outcomes of adolescent mothers, and their ability to choose in their lives. The findings of this study can help understand the processes involved in the decision-making of adolescent mothers and provide insight into better interventions for them.

References: [1] Dias N.M., et. al., TSN 19 (107). 206-12., 2013; [2] Casey, B. J., el al., doi: 10.1016/j.dr.2007.08.003; [3] Moffitt, T. E., el. al., doi: 10.1073/pnas.1010076108; [4] Gonzales, C. E., et al., doi: 10.1002/dev.21185.

POST STROKE CROSSED CEREBELLAR ATROPHY: A VOXEL BASED MORPHOMETRY STUDY

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Introduction: Crossed cerebellar diaschisis is already a well described process that consist in the hypometabolism and reduced functional activity of neurons in the cerebellum after ischemic insult to a contralateral supratentorial region. In addition, if this process persists over time, it may result in apoptosis of those neurons, chronically leading to crossed cerebellar atrophy. This study aimed to verify the presence of crossed cerebellar atrophy through a Voxel Based Morphometry analysis in post ischemic stroke patients and correlate the findings with each patients' collected

data. **Materials and Methods:** The patients' *magnetic resonance imaging* exams were selected systematically in the database of the neuroimaging laboratory, at the UNICAMP clinic hospital, and two exams were selected for each one of them. The first image had to be from the week in which the supratentorial stroke happened and the second from a time interval within 1 to 12 months after the event. The images were processed, allowing a second level statistical analysis, which was executed using the SPM12 software running on Matlab 2017b. Furthermore, the data collected from the medical charts consisted on the patients' age, sex, preexisting comorbidities, symptoms and National Institute of Health Stroke Scale (NIHSS) upon arrival at the hospital. **Results:** From an initial total of 1938 patients analyzed, 21 were suitable for the study. The presence of crossed cerebellar atrophy was confirmed in 14 (66,66%) of them, showing that this condition may be more present them it was thought to be. A positive correlation between the patients' age and severity of atrophy was found, suggesting that the older patients might be more susceptible to neuronal apoptosis, resulting in crossed cerebellar atrophy. Moreover, the number of preexisting comorbidities per patient also had a positive correlation with the severity of atrophy. Despite age and preexisting comorbidities have proven to be relevant variables to determine a higher or a lower atrophy level on the cerebellum, other factors like symptoms and NIHSS upon arrival didn't seem to have any correlation with the atrophy observed. **Discussion/Conclusion**: Crossed cerebellar atrophy is present in a significant percentage of post ischemic stroke patients and it seems to behave differently in varying age groups. However, its mechanisms are still not clear, so more studies are essential for better understanding of this condition and how it affects different patients. Figure A and B:

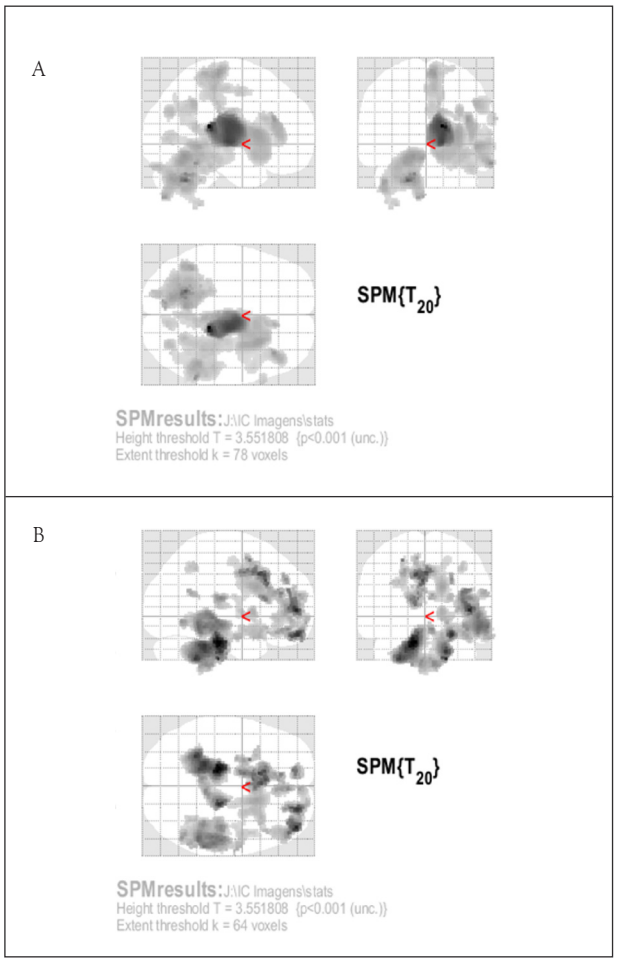

Figure 1. A - shows volumetric loss of gray matter, by the different shades of gray in the white anatomical representation of the brain, that occurred in the months between the ischemic event and the second MRI exam; B - shows volumetric loss of white matter. The loss of cerebellar gray and white matter is noticeable on the opposite side of the stroke.

PREDICTION OF SEIZURE FREEDOM FOLLOWING EPILEPSY SURGERY IN CHILDREN

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Introduction: Epilepsy surgery is the best treatment option for individuals with pharmacoresistant structural epilepsies. There is an attempt to establish nomograms to assess the postoperative prognosis for patients and assist in the decision for the procedure [1-5]. **Materials and Methods:** In this work, an existing nomogram was applied to a cohort of children undergoing epilepsy surgery. Data collection was carried out by reviewing the medical records of children and adolescents with pharmacoresistant epilepsy submitted to surgery in a tertiary hospital between 1998 and 2019. We excluded individuals undergoing hemispherectomy/hemispherotomy, resection including more than one lobe, with follow-up less than 2 years and incomplete data in the records. The possible outcome was calculated from the nomogram developed by Jehi et al. [6], considering the following data: duration of epilepsy, frequency of seizures, gender, presence of generalized tonic-clonic seizures, etiology, type of surgery, findings on brain MRI and EEG (location of seizures and interictal epileptic discharges). We considered Engel type I (free of disabling seizures after surgery) as the desired outcome. The analysis of agreement was calculated with Harrell's c-index. The SPSS 24.0 program was used for the statistical analysis. **Results:** We obtained data from 59 patients with 2-year follow-up and 39 patients with 5 years follow up. Of the total of patients, 35 were female and 24 were male. The mean age at surgery was 11 years, with median time from the first seizure to the surgery of 8 years. Fifty-four (91.5%) patients had tonic-clonic seizures. At 2 years after the surgical procedure, 45 (76.2%) were free of disabling seizures and at 5 years, 27 (69.2%). The mean prediction of Engel I at 2 or 5 years follow up was respectively 69% and 62% for those free of seizures and 56% and 53% for those who remained with disabling seizures. The c-index at age 2 was 0,54 and at age 5 it was 0,52. **Discussion/Conclusion**: in conclusion, this nomogram may not be appropriate for use in children. A larger number of patients and a detailed analysis of possible differences between surgeries for children and adults are required.

References: [1] Kwan P, Arzimanoglou A, Berg AT, et al., Epilepsia (51):1069-1077, 2010; [2] Brodie MJ et al., Neurology (78):1548-1554, 2012; [3] Kwan P, Brodie MJ. N Engl J Med., (342): 314-319, 2000; [4] Berg AT, Shinnar S, Levy SR, et al., Neurology. (56):1445-1452, 2001; [5] Meador KJ et al., J Epilepsy. (2): 21-25, 1989; [6] Lara Jehi et al., doi: 10.1016/S1474-4422(14)70325-4.

PRELIMINARY INVESTIGATION OF CONVOLUTIONAL NEURAL NETWORKS FOR BCI-SSVEP

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Introduction: The Steady-State Visually Evoked Potentials (SSVEP) is a popular paradigm used to conceive Brain-Computer Interfaces (BCI). In the non-invasive approach, the brain signal can be acquired by electroencephalography (EEG). Applications of a BCI-SSVEP range from assistive technology to entertainment, such as moving a wheelchair or augmented reality. In this study, we have analyzed and compared the performance of a BCI-SSVEP employing as classifier two scenarios of a Convolutional Neural Network (CNN): (1) employing features extracted from EEG signals and (2) using the raw EEG signals. **Materials and Methods:** The database employed [1] consisting of EEG signals of one healthy subject. During the EEG data acquisition, the subject was exposed to four visual stimuli frequencies (6, 10, 12 and 15 Hz), with 8 repetitions of 12 s for each frequency. The preprocessing consisted of the application of a notch filter at 60 Hz, a passband filter (5 – 100Hz), the segmentation of signal in 3 s window and the filtering with a digital filter based on Common Average Reference. In the first classification scenario, the CNN was fed with the magnitudes of Fast Fourier Transform (FFT) extracted in evoked frequencies. In the second scenario, the CNN was fed with the raw data. **Results:** Fig.1 shows the structure of CNNs in both scenarios evaluated. Table 1 shows the average accuracy of BCI-SSVEP for both scenarios evaluated, considering 10-cross-fold-validation and convolution with the Kernel at 1D. In Scenario 1 the average accuracy was 87,5±9,3 % and in Scenario 2 was 70,25±12,2%. **Discussion/Conclusion**: Our preliminary results showed that models of both

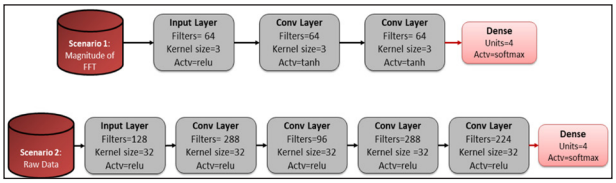

Figure 1. CNN topologies in Scenarios 1 and 2.

Table 1. Average performance and standard deviation of BCI-SSVEP in the two scenarios.

Frequency (Hz)/ Average accuracy (%)	6	10	12	15	Total
Scenario 1	81.4	98.6	75.7	94.3	87.5±9.3
Scenario 2	84.3	61.7	80.0	55.0	70.3±12.2

scenarios can discriminate the four visual stimuli with satisfactory accuracy (higher than 70%). However, the CNN of Scenario 1 seems to be able to get slightly better accuracy than the CNN of Scenario 2. The strategy of including feature extraction, in our case via FFT, looks attractive in some applications and should be further investigated by expanding the analysis to other subjects of the database. **Acknowledgments:** The authors thank FAPESP and UFOP for the financial support.

Reference: [1] LEITE, H. M. A., et al. Analysis of user interaction with a brain-computer interface based on steady-state visually evoked potentials: case study of a game. Computational intelligence and neuroscience, v. 2018, 2018.

REDUCED WORKABILITY ASSOCIATED WITH INCREASED LEVELS OF FATIGUE AND ANXIETY IN PATIENTS WITH POST-COVID SYNDROME

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Introduction: Although symptoms of fatigue, depression, sleepiness and anxiety are part of Post COVID syndrome, little is known about the negative impact on work capacity. Here we quantified these symptoms with validated questionnaires and analyzed the relationship with reduced work capacity. **Materials and Methods:** We analyzed 626 individuals bank workers diagnosed with confirmed COVID19 (hospitalized (17%) and non-hospitalized (83%)). information was extracted from the Neurocovid-UNICAMP study database. Patients answered the "Chalder Fatigue Scale (CFQ)", "Epworth Sleepiness Scale (ESS)", "Hospital Anxiety and Depression scale (HADS)" and "Work Ability Index (WAI)". We used SPSS22 for statistical analysis with Chi-Square tests for analyses of proportions. **Results:** Our patients presented average age 42 years (22 to 66 years old), sex (53.5% female), education (48,9% complete undergraduate, 35,6% graduate and 8,1% complete high school), vaccination (83.4%) and function at work (74,6% contact with the public and 25% administrative work). With an average interval of 200 days between diagnosis and interview, subjects SELF-reported several symptoms, including related fatigue (37%), anxiety (36%), depression (17%) and cognitive dysfunction (29%). Approximately 20% reported no post-COVID symptoms at interview. The quantification of symptoms with questionnaires revealed excessive somnolence (45,1%), fatigue (79,2%), symptoms of anxiety (60,6%) and symptoms of depression (65,9%). We also identified reduced capacity of work in 62,5%. Furthermore, the relationship between reduced work capacity with somnolence, fatigue, symptoms of depression and anxiety is illustrated in Figure1.

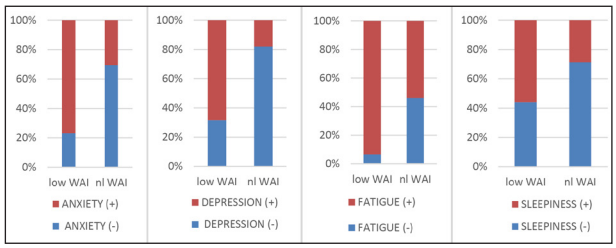

Figure 1. Relationship between neuropsychiatric symptoms and work capacity.
WAY: "Work ability index"; nl: normal; (+): presence of the specific symptom; (-): absence of specific symptom

Discussion/Conclusion: Our results reveal a negative impact of neuropsychiatric symptoms on reduced work ability months after the acute infection. These findings point to the urgent need to provide specific treatment for patients to minimize the individual burden and the economic loss.

REPRODUCIBILITY OF FUNCTIONAL CONNECTIVITY MEASURES IN THE CONTEXT OF MOTOR-IMAGERY BCIS: A PILOT STUDY

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Introduction: Brain-computer interfaces (BCIs) aim at translating brain signals directly into commands to control an external device. In general, BCIs consist of the following stages: signal acquisition, signal preprocessing, feature extraction and selection, classification, and, in some cases, feedback to the user. Several paradigms have been used to elicit brain signals for BCIs, which are supposedly easy to recognize/classify; among those, motor imagery (MI) produces signals that are very similar to those produced by overt movement. Thus, MI-BCIs have been explored as motor rehabilitation tools for several conditions. However, intra and inter-subject variability of brain responses has precluded BCIs to be routinely adopted in clinical environments. The aim of this work was to compare the reproducibility of different MI-BCI features obtained from functional connectivity (FC) applied to the alpha and beta bands of the EEG signals using two different methods. **Materials and Methods:** EEG signals were acquired with a 16-electrode equipment from one healthy subject (age 18, male) during 12 MI-BCI sessions performed in different days. Each session consisted of 5 runs divided into 16 blocks, alternating between rest and task. The MI task was closing and opening the left or right hand. Each task block lasted 6 s. FC was computed for 1 s epochs of the task blocks, for the alpha (8-12 Hz) and beta (13-31 Hz) bands, using coherence and motifs synchronization [1]. For each FC the following graph parameters were obtained: strength, clustering coefficient (CC), eigenvector centrality (EC), betweenness centrality (BC) and global efficiency (GE). Mean, standard deviation (STD) and coefficient of variation (COV = mean/STD) were computed for all parameters. **Results:** Table 1 shows mean, STD and COV for all parameters computed. **Discussion/Conclusion**: In general, the beta band produced smaller STDs than the alpha band, pointing to better feature reproducibility in this band. Furthermore, the lowest STD value was found for EC with the motifs method, and the lowest COV value was found for BC, also with motifs, but in the alpha band. Nevertheless, looking individually at the BC distributions there were several zero values, which happens when the network is (almost) fully connected or its links have similar values. Thus, it appears that this is possibly not a good reproducibility metric These results must be interpreted with caution, since this is a pilot study, which will be extended to more subjects as well as more connectivity methods and more robust reproducibility criteria. **Acknowledgements**: We thank FAPESP for financial support (grants 2013/07759-3 and 2021/06397-6).

Table 1. Mean, STD and COV for all parameters. Underline indicates smallest STD and COV values.

	Mean				STD				COV			
	Alpha (8-12 Hz)		Beta (13 -31 Hz)		Alpha (8-12 Hz)		Beta (13 -31 Hz)		Alpha (8-12 Hz)		Beta (13 -31 Hz)	
	Motifs	Coherence	Motifs	Coherence	Motifs	Coherence	Motifs	Coherence	Motifs	Coherence	Motifs	Coherence
Strength	12,16	7,81	7,67	7,23	1,69	1,70	0,83	1,34	7,20	4,59	9,24	5,40
CC	0,80	0,49	0,48	0,46	0,09	0,11	0,06	0,08	8,89	4,45	8,00	5,75
EC	0,25	0,25	0,25	0,25	0,04	0,04	0,02	0,03	6,25	6,25	12,50	8,33
BC	8,87	7,55	2,29	2,04	37,61	16,14	5,37	7,40	0,24	0,47	0,43	0,28
GE	0,74	0,47	0,45	0,42	0,04	0,08	0,04	0,07	18,50	5,88	11,25	6,00

References: [1] Rosário et al., doi: 10.1016/j.physa.2015.07.018.

SEARCHING FOR BIOMARKERS OF DRUG RESISTANCE IN MESIAL TEMPORAL LOBE EPILEPSY USING ^{1}H-NMR SPECTROSCOPY

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Introduction: A major challenge in the clinical management of patients with mesial temporal lobe epilepsy (MTLE) is identifying those who do not respond to antiseizure medication (ASM), allowing the timely pursuit of alternative treatments, such as epilepsy surgery. Here, we investigate changes in plasma metabolites as biomarkers of pharmacoresistance in patients with MTLE. Furthermore, we used the metabolomics data generated to gain additional insights into the mechanisms underlying MTLE and response to ASM. **Materials and Methods:** We used an untargeted metabolomic approach through Proton Magnetic Resonance Spectroscopy (^{1}H-NMR) and multi- and univariate statistical analysis to compare data obtained from plasma samples of 28 patients with MTLE compared to 28 controls. The patients were further divided according to response to ASM response: 19 patients were refractory to treatment, and nine were responsive to ASM. We only included patients using Carbamazepine in combination with Clobazam. **Results:** We compared the group of patients with controls and found that the profiles of glucose ($p=0.037$ and 0.036), saturated lipids ($p=0.001$), isoleucine ($p=0.011$), β-hydroxybutyrate ($p=0.01$), and proline ($p=0.01$) were different in patients compared to controls ($p<0.05$). In addition, proline ($p=0.037$), unsaturated lipids ($p=0.054$), isoleucine ($p=0.048$), and valine ($p=0.033$); could discriminate the two groups of patients. **Discussion/Conclusion**: The identified metabolites were linked to different biological pathways mainly related to the cell energy metabolism. Furthermore, pathways related to inflammatory processes and modulation of neurotransmitter release and activity were also found as potential contributors to the mechanisms underlying MTLE. In conclusion, our results show suggestive evidence that plasma metabolites may be used as biomarkers for response to ASM in patients with MTLE.

SLEEP/WAKE CYCLE DISRUPTS INTRA-NETWORK FUNCTIONAL CONNECTIVITY

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Introduction: The combined acquisition of electroencephalography (EEG) and functional magnetic resonance images (fMRI) provide visualization of a range of metabolic changes in the brain with high temporal and spatial resolution [1]. Functional connectivity (FC) analysis is a technique used to locate brain regions whose activity vary in synchrony across time. FC can measure small disturbances in brain function, enabling the investigation of neural networks associated to distinct functional aspects [2]. In this study, we evaluated FC differences on fMRI data acquired during sleep and wake conditions, assessing their impact on resting state network connectivity. **Materials and Methods:** We included 36-44 minutes EEG-fMRI dataset of 127 epilepsy patients acquired with a 3T scanner (Philips) and pre-processed using UF^{2}C toolbox (www.lniunicamp.com/uf2c). We developed an algorithm to separate volunteer's fMRIs into two new images: concatenated moments of wake or sleep conditions defined by an EEG-based consciousness classification algorithm [3]. The final concatenated images should have six minutes of each condition, trimming longer durations and excluding shorter ones. We included 55 patients that met the criteria and processed the ROI-to-ROI FC using 30 ROIs derived from the DMN, Basal Ganglia and Dorsal Attention networks using UF^{2}C. The correlation matrices were created using Pearson's coefficient (pair-wisely) and converted to Z-score using Fisher's Z-transformation. Lastly, we performed a paired t-test ($p<0.01$) to compare the sleep and wake stage matrices. **Results:** Five ROIs presented decreased connectivity during sleep stages: between the left inf. temporal gyrus (r4DorAtte) and the right post. precuneus (r6DMN), and among the right hippocampus (r9DMN) with right sup. frontal gyrus (r1DMN), right post. cingulate gyrus (r4DMN), left post. precuneus (r1DMN) and the right post. precuneus (r5DMN). As seen in Figure 1, the hippocampus is involved in four out of the five connections that presented decreased connectivity. **Discussion/Conclusion**: The sleep/wake conditions dynamically change the brain activity [4]. During awake rest, the hippocampus is a DMN hub performing a memory retrieval role [4]. However, during sleep stages, the evidence suggests that the hippocampus performs the very specific task of memory consolidation. Our findings corroborate the hypothesis that the hippocampus can suddenly switch its behavior during the wake/sleep cycle, also indicating that subtle consciousness oscillation or consciousness stages can bias and confound resting state FC by disrupting the intrinsic intra-network synchrony [5].

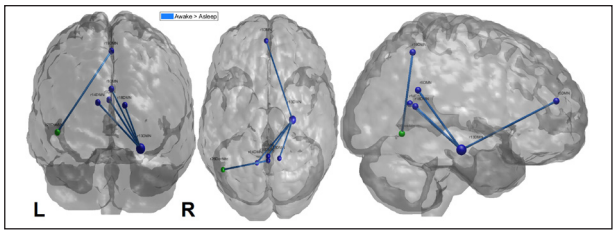

Figure 1. Decreased connectivity on asleep condition compared to awake condition.

References: [1] Coan AC *et al.*, DOI: 10.1111/epi.12670; [2] Kaiming L *et al.*, DOI: 10.1016/j.compmedimag.2008.10.011; [3] Gouvêa G *et al.*, Abstract #2 in this event; [4] Huijbers W *et al.*, DOI:10.1371/journal.pone.0017463; [5] Koyanagi I *et al.*, DOI: 10.4103/1673-5374.243695

STATIC VS. DYNAMIC FUNCTIONAL CONNECTIVITY FOR EEG-BASED MOTOR IMAGERY BCIS

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Introduction: Graph theory has been extensively employed in neuroscience to characterize brain functioning, pathologies and cognitive processes [1]. More specifically, the use of graph-based techniques for functional connectivity (FC) analysis has been very promising for feature extraction in motor imagery brain-computer interfaces (MI-BCIs) - a system that maps brain signals directly to control external assistive devices [2]. However, the dynamics of the MI process is usually disregarded during the FC analysis, which is an essential requirement for online BCI operation. Hence, this study proposes to evaluate the applicability of dynamic FC (dFC) to differentiate right-hand *vs.* left hand motor imagery in electroencephalography (EEG)-based BCIs. **Materials and Methods:** Cho et al.'s dataset [3] was used in this analysis, which contains EEG data of 52 subjects for 2 different MI tasks (right/left-hand) and 64 electrodes. We evaluated the classification performance of static FC (i.e., evaluated under the whole available trial interval) and the dFC using three similarity measures: 1) Pearson correlation; 2) Phase-lag index (PLI); 3) and a strategy based on the distance of electrodes' ERD - $Dist_{ERD}$. Four graph-based metrics were computed to characterize the network topology of 35 subjects, selected based on the strength of the mu-band desynchronization. As a comparison, we calculated the classical event-related desynchronization (ERD) in both static and dynamic scenarios. The EEG signals were bandpass filtered (8 - 16 Hz), followed by application of a Laplacian spatial filter. The dFC matrices were estimated with a 0.5 s window, with steps of 0.2 s. We used an 80/20 % split of trials to choose the best number of electrodes. Wrappers feature selection with LDA in a 10-fold cross-validation scheme was repeated 5 times. **Results:** Table 1 shows the performance of the graph-based metrics under the aforementioned FC pipeline. Based on the training set, the number of features used for classification was eight. Classification performance of the static and dynamic ERD was 0.65 ± 0.13 and 0.74 ± 0.09, respectively. **Discussion/Conclusion**: According to the training set, the number of features required for a relatively good classification (approximately 70%) was eight. A comparative analysis of static and dynamic FC showed that smaller windows not necessarily decreased the classification performance, while the outcome depends on the specific information underlying the connectivity measure.

Table 1. Mean accuracy of the three FC measures analyzed for the clustering coefficient (CC), eigenvector centrality (EC), closeness centrality (CL) and strength (S) when using eight best attributes chosen in the training set. Mean ± standard deviation in two scenarios: static FC and dFC.

	Static functional connectivity				Dynamic functional connectivity			
	CC	EC	CL	S	CC	EC	CL	S
$Dist_{ERD}$	0.60±0.13	0.62±0.13	0.60±0.12	0.62±0.11	0.73±0.10	0.73±0.09	0.72±0.10	0.71±0.09
Pearson	0.74±0.14	0.73±0.14	0.77±0.13	0.77±0.14	0.73±0.11	0.73±0.11	0.75±0.09	0.74±0.11
PLI	0.54±0.12	0.56±0.10	0.54±0.12	0.55±0.10	0.69±0.07	0.70±0.09	0.69±0.07	0.68±0.07

Moreover, dFC analyses revealed that the best performance was achieved approximately 0.6 to 1 s after the MI cue, which can be related to the time required for mu-band desynchronization stabilization. Although additional analyses would be required to further characterize the applicability of the dFC for BCI classification, the obtained results endorse the use of dFC for online MI-BCIs.

References: [1] Rubinov et al, doi:10.1016/j.neuroimage.2009.10.003; [2] Hamedi et al., doi:10.1162/NECO_a_00838; [3] Cho et al., doi:10.1093/gigascience/gix034.

SUPERVISED LEARNING TO IDENTIFY ELECTROPHYSIOLOGICAL BIOMARKERS TO CLASSIFY MOVEMENT STATE FROM SUBTHALAMIC LOCAL FIELD POTENTIALS IN PARKINSON'S DISEASE

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Introduction: Parkinson's disease (PD) is the second most prevalent progressive neurodegenerative movement disorder [1] which impact on motor execution and patient's quality of life. Altered electrophysiological composition from subthalamic nucleus local field potential (STN-LFP) is frequently observed in PD. In particular, decreased beta (13-35 Hz) and increased gamma (35-200 Hz) are associated to movement execution. However, accurate prediction of movement regarding the spectral composition STN-LFP is still a challenge and a matter of debate for designing new strategies for deep brain stimulation (DBS), i.e. an essential therapy in PD. This work aims to compare the performance of the supervised-based classifiers in order to detect movement state across the STN-LFP sub-bands. **Materials and Methods:** Data were collected from 23 patients during intraoperative process before DBS electrodes implanting. Fourteen patients received bilateral stimulation and 9 unilateral. The STN-LFP signals were acquired as 1 mm below the target (STN) and sampled at 24 kHz, bandpass filtered ([5 Hz - 15 kHz]) and recorded for 60 seconds in rest state, and, after a pause, for 60 s under active flexion of the elbow. The 74 STN-LFP recordings (37 rest *vs.* 37 movement) were exported and processed in Python to be downsampled at 1 kHz, notch filtered at 60 Hz, bandpass filtered (2–200 Hz) and z-scored normalized. Bandpower of LFP sub-bands - low beta (13–22 Hz), high beta (22–35 Hz), beta (13-35 Hz) and gamma (35–200 Hz) – were evaluated through the area under the power spectral density curve obtained by Welch periodogram. Four classifiers were used: Linear Discriminant Analysis (LDA), Naïve Bayes (NB), k-Nearest Neighbors (kNN) and Support Vector Machine (SVM) and two training techniques named k-fold cross validation (k=10) and leave-one-out (loo) were implemented. In this study, the initial 10 seconds of STN-LFP signal were used for classification. The performance is presented in terms of accuracy and presented as mean ± standard deviation (SD). **Results:** In table 1, the accuracies are show for low-, high-, entire beta and gamma band. For low beta, the best classifier is the k-NN (k=1) considering the partition loo, achieving an accuracy of 0,622. **Discussion/Conclusion**: In this study, the low beta sub-band was the best to predict the movement regarding the k-NN (k=1) classifier implementation, although the relative low performances (accuracy lower than 0,700) were obtained which in turn suggest further investigations to implement new techniques to better prediction of the movement from STN-LFP signals. Overall, these finding indicate a potential path in the search of the adaptive DBS improvement.

Table 1. mean accuracies (ad.) and standard deviation (except for loo partition) for the low, high and entire beta sub-bands of LFP. Moreover, the performances for gamma, a prokinetic sub-band are also depicted.

Sub-band	Low Beta (13 - 22 Hz)		High Beta (22 - 35 Hz)		Beta (13 - 35 Hz)		Gamma (35 - 100 Hz)	
Trainning	k-fold	loo	k-fold	loo	k-fold	loo	k-fold	loo
LDA	0,583 ± 0,005	0,608	0,388 ± 0,007	0,000	0,595 ± 0,005	0,608	0,479 ± 0,006	0,486
NB	0,591 ± 0,003	0,595	0,405 ± 0,006	0,297	0,545 ± 0,006	0,595	0,522 ± 0,006	0,581
k-NN (k=5)	0,498 ± 0,006	0,446	0,423 ± 0,006	0,405	0,540 ± 0,005	0,581	0,523 ± 0,006	0,595
k-NN (k=1)	0,606 ± 0,005	0,622	0,418 ± 0,006	0,392	0,464 ± 0,005	0,446	0,571 ± 0,005	0,581
SVM	0,487 ± 0,008	0,581	0,451 ± 0,009	0,405	0,513 ± 0,007	0,500	0,486 ± 0,007	0,419

References: [1] Vitek et al., doi: 10.1073/pnas.1902300116.

THE BLIND CHILD'S DRAWING IN THE PROCESS OF APPROPRIATION OF THE WRITTEN LANGUAGE

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Introduction: The present study is a clipping of the doctorate thesis presented in 2021, regarding the drawing aspect. The subject of the research is a blind child who started braille literacy instruction at the age of six in a municipal school, in the interior of São Paulo. The child was assisted in the school resources room by a professional specialized in the treatment of people with disability. Parallel with the teaching from the regular school, the child attended a specialized institution and was referred to the pedagogical sector in the same year when literacy instruction began and was assisted by a pedagogue specialized in visual impairment, in the teaching of braille and in computer resources. The study was founded on Vigotski's historical-cultural perspective. Inspired by [1], to assist one child alone makes it possible to describe, understand, and interpret very particular evidences, but that may also help understand the process other children have gone or will go through regarding writing. **Materials and Methods:** [1] proposes the search for evidences: the existence of the child's cultural constitution process, thus revealing how it occurs. The theoretical assumption was based on [3] who, by analyzing the writing of young children, have proposed the drawings as indicative of pre-writing. For data analysis purposes, the child's texts were sorted out into two units: drawings and letters/texts. For the unit "drawing", the choice and data discussion, were grounded in [2] statement that says; "the drawing is a graphic language that emerges based on the verbal language" (p.136). **Results:** It was observed that the blind child developed drawings in the same way that the sighted ones do. However, it was noticed that the blind one was not given many opportunities for drawing. This was an important issue because the drawing works as a pre-writing for the blind and without it the learning may become more difficult. Adults cannot enter the fantasy world of the child since they are too much centered on reality. Being a blind child does not mean not being able to draw. On the contrary, the drawing activities developed and presented in this study can confirm that. **Discussion/Conclusion**: For the activities developed, drawings using sand paper were taught and worked on. The texts in which the child drew images which could be associated with a "pre-writing function" were chosen for the drawings data discussion. Such images help understand the process of writing acquisition. Drawing must be presented to the blind child in the early childhood education. It has been concluded that drawing is crucial for all children, without exception, in the process of appropriation of the written language.

References: [1] PINO, A. As marcas do humano: às origens da constituição cultural da criança na perspectiva de L. S. Vigotski. – São Paulo: Cortez, 2005. [2] VIGOTSKI, L. S. A formação social da mente. 7ª edição – São Paulo: Martins Fontes, 2007. [3] VIGOTSKII, Lev Semenovich; LURIA, Alexander Romanovich; LEONTIEV, Alexis N. Linguagem, desenvolvimento e aprendizagem. Tradução de Maria da Penha Villalobos. 2. ed. São Paulo: Ícone, 1988.

THE IMPACT OF WINDOW SIZE ON THE PERFORMANCE OF BCI-SSVEP

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Introduction: Brain-Computer Interface (BCI) makes human-computer interaction possible by processing brain signals [1]. In the BCI based on Steady-State Visually Evoked Potential (SSVEP) is possible to associate commands of an application with visual stimuli that flicker at well-defined frequencies. This work analyzes the correlation between the window size of the brain signals employed to identify the visual stimuli and the accuracy of the BCI-SSVEP system. **Materials and Methods:** Our database with electroencephalographic (EEG) signals of 32 health subjects was used [2]. For each subject, 8 repetitions of 12 s were acquired for the four visual stimuli flickering at 6, 10, 12 and 15 Hz [2]. The preprocessing was performed using the Common Average Reference filter, the features extraction was obtained via Fast Fourier Transform (FFT) and a linear classifier based on the method of least squared was used. To evaluate the impact of window size of EEG signal used to identify the visual stimulus on the performance of the BCI-SSVEP was considered all possibilities of submultiples windowing of 12 s. The classifier performance was analyzed in two scenarios of the data partition: Scenario 1: considering 30% of the total samples for validation of the BCI system- this results in 228 samples for 0.5 s, 112 samples for 1 s, 56 samples for 2 s, 36 samples for 3 s, 28 samples for 4s and 16 samples for 6 s. Scenario 2: fixing 16 samples in all cases. In

both scenarios, the remaining samples were used to train the BCI-SSVEP. **Results:** Figure 1 shows the average accuracy and standard deviation of the BCI-SSVEP considering a scheme of 20-cross-fold-validation for the 32 subjects, for each window size in the two scenarios of the data partition. The average hit rate to discriminate the four stimuli were similar in all scenarios, being within the standard deviation. Particularly, the average accuracy was around 50% for windows size of 1, 2, 3 and 6 s. And slightly lower (about 40%) for windows sizes of 0.5 s and 4 s. **Discussion/Conclusion**: Our results indicate that the size of the windows used during the analysis to identify the visual stimuli appears to have a low impact on the BCI-SSVEP performance. A window size of 1 s seems sufficient to guarantee a good performance while ensuring flexibility and interactivity for application control. As future work, studies involving a database with more samples are necessary. However, the EEG data acquisition for training BCI is an annoying procedure for the user. So, the use of synthetic signals can be a promising alternative. We intend to use Generative Adversarial Networks (GANs) to improve BCI performance without increasing data collection time for BCI. **Acknowledgements:** The authors thank FAPESP and UFOP for the financial support.

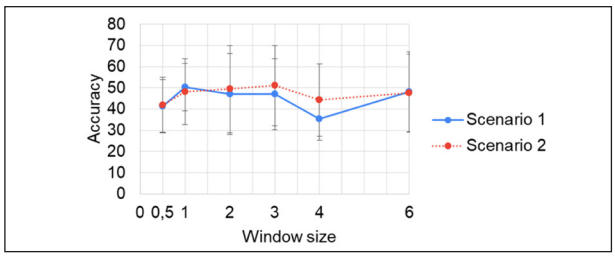

Figure 1. Accuracy of the BCI-SSVEP for the six different window sizes in the two scenarios.

References: [1] Grainmann B. *et al*., doi:10.1007/978-3-642-02091-9_1. [2] Leite, HMA, Phd thesis, FEEC/UNICAMP, 2018.

THE ROLE OF GENOMIC FOOTPRINT IN THE MECHANISMS UNDERLYING MESIAL TEMPORAL LOBE EPILEPSY: A SINGLE-CELL APPROACH

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Introduction and Hypothesis: The regulation of gene expression is an intricate and multifactorial process that requires a specific sequence of events. Open chromatin regions contain *cis*-regulatory elements, which are non-coding portions of the DNA, capable of regulate gene expression by epigenetic mechanisms [1]. One of these regions are the so-called genomic footprint (GF), which is characterized by a small sequence of nucleotides compatible with one or multiple transcription factors, and involved in the dynamic of coupling and uncoupling of many regulatory elements [2]. Differences in the GF may be related to disease development and progression. Mesial temporal lobe epilepsy (MTLE) associated with hippocampal sclerosis (HS) is one of the most frequent and severe types of epilepsy. For these patients, a surgical procedure may be used to achieve seizures control in patients that do not respond to medication. The tissue resected by epilepsy surgery can then be further studied [3]. **Objectives:** 1. To characterize the GF in brain tissue obtained from surgery (hippocampus, dentate gyrus, and amygdala) from patients with MTLE+HS;
2. To characterize the GF in tissue of patients with different disease duration;
3. To evaluate if the GF is indeed linked to the pattern of gene expression in the tissue studied (transcriptome);
4. To perform a multiomics analysis of the GF, including also the methylome and proteomics data obtained from the same tissue.
Materials and Methods: In this study, we will access the GF at a single cell level using the Assay for Transposase-Accessible Chromatin using Sequencing (ATAC-Seq) technology [1]. The nuclei from neuronal cells will be isolated, and the non-coding DNA portion will be sequenced in an Illumina® Platform. Data will be treated with bioinformatic tools to obtain the complete GF of the brain tissue studied (hippocampus, dentate gyrus, and amygdala). Patient samples will be divided into groups according to disease duration and results will be compared to controls tissue from autopsy. Finally, a multivariate analysis with be performed including multiple layers of omics data from the same tissue. **Relevance:** Single-cell molecular assays are a novel and powerful approach, especially in the context of multiomics studies. By using these methods, we can study the molecular mechanisms involved in MTLE+HS, constructing a detailed landscape of the molecular processes occurring in the abnormal tissue. Thus, we believe that our work will contribute with new and relevant biological information that can be used to better understand the mechanisms underlying MTLE+HS, and to identify novel therapeutic targets.

References: [1] Buenrostro, J.D. et al., DOI:10.1038/nmeth.2688; [2] Vierstra, J. et al., DOI: 10.1038/nmeth.3768; [3] Wieser, H.G. et al., DOI: 10.1111/j.0013-9580.2004.09004.x

THE TRANSCRIPTOME OF MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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Introduction: The most common form of medically refractory focal epilepsy is mesial temporal lobe epilepsy (MTLE)[1]. In MTLE, an important pathological hallmark pathologic is hippocampal sclerosis (HS)[2]. Patients with pharmacoresistant MTLE+HS may undergo surgical treatment to achieve better seizure control [3]. Hippocampal tissues resected by surgery offer a unique opportunity to investigate the molecular mechanisms underlying MTLE+HS. This study aims to characterize the hippocampal transcriptome in patients with MTLE+HS compared to control hippocampi from an autopsy. **Materials and Methods:** We studied hippocampal tissue obtained by surgery from 17 patients with medically refractory MTLE+HS and six postmortem hippocampi from individuals without neurological disease. We extracted RNA from samples with TRIzol®, using the manufacture instructions. We evaluated the quality and integrity of the RNA by RNA Integrity Number (RIN) detection on the Bioanalyzer 2100 chip electrophoresis (Agilent). Subsequently. We produced complementary DNA (cDNA) libraries from 200 ng of extracted RNA using the TruSeq Stranded Total RNA (Illumina®). We sequenced the cDNA libraries in a HiSeq® 4,000 (Illumina®) in high output mode, producing 100-base pair (bp). Read quality was assessed using FastQC v0.11.8 software, and TrimGalore v0.6.6 was used to filter adapters and reads of low quality [4]. Using the human GRCh38 cDNA from GENCODE release 36 as a reference, we built an index to align all our fastq files. Next, we used the quantifier of transcripts abundances performed by Salmon (version 1.4.0) with our pre-built index to align fastq files [5]. Differential expression was analyzed using the R package DESeq2 [6]. Genes were considered differentially expressed when statistical significance reached $\log_2FC \geq 1.0$ or ≤ -1.0 and adjusted $p \leq 0.05$ using the false discovery rate (FDR). Furthermore, we performed an enrichment analysis to identify gene ontology (GO) processes and pathways that occur more often than expected in a random distribution based on the list of genes found to be differently expressed. The analysis was performed using clusterprofiler [7] and Metascape[8]. **Results:** We found a total of 1,812 genes differentially expressed in hippocampi of patients with MTLE+HS. We observed 1,261 genes up-regulated ($\log_2FC \geq 1$) and 551 genes down-regulated ($\log_2FC \leq -1.0$) in patients with MTLE+HS. We found enrichment of GO according to **molecular function**, processes related to *"receptor-ligand activity"*, *"cytokine activity"*, "G *protein-coupled receptor binding"*, *"ATP-dependent microtubule motor activity"*, *"oxidoreduction-driven active transmembrane transporter activity"*, *"amino acid:sodium symporter activity"*, "extracellular matrix structural constituent" among others. For GO according to **biological process** we observed enrichment on "*cilium movement*", *"axoneme assembly"*, *"microtubule-based movement"*, *cytokine-mediated signaling pathway, cellular response to cytokine stimulus*, *"inflammatory response"*, among others. Enrichment of GO according to **cellular component** are "ciliary plasm", "axoneme", "cytoplasmic region", "extracellular matrix", "complex apical plasma membrane", "respiratory chain complex", "oxidoreductase complex", "respirasome", "excitatory synapse", among other. **Discussion/Conclusion**: We used state-of-the-art high throughput sequencing technologies to characterize the transcriptome of hippocampal tissue resected by surgery of patients with medically refractory seizures. Our results showed a remarkable complexity in the biological mechanisms involved in MTLE+HS, clearly demonstrating the

importance of performing agnostic omics studies. The most relevant biological pathways involved are inflammation and cytokines responses, respiratory chain complex, regulation of ion transport, and aberrant neurogenesis [9,10].

References: [1] Kwan et al., 2010. Epilepsia 51(6):1069-77,2010; [2] Blümcke et al., Epilepsia 54: 1315-1329, 2013; [3]de Souza et al., J Neurosurg 134(3):1044-1053, 2020; [4] Babraham Institute. Avalilable from:https://www.bioinformatics.babraham.ac.uk/projects/trim_galore/. Accessed:2020, Aug 04; [5] Soneson et al., F1000Research 4:1521, 2016; [6] Love et al., Genome Biol 15(12):550; 2014; [7] Wu et al., The Innovation 2(3), 2021;[8] Zhou et al., Nat Comm 10 (1): 1523, 2019; [9] Dixit et al., Genomics 107:178–88, 2016; [10] Morin-Brureau et al., Brain 141: 3343–60, 2018.

UNRAVELING THE MOLECULAR MECHANISMS UNDERLYING PARASITE-HOST INTERACTION IN *TAENIA SOLIUM* NEUROCYSTICERCOSIS

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Introduction: Neurocysticercosis is the most frequent parasitic disease in the human CNS. It is most prevalent in low and middle-income countries, where poor sanitation and free-roaming pigs are common. The analysis of how the transcriptome of the host's brain adjacent to the cyst and how the cyst changes throughout infection would help unravel the parasite-host immune systems interactions and facilitate understanding of the resulting disease. However, despite the Peruvian and Mexican initiatives to sequence the *T. solium* genome [1], it is still not entirely resolved. This way, we saw the need to improve the annotation of the *T. solium* genome using public transcriptome data. **Materials and Methods:** To do so, we used publicly available *T. solium* RNA-Seq data [2] deposited at the NCBI's Sequence Read Archive Database, following Ji et al., 2020 pipeline [3] for new genetic elements discovery. **Results:** HISAT2[4] aligned the transcriptome data to the *T. solium* reference genome with an 89.26% alignment rate. Stringtie[5] and QUAPRA[6] assembled the aligned reads, creating new *gtf* files, followed by Cuffcompare, to compare these new *gtf* files to the one from the reference genome. 23,252 new mRNAs were found for Stringtie and 20,743 for QUAPRA, and, of these, Cuffcompare[7] classified 3,216 (Stringtie) and 3,334 (QUAPRA) as potentially new transcripts. For coding-ability prediction, the new transcripts with FPKM > 1 were then submitted to CPAT[8]. CPAT generates a coding score cutoff after training with the target organism coding and non-coding mRNA dataset. To overcome *T. solium* and other cestodes lack of non-coding genes annotation, we created a *C. elegans* training dataset. From 2134 transcripts analyzed by CPAT, 121 (Stringtie) and 912 (QUAPRA) were above the coding-score cutoff. Of those, 94 (Stringtie) and 616 showed high similarity to close cestoda species or *C. elegans* compared with the UniProtKb/SwissProt curated cestoda proteome database. Transcripts below CPAT cutoff and that also do not present any protein family domain, and low similarity with any known protein will be considered as potential non-coding genes. These will also be submitted to miRTools 2.0 to predict and characterize non-coding genes. **Discussion/Conclusion**: Our adapted pipeline for discovering new genetic elements based on transcriptomic data demonstrated to have an excellent potential for improving the current *T. solium* reference genome annotation, with the possibility of including at least 600 new protein-coding genes. The next steps are to compare the results obtained from Stringtie with those from QUAPRA, quantify the potential non-coding transcripts, annotate the new findings in a new gtf file and submit it to the Wormbase database for public use.

References: [1]*T. solium* genome - https://parasite.wormbase.org/Taenia_solium_prjna170813/Info/Index [2]*T.solium* public RNA-seq (GSM2227058,SRX1899230) - https://www.ncbi.nlm.nih.gov/sra?term=SRX1899230 [3] Ji X. *et al.*, doi: 10.1093/nar/gkaa638. [4] Kim D. *et al.*, doi: 10.1038/s41587-019-0201-4. [5] Pertea M. *et al.*, doi: 10.1038/nbt.3122. [6] Ji X. *et al.* doi: 10.1007/s11427-018-9433-3. [7] Trapnell C. *et al.*, doi:10.1038/nbt.1621. [8] Wang L. et al., doi: 10.1093/nar/gkt006. [9] UniProt website - https://www.uniprot.org/ (accessed and data downloaded in Sep. 2021)

USE OF ASSISTIVE TECHNOLOGY IN THE REHABILITATION OF PATIENTS WITH STROKE

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Introduction: Strokes are thromboembolic phenomena [1] that have varying origins, classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Assistive technologies enable new solutions for the rehabilitation of neural amputations or neurological injuries through medical interventions performed through neuroengineering. **Materials and Methods:** This study was approved (CAAE: 39067720.6.0000.5481) and performed in stroke patients. Exclusion criteria: plegic patients or with limiting musculoskeletal deformities, cognitive impairment, comprehension aphasia. The evaluation of motor performance used Fugl-Meyer scale and the "*KinesiOS*" at the beginning and end of treatment. The Virtual Reality (VR) software used was the interactive game "*Puzzle_Win*", which consists of a screen with pieces that form a simple image. Participants performed two weekly sessions for four months, structured with 15 minutes of virtual reality software application and 45 minutes of conventional therapy. **Results:** Based on the inclusion criteria, three patients were selected, based on the inclusion criteria, among those registered in the system. Two patients were excluded due to the change in the etiology of their initial lesions. At the end of therapy, only one remained in the program, and their results were shown in the graphs displayed. Again, there is a range of motion, comparing the evolution lines in both charts. **Discussion/Conclusion**: Neurorehabilitation is a sensitive topic in health spending, due to the increasing number of stroke patients, the severity of the disease and its psychosocial impacts on population. Patient amount is a statistical problem for the results evaluation, however, our patient obtained gains with the proposed therapy.

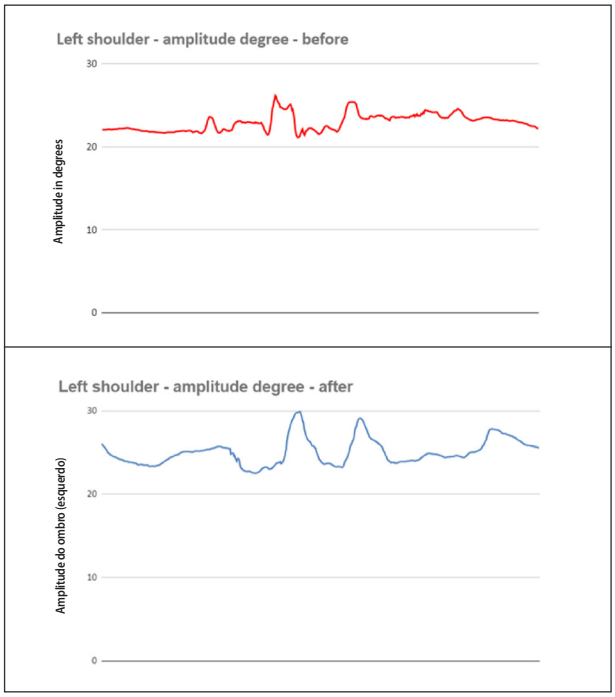

Figure 1. Motion gain; graphic evidence. Left shoulder – before treatment. Left shoulder – after 4 months.

References: [1] Chung, J. W. et al. Trial of ORG 10172 in Acute Stroke Treatment (TOAST). J Am Heart Assoc. Aug 11;3(4), 2014.

VOLUMETRIC SEGMENTATION OF THE CORPUS CALLOSUM: COMPARING 2D AND 3D NNU-NET MODELS TRAINED ON DIFFUSION MRI

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Introduction: Diffusion tensor imaging (DTI) provides relevant information about the CC as it is a type of imaging technique that analyzes the diffusion of water molecules in the brain, and is influenced by tissue microstructure [1]. In CC MRI-based studies, CC segmentation is an important step, however most available automated methods and tools perform the CC segmentation using T1-weighted images, and are able to segment it only on the midsagittal slice [2]. Only a few works handle volumetric CC segmentation, such as FreeSurfer

[3] and MRICloud [4]. This work presents a volumetric segmentation method of the CC using a nnU-Net [5] and multiple diffusion tensor maps as input channels, to perform DTI-based studies of the CC without the need of a time--consuming registration step of DTI with T1w masks. It also compares 3D and 2D approaches. **Materials and Methods:** The dataset contains T1 and DWI acquisitions from 84 subjects, split into training (53 subjects), validation (17 subjects), and testing (14 subjects). The training was performed using diffusion maps simultaneously (FA, MD, and MO) as input channels. The framework used to carry out the training was the nnU-Net, designed to deal with the dataset diversity and with automatic hyperparameters selection. We trained and compared two independent models for the same task: 2D nnU-Net and 3D nnU-Net. The evaluation metric used was Dice Similarity Coefficient (Dice). **Results:** Fixed parameters for both models include using the SGD optimizer with Dice loss and cross-entropy loss, 1000 for number of epochs, and initial learning rate of 0.01. The patch size used by the 2D nnU-Net was 192x160 in the axial view, and a batch size of 108; for the 3D nnU-Net the patch size was 80x192x128 and a batch size of 2. Evaluation of the models was done through volumetric Dice, in the testing dataset. The best mean Dice was obtained by the 3D nnU-Net, 83,66%, while for the 2D nnU-Net was 83,06%. Our previously proposed model [2], also using all diffusion maps to train a 2D UNet with no parameters optimization (in contrast to nnU-Net), obtained a Dice of 83,12% in the same test set. Qualitative analysis of the results confirms the slightly superior performance of the 3D nnU-Net model (Fig.1). **Discussion/Conclusion**: Comparison of the 2D and the 3D nnU-net models shows that volumetric information used by the 3D convolutions improved the results, as expected. However, while the 2D nnU-Net tends to underestimate the CC (Fig.1 - center), the previously proposed model [2], also 2D, presented a better performance, obtaining segmentation masks (Fig.1, right) similar to the ones obtained by the 3D nnU-Net (Fig.1, left). This can be due to the fact that the views used for training the 2D models were different. While our previous model uses the sagittal view (which better represents the CC), the nnU-Net model uses the axial view. Since quantitative results are similar and the superiority of the 3D nnU-Net model is not so evident, computational costs of each model should be taken into consideration. Also, experiments with a larger and more diverse dataset should be conducted to conclude if the differences between models are statistically significant.

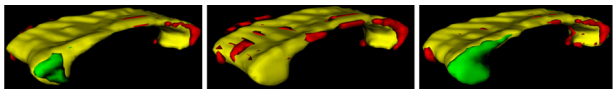

Figure 1. Volumetric results superimposed: 3D nnU-Net (left); 2D nnU-Net (center); Rodrigues et al. [2] (right). Manual mask is in red and models output in green, with overlap shown in yellow.

References: [1] Basser P et al., doi:10.1016/j.jmr.2011.09.022; [2] Rodrigues J et al., doi:10.1117/12.2606233; [3] Fischl B, doi:10.1016/j.neuroimage.2012.01.021; [4] Wang H and Yushkevich P, doi:10.3389/fninf.2013.00027; [5] Isensee F et al., doi:10.1038/s41592-020-01008-z.

AFFECTIVE MODULATION OF INTENTIONAL BINDING USING LINGUISTIC STIMULI: PSYCHOPHYSICS AND NEUROPSYCHOPHYSIOLOGY

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Introduction and Hypothesis: Sense of agency (SoA) is the feeling of one's influence in producing external consequences, which generates subjective contiguity in the time course of sensorimotor events involved. One phenomenon related to time contiguity is intentional binding, the subjective experience of time interval compression when an agent perceives a consequence as caused by an agent's action [1]. This effect is measured in the temporal binding paradigm, in which observers must judge the time interval between either a voluntary action or an externally caused event and a consequence. Although some experimental studies have shown that this effect might be modulated by the emotional valence of the consequence in that a bigger subjective experience of time compression occurs for positive than for negative consequences [2], some controversies have arisen over these results and the methodology they were obtained with, such as failure to fully reproduce the affective modulation of intentional binding and contradictory results [3]. Also, there is a lack of neuroimaging results to improve its physiologic understanding. Thus, alternative methodologies and stimuli are needed to shed more clarity on these issues [4]. **Objective:** This project aims to investigate the expected modulation of temporal binding when an emotional outcome is presented with linguistic stimuli and to deepen into its neural basis to get a better understanding of how affective stimuli are processed during temporal estimation in the brain, which would be helpful to explain literature divergences. Hence, validation of linguistic stimuli with behavioral and neuroimaging measures will be made, to later evaluate the emotional modulation of temporal binding with the same stimuli with both behavioral and neuroimaging measures. **Materials and Methods:** Two experiments will be made together with a pre-experiment to obtain required psycholinguistic indicators (word's Age of acquisition and Familiarity) that lacks Brazilian linguistic normalizations [5]. In Experiment 1 an intentional binding paradigm will be implemented with linguistic stimuli, using a perceptual discrimination two-alternative forced-choice (2AFC) task from which a point of subjective equality (PSE) will be extracted. A shorter PSE is expected as a function of a word's emotional valence. In Experiment 2 fNIRS procedure will be performed, in which, first, a validation of the neural response will be made with former stimuli, to identify emotional valence deoxyhemoglobin (Hb) dependent response. Then, a similar procedure to Experiment 1 will be performed with the same fNIRS arrangement [6], to obtain the deoxy-Hb of the affective modulation of temporal binding. All images will be acquired from a NIRScout System and an array of optodes (12 light sources and 12 detectors) covering frontal and occipital areas. Signal pre-processing and analysis will be performed with MNE pipeline analysis for Python. **Relevance:** Understanding phenomena as SoA allows clarifying the role of agency in conscious experience, with is relevant in the identification of underlying cognitive disturbances of psychopathological disorders. Also, the intentional binding paradigm helps us understand temporal binding and how we perceive and glue together both the concurrent physical events and the building blocks of our identity. Because emotions shape our relationship with the environment, implementing variability in methodologies and stimuli is fundamental to better understand these phenomena and their implications for society.

References: [1] Haggard P et al., doi:10.1038/nn827, [2] Yoshie M et al., doi:10.1016/j.cub.2013.08.034, [3] Moreton J et al., doi:10.1016/j.concog.2016.12.008, [4] Moore J et al., doi:10.1016/j.concog.2011.12.002., [5] Estivalet GL et al., doi:10.12957/soletras.2017.29702., [6] Trambaiolli L et al., doi: 10.1038/s41598-018-23747-7.

ANALYSIS OF THE IMPACT OF THE SARS-COV-2/COVID2019 PANDEMIC ON THE DIETARY PATTERN OF CHILDREN WITH EPILEPSY

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Introduction: Epilepsy is associated with an increased risk of malnutrition. Feeding difficulties may result from swallowing disorders, as well as appetite or metabolic changes associated with antiseizure medication (ASM) [1,2]. The SARS-CoV-2/COVID2019 pandemic generated interruption of the population's daily activities, with a high impact on children due to the closure of schools and the need for families to readjust. Therefore, the aim of this study was to investigate possible changes in the food consumption of children with epilepsy during the SARS-CoV-2/COVID2019 pandemic. **Materials and Methods:** Parents and guardians of individuals up to 21 years of age diagnosed with epilepsy were invited to fulfill online forms aiming to evaluate the change on the dietary pattern of their children with epilepsy. The questionnaire collected data related to the past and current clinical history of epilepsy, dietary pattern before and after the pandemic and factors associated with this change. Online informed consent was obtained from all participants and the Research Ethics Committee approved the study. **Results:** From April 2021 and January 2022, 79 parents or guardians of children and adolescents with epilepsy (53% male, median age 8 years old, range 1-19 years old) fulfilled the questionnaire. Age of epilepsy onset varied from zero to 15 years old (median 9 months). Most children (28%) were using one ASM and had their seizures controlled (49%), while 27% were using four more ASM and had daily seizures (27%). There was no significant change of seizure frequency during the pandemics. Twenty-three children (29%) had changes in their dietary intake during the pandemics. There was increase of the consumption of foods with added sugar (24%) and indus-

trialized foods (25%). On average, there was an increase of 3kg per individual since the start of the pandemics (range -9 to 23 kg). The medium body mass index (BMI) varied from 18 pre-pandemics to 20. During the pandemics, there was a decrease of low BMI from 18% to 6% and an increase of overweight or obesity from 44% to 51%. **Discussion/Conclusion**: In this cohort of children and adolescents with well-controlled as well as pharmacoresistant epilepsies we observed that almost one-thirty had change in their dietary pattern during the SARS-CoV-2/COVID2019 pandemic. There was a high frequency of increased consumption of sugar added and industrialized foods. On average, children with epilepsy had significant weight gain with increased frequency of overweight and obesity.

References: [1] Bertoli S, et al. Evaluation of nutritiona status in children with refractory epilepsy. Nutrition Journal, 2006;5:26. [2] Bergqvist, AC, et al. Growth failure in children with intractable epilepsy is not due to increased resting energy expenditure. Developmental Medicine & Child Neurology, 2008;50(6):439-44.

CONNECTION BETWEEN THE "ROTATION SCHEMA" AND THE DEVELOPMENT OF THE VESTIBULAR SYSTEM AND ITS RELEVANCE TO ONE'S GOOD COGNITIVE AND MOTOR DEVELOPMENT. AN OVERVIEW ON THE FIRST 6 YEARS OF LIFE

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Introduction: The vestibular system consists of an important circuitry that involves structures of the inner ear, brain stem, cerebellum and somatosensory cortex. The whole system plays several different roles that range from proprioception to motor function. One of the main structures that take part in this system is the vestibular labyrinth that detects the sensory information concerning the head acceleration. Special hair cells located in the both otolithic organs and the semicircular canals that form the vestibular labyrinth transmit informations relative to speed and acceleration of the head to the vestibular nuclei on the brain stem that help us to maintain balance and perceive the space around us. It is known that mammals acquire the main skills required in adult life through play, and are hardwired to do so in order to develop physical, mental and social abilities. Schemas in play are patterns of behaviors commonly observed throughout childhood, in all sorts of societal arrangements around the world, regardless of children's age or any other cluster. One of the most common schemas is the rotation schema, in which the child gets particularly interested in all rotational movements including it's own body. The main goal of this study is to establish the connection between such schema and its importance in the development of the vestibular system. A secondary but just as important goal, is to shine a light over this important pedagogical concept of schemas, make it more relevant in the academic environment in Brazil, integrate these pedagogical concepts with human neurodevelopment knowledge and broadcast this ideas to the general public through all sorts of digital media (videos, popular articles, elaborated images, audios), in platforms such as Instagram, Kwai, and others in the form of a project called #SemeandoBrincadeiras. **Materials and Methods:** We used research platforms to acquire the knowledge on all of the topics discussed, cell phone cameras, computers and the internet, to produce, edit and share videos, pictures and others, portraying information of childhood development and the importance of play in social media and other kinds of media as well. **Relevance:** So far we have created and now own a brand called #SemeandoBrincadeiras and use it to diffuse information of the importance of play in development, with a special focus on the usage of schemas to help caregivers in the task of promoting a global development for the children under their responsibility. We have also participated on a co-authoring book by Literare publisher with a popular article about schemas that is yet to be released. Currently we are working on establishing the correlation between the discussed schema and the vestibular system through bibliografic review, yet we have found with our work in social media that, knowledge concerning schemas is not spread in Brazil's education system nor among professionals, neither among parents or caregivers in general, that is in spite of being a well established concept in many other countries on the realms of pedagogy, and such knowledge would change the view on some behaviors considered challenging, improving the relationship between child and caregiver promoting an environment prone to development.

CONSTRUCTING NEW AND IMPROVED PLATFORM FOR DATA SHARING IN THE BRAZILIAN INITIATIVE ON PRECISION MEDICINE (BIPMED)

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Introduction: The Brazilian Initiative on Precision Medicine (BIPMed), created in 2015, is based on a software platform, built following the guidelines and principles of the Global Alliance for Genomics and Health (GA4GH), and observing the responsible sharing of genomic and clinical data. This platform is the first of its kind in Latin America and aims to offer public access to genomic and phenotypic data. It is intended to be used by clinicians and scientists worldwide to share and obtain information about various aspects of genomic medicine and human health, as well as to support dissemination and training in the areas of human molecular genetics, computational biology, and genomic medicine (www.bipmed.org). Over the past two years, we realized that the BIPMed genomic platform needs significant changes to incorporate updates and improvements as new data is included, and new applications are necessary. Thus, we report here the first major overhaul of the BIPMed website and genomic platform so that it can continue serving the medical and research community. **Materials and Methods:** In order to launch BIPMED 2.0, several steps are being taken. First, to follow the most current GA4GH guidelines on data sharing, we are implementing CRAM and VCF files formats, Family History Tools Inventory, htsget API, and Variant Benchmarking Tools. Second, we are re-processing the data on the 257 original exomes from the São Paulo state reference population, which were initially processed using the outdated hg19 human reference panel. These exomes plus 87 newly sequenced ones (from Belo Horizonte, Barretos, and Ribeirão Preto) were re-processed using the hg38 human reference. We are looking carefully for possible discrepancies between the results of the two analyses. Also, we will make the two datasets, hg19 and hg38 references, available to the public. Third, we have developed a new tool to import variants from VCF files to the BraVE application programming interface (API) based on the GA4GH Genomics API. This update is considerably faster than the previous implementation and fixes some critical issues regarding missing information in the variants file. Finally, we are also implementing improved applications for uploading external data or downloading BIPMed datasets. **Results**: Currently, the platform has nine databases, including genomic and genetic information in about 900 individuals. Two of these databases are from what we call 'reference' Brazilian population, where individuals were ascertained based on place of birth and not on disease phenotypes. Seven are disease-specific databases, including diverse phenotypes ranging from cancer to neurological disorders. The two reference databases are composed of unique SNPs identified using whole-exome sequence and single nucleotide polymorphisms (SNP)-arrays. Genetic variation within the databases can now be searched using three online tools (BEACON – GA4GH -, LovD – Leiden University – and the BraVe application, which has been developed in-house). **Conclusion**: Keeping public genomics databases running demands time and effort, requiring computational solutions for hosting, displaying, searching, and interacting with the datasets. Furthermore, the web interface should provide a good experience to suit users with different scientific backgrounds. Therefore, over the past year, we have been undertaking a great effort to implement new features on the BIPMed platform to make it more informative and user-friendly. Thus, keeping with the BIPMed mission of supporting the implementation of precision medicine in Brazil.

EFFECT OF RESISTANCE TRAINING AND DETRAINING ON COGNITIVE, FUNCTIONAL, AND PHYSICAL PERFORMANCE OF ELDERLY PEOPLE WITH MILD COGNITIVE IMPAIRMENT

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Introduction and Hypothesis: Mild cognitive impairment (MCI) refers to the diagnostic term applied to individuals who have a cognitive decline in one or more cognitive functions but are still independent. MCI may be a precondition for the development of Alzheimer's disease (AD). Due to the predicted

increase in the incidence of AD, the importance of an early diagnosis and intervening with accessible tools stands out, to reduce health investments and improve the patient's quality of life. Physical exercise has a positive influence on cognitive functions and in neuroinflammation reduction. A less investigated type of exercise in relation to the MCI population is the resistance training. The brief existent literature points to improvements in cognition, functionality, and physical performance of elderly people with MCI. However, some studies contradict each other regarding brain changes and hormones related to neurodegeneration, like irisin concentrations. To individuals with MCI changing physical daily habits seems to be a beneficial factor on cognition. Therefore, intervening with modifiable lifestyle factors, with low cost and easy access, such as the practice of resistance exercises, can represent an advance in therapeutic and socioeconomic terms. **Objective:** The aim of this study is to investigate if cognitive and physical performance, brain structure and functionality, serum, and CSF irisin and AD biomarkers concentrations are influenced by resistance training practice in elderly people with MCI. **Materials and Methods:** 80 elderly people with MCI will participate in resistance training twice a week for 6 months and will be evaluated at baseline, after resistance training period and after a detraining period (6 months). Participants will be evaluated through: Neuropsychological tests (cognitive tests and neuropsychiatric scales); Functional and physical tests (physical performance in tests and questionnaires); MRI (Structural: for volumetric and thickness analysis of brain structures; T2 - FLAIR with fat suppression, to evaluate white matter lesions; Functional: in resting-state to assess the integrity of functional connectivity networks, especially the default mode network); White matter integrity assessment: Diffusion Tensor Imaging); Blood tests (irisin concentrations). In addition, at the beginning of the study, they will be evaluated for CSF levels of irisin concentrations and of AD biomarkers (total tau protein, phosphorylated tau protein, amyloid beta peptide of 42 units by immunoassay - ELISA). Based on the descriptive classification for AD biomarkers, patients will be divided into groups (Continuum AD, SNAP, and Negative biomarkers) enabling comparison between them. **Relevance:** AD is a neurodegenerative disease that affects cognition, physical function, social behavior, and the individual's general quality of life, generating, also, socioeconomic cost for society. This study aims to evaluate a less studied type of physical activity in the AD spectrum in a population without dementia to understand its clinical effects and the pathophysiology of the disease. If we prove our hypothesis that resistance training is beneficial, our study may provide evidence for this type of activity to be incorporated as a therapeutic intervention. In addition, it will be of great importance a study showing, in different analyses, the effect of this physical training in elderly people with MCI.

EFFECTS OF CORTICAL NEUROMODULATION THROUGH TRANSCRANIAL DIRECT CURRENT STIMULATION IN DEPRESSIVE DISORDERS: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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Introduction and Hypothesis: The present study will aim to analyze the effects of cortical neuromodulation offered by transcranial direct current stimulation (tDCS) in individuals with mild depressive disorders. Depressive disorder is a highly prevalent mental illness characterized by persistent negative emotions and thoughts. People with depression show increased attention and memory for negative emotional stimuli associated with severity of symptoms and cognitive uncontrol over information processing due to decreased activity of the dorsolateral prefrontal cortex[2]. Recent neuromodulation studies have shown that the application of TDCS has significant results in attention and emotional functioning, performance and cognition in individuals with major depression. **Objective:** Primary Objetive: To analyze the influence of cortical neuromodulation through transcranial direct current stimulation in individuals with mild depressive disorders. Secondary Objective: Observe the variation of behavior in relation to the dosimetry of 1mA and 2mA in the experimental times of 10 and 20 sessions. **Materials and Methods:** This is a clinical, controlled, randomized and double-blind study, which will follow the standards recommended by the National Health Council (CNS) for research involving human beings and the National Research Ethics Commission (CONEP), established in Resolution number 196, of October 10, 1996 of the National Commission for Ethics in Research. The sample will consist of 35 individuals, of both genders, aged between ±45 and 80 years, who will be divided into the following groups: control group *(GC=5), tDCS -1 group (n=15 G-tDCS) 1mA 20 sessions, tDCS-2 group (n= 15 G-tDCS)2mA 20 sessions. Note: *control group, sample of 5 individuals, placebo application, experimental time 10 and 20 days. ** tDCS-1 group transcranial direct current stimulation group, experimental time 10 and 20 days, dose 1mA. *** tDCS-2 group (transcranial direct current stimulation group, experimental time 10 and 20 days, dose 2mA). **Relevance:** The present study may contribute to the formulation of new neuromodulation protocols for mild depressive disorders with safe doses and with greater results. Neuromodulation is presented as an option for the non-drug treatment of depressive disorders, contributing to a safe approach with few side effects for the patient.

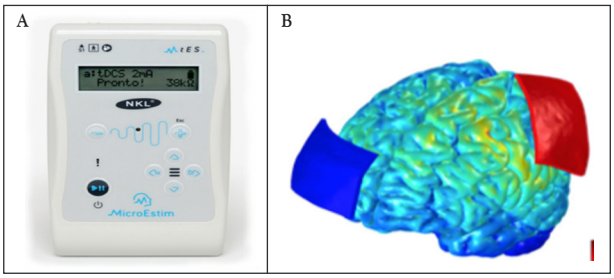

Figure 1. A - Cortical Neuromodulation Equipment - Transcranial Direct Current Stimulation (tDCS). B - Application location in the cerebral cortex.[17,18,19]

EVALUATING EEG NETWORKS FROM EPILEPSY PATIENTS WITH MACHINE LEARNING

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Introduction and Hypothesis: In the last decade, several methods for analyzing epileptiform signals in electroencephalography (EEG) have been proposed. These methods primarily use time and/or frequency domain characteristics of the EEG signal to separate regular, interictal, and ictal brain activity. In our previous work [1] we evaluated the feasibility of using functional connectivity (FC) based feature extraction methods, in conjunction with supervised machine learning techniques, for the analysis of interictal epileptiform discharges (IEDs) on EEG signals obtained from EEG-fMRI sessions (i.e. concomitantly with functional magnetic resonance imaging data), of 10 patients with mesial temporal lobe epilepsy (MTLE). Of the different connectivity functions used, motif synchronization [2] had the greatest potential for separating three types of 1 s epochs of the EEG signal, namely: without IEDs, right before IEDs and mid IEDs. Based on these previous results, we wish to continue exploring the FC networks, in search for other useful information regarding spatiotemporal location of IEDs. **Objective:** The objective of this project is to use FC-derived features from either EEG-fMRI or simple EEG data (which have a better signal-to-noise ratio) for spatiotemporal location of IEDs. In this work, we intend to increase the number of analyzed patients, and to include other (than MTLE) types of epilepsy. Initially, we will attempt to confirm the results previously obtained [1] and refine the IED detection tools (including the automation of these). Furthermore, we will verify if the methods of analysis of FC networks can help in the localization of epileptogenic foci. **Materials and Methods:** We will use motifs synchronization [2], coherence and phase locking value [3] to estimate FC. Several machine learning methods, such as naive Bayes, k-nearest neighbors, decision tree, linear discriminant analysis and support vector machines, will be evaluated for this task. The EEG and EEG-fMRI signals have been accumulated during years of acquisition by clinical care at UNICAMP's Neuroimaging Laboratory, consisting of a vast sample population. Despite having already received some type of evaluation, much of these data requires cataloging of the epilepsy diagnoses, as well as IED marking. For this reason, a direct collaboration with neurologists, neurophysiologists and other researchers from the field of neuroimaging at UNICAMP is necessary, which makes it possible for other parallel projects to follow this line of research. **Relevance:** The analysis of the EEG exam is a fundamental step in the treatment

of epilepsy. The visual inspection that a neurologist makes for marking IEDs is a standard procedure, but it can be very time consuming. As so, any tools that aid in performing this task can be of great help. **Acknowledgements:** We thank CAPES and FAPESP (grant 2013/07759-3) for financial support.

References: [1] Costa LR et al., doi: 10.3389/fneur.2021.673559. [2] Rosário RS et al., doi: 10.1016/j.physa.2015.07.018. [3] Aydore S et al., doi: j.neuroimage.2013.02.008.

EVALUATION OF GENE EXPRESSION PROFILE OF ENDOTHELIAL COLONY FORMING CELLS OF PATIENTS WITH SICKLE CELL ANEMIA AND STROKE

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Introduction and Hypothesis: Neurological alterations, especially ischemic stroke (IS), are common complications of Sickle Cell Anemia (SCA) [1]. Hemolysis, inflammation, endothelial activation and vaso-constriction are involved with vaso-occlusion prior to ischemic accidents. The role of the vascular endothelium in the cascade of events that culminate in such phenotypic changes have been emphasized [2]. In this context, we hypothesize that there is a differential gene expression profile in endothelial cells from SCA patients with IS when compared to SCA patients without IS, which may lead to the identification of molecular pathways involved with this neurological complication. **Objective:** To identify differentially expressed genes (DEGs) and regulatory factors in endothelial cells of patients with SCA and SI and investigate their biological relevance in mechanisms of ischemic stroke. **Materials and Methods:** RNA samples from circulating Endothelial Colony Forming Cells (ECFCs) of four SCA patients with IS and six SCA patients without IS were sequenced by RNA-Seq. Detection of differentially expressed genes were obtained by edgeR package in R, followed by Gene Ontology analysis of Biological Process in ShinyGO and construction of Protein-Protein Interaction networks in Cytoscape. Clustvis was used for Heatmap and PCA construction. **Relevance:** Ischemic stroke is related to greater severity of SCA, especially at an early age, being fatal in 15% of cases [3]. Despite the monogenic inheritance of this hemoglobinopathy, the phenotypic manifestation encompasses a complex interaction of biological mechanisms. In this context, next generation sequencing technologies are important tools for uncovering the complexity of several diseases [4]. In our preliminary results, we found 600 DEGs (-2 < Log2FC > 2 and FDR <0.01) used to construct the Principal Component Analysis (PCA) (A) and Heatmap (B) depicted below. Enriched pathways of regulation of growth, cell migration and positive regulation of immune response, relevant mechanisms of IS in SCA, were observed. However, based on PCA and Heatmap results, we highlight that especial attention must be taken regarding clinical aspects of control 6 (C6).

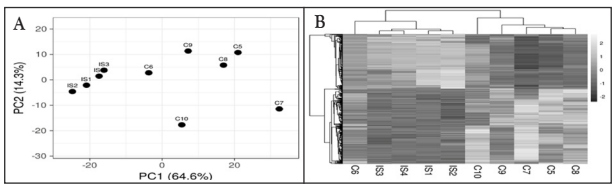

Figure 1. Distribution of Sample Group. (IS = Ischemic Stroke, C = Control). A - Principal Component Analysis. B - Heatmap of 600 DEGs.

References: [1] Ohene-Frempong K *et al.*, Blood 91(1): 288-94, 1998; [2] Kato GJ *et al.*, doi: 10.1002/ajh.21475; [3] Steinberg MH.,doi: 10.1100/tsw.2008.157; [4] Byron SA *et al.*, doi:10.1038/nrg.2016.10.

EVALUATION OF VIRTUAL REALITY TREATMENTS FOR STROKE PATIENTS USING MOTOR IMAGERY ELECTROENCEPHALOGRAPHY

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Introduction and Hypothesis: Impaired motor functions caused by a stroke are major issues both for victims and for those around them. Among the new treatments available for rehabilitation is the virtual reality (VR) approach, in which patients are driven to perform movements as a display shows them what to do in a ludic, more engaging way. As the once-lost movements improve via this type of treatment, changes in the patient's brain follow. We hypothesize that these changes can be evaluated by electroencephalography (EEG), in particular using a motor imagery (MI) protocol. **Objective:** To evaluate cognitive changes due to VR motor rehabilitation of stroke patients using an MI-EEG protocol, at which participants imagine the movements of their arms and legs while being measured by an EEG device. This evaluation will be done before and after the treatment is done. **Materials and Methods:** Two sessions (before and after VR treatment) of MI-EEG will be performed, using g.tec's g.USBamp USB Biosignal Amplifier. This device has 16 electrodes and a sampling rate of 256 Hz. Each session begins with a two-minute resting-state period to measure the baseline of the patient. Then, a two-minute hand-MI period follows. This is divided into eight 16 s periods at which participants rest for 8 s while a black screen appears on a computer display. Then a cross appears for 2 seconds, indicating that the task is about to start. Finally, a right- or left-hand figure appears on the screen indicating which hand's movement the participant should imagine. The side is chosen randomly, but each session has 4 left and 4 right hands MI guaranteed. Finally, a two-minute foot-MI period follows in exactly the same way. **Relevance:** Understanding how rehabilitation reveals itself at the brain level is important to describe the means by which it happens and, perhaps, to improve and even generate new methods of rehabilitation for stroke patients.

INTERVENTION FOR VIRTUAL PHYSICAL EXERCISE IN ELDERLY

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Introduction: Virtual reality (VR) is an innovative method in the recovery and motivation of the elderly and the measures adopted and in the practice of physical exercises (PE)[1,2]. **Materials and Methods:** The pilot project evaluates two healthy elderly (80-85 years and of both sexes) who practice PE and VR intervention from gestural interaction with the computer system. This study followed the evolution of executive function and relationships with technology during the five months of the project. The instruments utilized were: the Stroop Test to estimate executive function and the Bioecological Questionnaire to evaluate the individual's relationship with technology. We used the Gesturemaps Software[3] three times a week to allow, by gestural interaction, virtual Street View navigation controlled through stationary gait. **Results:** We used the same instruments as the final intervention (5 months later) in re-evaluating the subjects. The preliminary results highlight the following points: the VR and PE improved the executive function by 38,5% and the relationship with technology by 13,5%. Intervention with VR associated with PE improves cognitive functions[4]. Ethics Committee approved it of UNICAMP, CAAE: 46692821.3.0000.5404. **Discussion/Conclusion**: The values found with VR values efficiently improve physical and psychological abilities in two elderly

Table 1. Comparison of means between the main questions of the Bioecological Questionnaire of the 1st and 2nd application.

Applications	Is technology important in my daily life?	I need the internet in my everyday life.	I use my cell phone/tablet/computer at least once a day.
1st Application	2 points	1.5 points	2 points
2nd Application	5 points	4.5 points	5 points

Table 2. Comparison of means between the Stroop Test and Bioecological Questionnaire of the 1st and 2nd application.

Applications	Stroop Test	Bioecological Questionnaire
1st Application	40.5 points	54 points
2nd Application	56.5 points	61.5 points

Figure 1. Subject uses the GestureMaps application to control Google Street View using legs' (lower limbs) movements.

during healthy ageing and the rehabilitation process. The participants (a male and a female subject) accepted the software well, presenting safe and viable applicability.

References: [1] FRIED, L.P. et al. (2001) J Gerontol A. 2001, 56(3): 146-56.; [2] Jorgensen M.G. el al. (2013) J Gerontol A. 2013, 68(7):845-52.; [3] BRANDÃO, A.F. et al. (2018) J. Health Inform. 2018, 10(1): 9-16.; [4] MAGNA, T.S.; BRANDÃO, A.F; FERNANDES, P.T. (2020); 12(3):77-8.

MACHINE LEARNING FOR AUTOMATIC HEMORRHAGE DETECTION IN CRANIAL COMPUTED TOMOGRAPHY EXAMS

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Introduction and Hypothesis: In the radiological context, the detection of findings that put a patient's life at imminent risk should be treated as "critical findings" [1-2]. The radiology workflow requires the identification of these findings and communication of the patient's condition to the physician as quickly as possible. One of the most common critical findings is intracranial hemorrhage (IH) and, although the radiology technician team has a high degree of training for the rapid detection of critical findings, they may not be detected during image acquisition, especially in cases where they are subtle. Thereby, the exam can be in the report queue for hours until a radiologist reports the findings, causing a delay in the disease treatment [1-2]. In this sense, our project aims to develop a machine learning algorithm to detect intracranial hemorrhage, including its sub-types, from computed tomography, a type of exam whose acquisition time is shorter than that of MRI, it has lower costs and greater availability in developing countries such as Brazil. **Objective:** Development of a machine learning algorithm for detecting intracranial hemorrhage, a type of critical findings in medical images, with high sensitivity (greater than 90%) and specificity (greater than 60%) compared to the radiologist's evaluation. Integration of the algorithm into the hospital radiology workflow, so it can be used by the medical team to indicate that a given patient's exam has a relevant radiological finding. Evaluation of the time spent in the identification of the radiological finding and in the release of the report to the physician responsible for the patient. **Materials and Methods:** 1301 anonymized dicom exams from 840 patients deposited on the hospital's PACS system have been selected (ethical committee nº CONEP – CAAE 12616619.8.0000.0071). The preprocessing step includes rebalancing the dataset, normalization of images, division of images into training, validation and test datasets. For model construction, architectures and components of convolutional neural networks are being used. For model's evaluation, accuracy, sensitivity, specificity and ROC curve are the chosen metrics [3-4]. **Relevance:** From a clinical perspective, our project has the potential to be an automatic method of screening CT exams and be used in radiological information systems to identify emergency situations, based on imaging findings, particularly those related to IH. In the future, this model can also integrate the development of new techniques that help the clinical diagnosis of patients.

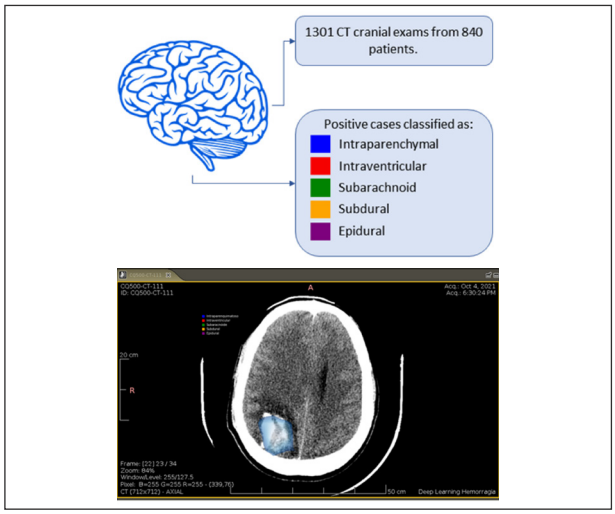

Figure 1. Scheme representing the dataset used in our study and the sub-types of hemorrhage we aim to predict with our model. The results will be displayed as heatmap maks overlayed with the original image. The heatmap colors will indicate the sub-type of hemorrhage detected.

Referências: [1] Hussain, S et al., doi: 10.1016/j.jacr.2009.10.012; [2] Reiner, B.I et al., doi: 10.1007/s10278-013-9609-4; [3] Prevedello, L et al., doi: 10.1148/radiol.2017162664; [4] Kholi, M et al., doi: 10.2214/AJR.16.17224.

NEW TECHNOLOGIES CONTRIBUTION TO THE DEVELOPMENT OF EXECUTIVE FUNCTIONS

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Introduction and Hypothesis: To explore the benefits of Active Learning Methods (*e.g.*, games, Gamification, group work, problem-based learning, and flipped classrooms) on student motivation and learning, we have developed a pedagogical approach encompassing some concepts related to active learning. The hypothesis is that specific approaches and technologies can contribute to cognitive development and the coping of challenges commonly identified in modern societies. **Objective:** The objective is to evaluate if an intervention with Gamification associated with other Active Learning Methods can promote changes in the understanding of new roles for teachers in the academic organization of schools, in student participation, and in deepening knowledge. **Methods:** We developed a pedagogical approach with concepts related to Active Learning Methods to explore the benefits that Active Learning Methods (*e.g.*, games, Gamification, group work, problem-based learning, and flipped classroom) can exert on students' motivation and learning. The pedagogical approach uses Gamification and the game style known as RPG (Role-Playing Game) elements. One of these elements is a narrative (fictional story) where students play like characters in the story. The teacher has the role of a storyteller, such as a game master of RPG. Some systems used in the intervention are Classcraft (https://www.classcraft.com/) as Learning Management System (LMS). Classcraft works as a kind of "Guild Castle". Reddit (https://www.reddit.com) is used for asynchronous discussions in a forum. Reddit works as a "Tavern", where students gather to discuss the proposed topics. Students publish their reflections about the story's journey on Padlet (https://padlet.com). In Mindmeister (https://www.mindmeister.com/), collaborative mind maps are created on the concepts that permeate the key concepts proposed in each activity. Miro (https://miro.com/) is used to carry out different group dynamics. Kahoot! (https://kahoot.com) is used to create and answer quizzes on the concepts covered in the activities. We applied the Teaching Approaches Inventory (ATI) [1] to verify the teaching perceptions of teachers in the training carried out to prepare them to apply the pedagogical approach. To verify the general perception of the participating teachers about the training and about their trainers, as well as about their degree of satisfaction with the training. To evaluate the impact of the pedagogical approach on student motivation and learning, we applied the School Motivation Questionnaire (SMQ) [2]. There will be 3 stages in the intervention: (1) *Teacher's training:* The intervention begins with the training on concepts related to games and Gamification in education. The training uses all the resources of the proposed pedagogical approach to enable teachers to use the tools in their pedagogical contexts; (2) *Support for teachers:* In the second stage of the intervention, we will assist the teachers in adapting the approach to their specific pedagogical contexts; and (3) *Application of the pedagogical approach in the context:* In the third stage, teachers promote the motivation and development of student learning using the pedagogical approach. **Relevance:** In the post-pandemic context, the teachers' and students' interactions are mediated by various technologies as learning tools in a hybrid context, part in a remote and part in face-to-face teaching. We propose to use Gamification and other Active Learning Methods to improve the learning experience. The Gamification approaches for distance learning courses [1] can promote motivation for learning [2] but may have adverse effects on students [3], creating the need to reevaluate the pedagogical approaches and environments.

References: [1] Urh M. et al., doi.org/10.1016/j.sbspro.2015.07.154; [2] Rozman & Donath, doi.org/10.32015/JIBM/2019-11-3-2; [3] Frost R.D. et al., JISE 26(1): 59-70, 2015.

RADIATION THERAPY EFFECTS ON THE HEALTHY BRAIN TISSUE OF TUMOR PATIENTS MEASURED BY MAGNETIC RESONANCE IMAGING

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Introduction and Hypothesis: Tumors were a leading cause of deaths worldwide in 2020, while nervous system cancers represent the 10th cause of cancer in the US. Nevertheless, the survivability of brain cancers has also increased due to advances in treatment and diagnosis technologies. One of the most common types of treatment is Radiation Therapy (RT), which is responsible for killing cancer cells by damaging their genetic material. However, it also causes damage to normal brain cells. This process can lesion the brain and generate radiation-induced brain injury (RBI), which occurs in roughly 50%-90% of patients, leading

to morphological brain changes, such as cortical thinning. Therefore, alterations in healthy brain tissue due to RT and assessed using Magnetic Resonance Imaging (MRI) can provide relevant information for patient's outcomes. **Objective:** Correlate the radiation exposure of non-tumor brain areas with their cortical thinning and volume reduction, willing to identify sensible dose-dependent regions. **Materials and Methods:** All images were acquired in a 3T scanner. For each patient, 3D T1-weighted high spatial resolution images, acquired before and after RT, are co-registered with CT (Computed Tomography) image so the Planned Target Volume (PTV) maps from RT could be in the same space of MRI scans. T1 images are then segmented using Statistical Parametric Mapping Computational Anatomy Toolbox (SPM – CAT12). DK-40 atlas was chosen for regional thickness estimation, and the neuromorphometrics atlas was chosen for regional volumetry. Regions localized on PTV are excluded from the analysis. Data values before and after RT will be compared and related to the dose received by each region. Segmentation, volumetry, and cortical thickness estimation before RT were already performed for 11 patients. Figure 1 shows an example for cortical thickness estimation. **Relevance:** We intend to assess morphological alterations in healthy brain tissue due to radiation. It may help the understanding of different outcomes observed in patients undergoing RT, such as cognitive deficits or other symptoms that may worsen their quality of life, and may assist future RT planning.

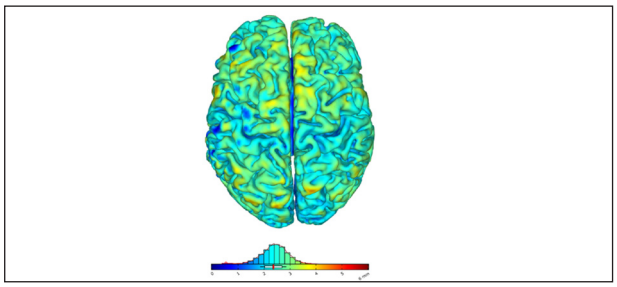

Figure 1. Cortical thickness estimation of a patient with brain tumor before radiation therapy.

RECONHECER: PROGRAM DIRECTED TO MATERNAL RESPONSIBILITY AND MOTHER-BABY BOND

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Introduction and Hypothesis: Adolescence and youth are periods when life skills are still under development [1]. The natural challenges of this period, when added to the experience of motherhood, can represent a great challenge for young people [2]. Teenage mothers have less sensitivity and worse performance in executive functions than adults [3]. Programs based on film and feedback about reciprocal interactions are studied as an intervention proposal to improve responsive attitudes and maternal sensitivity, consequently affecting the development of children and the bonding of the mother/caregiver-baby binomial. In addition, Transcranial Direct Current Stimulation (TDCS) programs are studied to improve plasticity and executive functions [4]. The research hypothesis is that maternal responsiveness is associated with executive functions and can be improved through film interventions and TDCS [5]. **Objective:** To evaluate the effectiveness of interventions focused on young mothers to improve maternal responsiveness and the bond between them and their children. **Materials and Methods:** This research is a clinical, prospective, and longitudinal trial with 60 young mothers aged 15 to 24 years. This project was approved by the local Ethics Committee in research. All participants will undergo an initial assessment using the following tools: sociodemographic assessment; of sleep quality; of depressive and anxious symptoms; executive functions; ability to recognize and infer facial expressions; child development; and maternal responsiveness. In the second meeting will be held a semi-structured interview and the intervention will follow through with 6 meetings with 10-minute footage and presentation with scenes filmed between mother and child where mothers were responsive, followed by a second evaluation. Young women who did not respond well to the intervention or performed below average in executive functions will be subjected to a new intervention with TDCS. **Relevance:** There are few studies concerning the complexity of motherhood during adolescence. It is important to promote interventions that enhance maternal sensitivity and allow the development of the young person, and of her child, strengthening the bond between them.

References: [1] Sanders, R. A., DOI: 10.1542/pir.34-8-354; [2] Freitas, G. V. S., et. al., DOI: 10.1590/S0104-42302002000300039; [3] Gonzales, C. E., et. al., DOI: 10.1002/dev.21185; [4] Fisher, P. A., et. al., DOI: 10.1111/cdep.12195; [5] Mondino, M., et. al., DOI: 10.3109/15622975.2013.876514.

RESTING BRAIN FUNCTIONAL CONNECTIVITY BY MAGNETIC RESONANCE IMAGING IN PATIENTS WITH *DE NOVO* PARKINSON'S DISEASE

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Introduction and Hypothesis: Parkinson's disease is a chronic, neurodegenerative condition with multifactorial reasons. Diagnosing this disorder becomes a very difficult task, as the symptoms are not the same for all patients and only appear when damage is already very significant [1]. In order to avoid the most severe degenerations, the early diagnosis plays a key role, making the damage contention easier, based on conventional or complementary therapies. A possible analysis is by functional magnetic resonance imaging (fMRI), observing high activity in some resting state brain regions in those patients, and then it could lead to new biomarkers. Some tests have shown that connectivity in specific brain regions at resting state may differ between parkinson's disease patients and healthy individuals [2]. **Objective:** The main objective is to evaluate the resting brain functional connectivity of newly diagnosed patients with parkinson's disease without any effect of treatment-related drugs. The analysis consists of observing low-frequency amplitudes in functional images in order to identify connectivity patterns and then to differentiate controls and patients, and relate these results with non-motors symptoms. **Materials and Methods:** All images used are part of the Parkinson's Progression Markers Initiative international database (PPMI). The group is made up of 50 subjects with *de novo* parkinson's disease and 50 healthy subjects, all of them with high-resolution T1-weighted and functional images acquired in a 3T MRI scanner. Beyond that, all individuals must have done non-motors assessments: Trail Making A and B tests; verbal fluency; Epworth Sleepiness Scale (ESS) and REM Sleep Disorder Questionnaire. The functional data comes from blood oxygenation level dependent contrast (BOLD), which evaluates brain connectivity based on hemodynamic changes. As it is possible to evaluate this activity during a task or at rest, the resting state fMRI was chosen because of the ease in acquisition in most part of patients. After the selection on database, the functional images will be pre-processed using the following software: MATLAB R2015a, Statistical Parametric Mapping – SPM 12 and CONN toolbox. At this step, reorientation, slice time correction, realignment, corregistration, structural image segmentation, spatial normalizing and spatial smoothing will be performed. Then, the final analysis consists in comparing the newly diagnosed patients with the control group. This comparison aims to find statistical differences in connections between the groups, and relate specific regions with non-motors symptoms on ill patients. **Relevance:** The relevance of this study is mostly about to improve the early diagnosis in order to prevent and control irreversible degenerations caused by the parkinson's disease. Establishing this relationship between the BOLD contrast and the presence of this condition, using data of patients who have never received any kind of treatment, can create a trustable biomarker that identifies the disease in early stages and, consequently, in less motor and non-motor damages.

References: [1] Miller, D. B. et al., doi: 10.1016/j.metabol.2014.10.030; [2] Wolters, A. F. et al., doi: 10.1016/j.parkreldis.2018.12.016.

TRANSCRIPTOMIC ANALYSIS OF PERIRHINAL (PER) AND ENTORHINAL CORTEX (EC) OF MALE MICE

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Introduction and Hypothesis: The perirhinal cortex (PER) plays an important role in acquiring knowledge about objects, recognition of memory, identification of objects by associating different sensory features of an object, and association of objects with other objects. Moreover, PER is ventrally bordered by the lateral entorhinal cortex, LEC, providing an inhibitory control on the information entering the LEC. PER comprises two horizontal bands areas 35 and 36, that have different cytoarchitecture and connections, and is ventrally bordered by the entorhinal cortex. The entorhinal cortex (EC) is important for processing visual and spatial information, receiving direct inputs from PER, and being one of the most major cortical inputs to the hippocampus. EC is also divided into bands, the MEC (medial entorhinal cortex) and LEC (lateral entorhinal cortex). Both PER and EC cytoarchitecture are composed of I-VI layers, each of which has different cell types, densities, inputs, and outputs. The PER projects to the LEC which in turn projects to the hippocam-

pus, an interaction that is important for integration of object-related information, spatial information, and creation of a context-specific representation for novel and familiar objects recognition, which in turn may contribute to the hippocampus episodic memory. **Objective:** This study aims to investigate the biological processes and molecular components of PER and EC regions, separating the cell population of II-III, V, and VI layers of 35/ 36 of PER areas, and the II-/III, V layers of MEC/ LEC of EC areas. **Materials and Methods:** We will use 10 male C57BL/6 mice (CEMIB-UNICAMP), in which five animals will be used for RNA-sequencing and five animals will use for further validation. The brain tissue will be horizontally sliced to preserve the PER and EC structures. Then we will perform Laser Capture Microdissection (Zeiss) and extract the II-III, V, and VI layers of 35/36 of PER areas, and II/III, V layers of MEC/LEC of EC areas, from the brain tissue using a surgical microscope (Zeiss). Total RNA will be isolated using the Trizol protocol and RNA libraries will be constructed using Truseq (Illumina) library preparation kit according to manufacturer instructions. Bioinformatic tools such as STAR and DESEq2 will be employed for transcriptome alignment to *Mus musculus* genome and statistical analysis of transcriptomic differences between each layer of each PER and EC region. **Relevance:** The cortex is organized into segregated functional domains at different levels - as areas, columns, and layers - each processing distinct information and cooperating to generate integrative signals. To understand the different cortical structures that might contribute to the anatomical specialization of neuronal circuits, specific cellular development, and synaptic connections, the separation of cortical layers according to the cell type is important. Therefore, the separation of the cell population of PER and EC using LCM techniques will help the understanding of the molecular processes involved in which layer through transcriptomic approaches.