JECN

Journal of Epilepsy and Clinical Neurophysiology

ISSN 1676-2649

Volume 24 | Number 2 | Year 2018

ABSTRACTS PRESENTED AT THE 5TH BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (BRAINN-UNICAMP)

APRIL 9th TO 11th 2018 - CAMPINAS, SP, BRAZIL

J Epilepsy Clin Neurophysiol 2018; 24(2): 31-91

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

EXPEDIENTE

Editor Consultivo – Arthur Tadeu de Assis
Editora Executiva – Ana Carolina de Assis

Editora Administrativa – Atha Comunicação Editora
Contato – revistajecn@outlook.com

Ficha Catalográfica

Journal of Epilepsy and Clinical Neurophysiology (Revista de Epilepsia e Neurofisiologia Clínica) / Liga Brasileira de Epilepsia. – Vol. 23, n.3, jul 2019.

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

Contents/Sumário/Contenido

ABSTRACTS PRESENTED AT THE 5TH BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (BRAINN-UNICAMP)

APRIL 9TH TO 11TH 2018 - CAMPINAS, SP, BRAZIL

JECN Journal of Epilepsy and Clinical Neurophysiology

JECN Journal of Epilepsy and Clinical Neurophysiology

JECN Journal of Epilepsy and Clinical Neurophysiology

JECN Journal of Epilepsy and Clinical Neurophysiology

JECN Journal of Epilepsy and Clinical Neurophysiology

ABSTRACTS PRESENTED AT THE 5TH BRAINN CONGRESS BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY (BRAINN-UNICAMP)

APRIL 9TH TO 11TH 2018 - CAMPINAS, SP, BRAZIL

ANALYSIS OF THE GENOMIC DNA'S METHYLATION PATTERN IN MESIAL TEMPORAL LOBE EPILEPSY ASSOCIATED WITH HIPPOCAMPAL SCLEROSIS

J. C. Geraldis[1], D. B. Dogini[1], A.M. Canto[1], S.H. Avansini[1], M. Alvin[2], F. Rogerio[3], C.L. Yasuda[2], B. S. Carvalho[4], F. Cendes[2], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, [2]Department of Neurology, [3]Department of Anatomical Pathology; School of Medical Sciences, (FCM), [4]Department of Statistics Institute of Mathematics, Statistics and Scientific Computing (IMECC), University of Campinas (UNICAMP), Campinas, SP, Brazil.

Introduction and Hypothesis: Mesial temporal lobe epilepsy (MTLE), which may be associated with hippocampal sclerosis, is one of the most frequent and most severe types of epilepsy, since many patients present are refractory to antiepileptic drug treatment [1]. In these patients, surgical treatment may be a therapeutic alternative, which includes the surgical resection of brain tissue presenting epileptic activity and histopathological changes [2]. We and others have identified gene expression differences in brain tissue from patients with MTLE when compared with tissue from autopsy controls. Currently, DNA methylation is the most studied epigenetic mechanism, since it acts on gene regulation and may be reversible [3]. Thus, our main hypothesis is that the differences in gene expression identified in surgical specimens of patients with MTLE may be caused, at least in part, by differentially methylated regions in the genome. **Objective:** 1. To characterize the pattern of DNA methylation throughout the genome (methylome) in surgical tissue obtained from patients with MTLE with hippocampal sclerosis; 2. To evaluate the methylation profile in different regions of the dentate gyrus in the hippocampal samples obtained from patients and autopsy controls; 3. To evaluate if differentially methylated regions play a role in the transcriptional repression of candidate genes that contribute to the pathophysiology of the disease; 4. To correlate the methylome obtained from patients with previous data on the transcriptome (RNA-Seq) and proteomics data from the same patients. **Methods:** we will sequence the genomic DNA modified by sodium bisulfite tissue from patients and control individuals, using an HiSeq 2500 Illumina platform. Data will be treated by bioinformatic tools, such as Bowtie and Bismark, to obtain whole genomic methylation data, the methylome [4]. Then, we will combine the trancriptomic and proteomic data with the methylome of our samples, and search for common genes and pathways. **Relevance:** with our results, we hope to identify and catalog differentially methylated regions in the genome that may be influencing the expression of relevant genes. In addition, we hope to find molecular pathways amenable to intervention, contributing improvement in therapeutic interventions for patients with severe forms of epilepsy. We believe that our work will be of great value since the literature is scarce in the face of the analysis of methylome in brain tissue of the patients, as well as its correlation with other genomic and molecular aspects.

References: [1] Wieser, H.G. et al. Epilepsia, 2004. 45(6): p. 695-714; [2] Lee, S. et al. Journal of Epilepsy Research, 2014. 4: p. 1- 6; [3] Mohn, F. et al. Mol Cell, 2008. 30(6): p. 755-66; [4] Hansen, K.D. et al. Irizarry, Genome Biol, 2012. 13(10): p. R83.

MULTIPLEXED PROTEOMICS OF LASER-MICRODISSECTED BRAIN TISSUE FROM PATIENTS WITH MTLE

A. M. Canto[1], B. A. Bertelli[1], A. S. Vieira [2], S.H.Avansini[1], E. Ghizoni[3], H. Tedeschi[3], M. Alvim[3], M.E.Morita[3], C.L.Yasuda[3], F. Rogerio[4], F. Cendes[3], I. Lopes-Cendes[1]

[1] Department of Medical Genetics, School of Medical Sciences, UNICAMP and The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN); [2] Biology Institute (IB), UNICAMP; [3]Department of Neurology, UNICAMP; [4]Anatomical Pathology, UNICAMP, Campinas, SP, Brazil.

Introduction: Mesial temporal lobe epilepsy (MTLE) is the most common form of epilepsy in adults. Usually, patients with MTLE have a distinct lesion in the mesial temporal structures, including the hippocampus, named hippocampal sclerosis (HS). In this context, the dentate gyrus (DG) is a cortical region that is an integral portion of the larger functional structure named hippocampal formation (HF) and it is affected by HS. There are some advantages in the study of the DG in the context of HS, since it is better preserved, with less neuronal death when compared with other structures from the HF such as CA1 and CA3 [1]. Thus, possibly yielding more information about the molecular mechanisms leading to HS. The present study aimed to analyze the total proteome of neuronal cells in the DG of patients with MTLE who underwent epilepsy surgery. **Materials and Methods:** The DG from patients with MTLE (N=5) and pathology proven HS, as well as from autopsy controls (N=5 autopsy) were laser microdissected to refine the cell population of interest, in this case neuronal bodies. Proteins were extracted using Urea 8M and quantified using BCA assay (Pierce). We used state-of-the-art, recently introduced (2017) multiplexing proteomics technology, the **TMT-11plex** [2]. Protein samples (15μg) were tagged using the isobaric label TMT-11plex (Thermo Fisher Scientifics) and were pooled with a personalized QC (quality control), which was used both to calibrate the equipment and to normalize the differences between the set of samples. The proteins were analyzed in a high-resolution Mass Spectrometer (LTQ-Orbitrap) coupled with a HPLC. Bioinformatics analyses were performed using the Proteome Discoverer 3.1. **Results:** 5896 peptides belonging to 361 protein groups were identified. The comparisons between patients and controls revealed 9 proteins present in both groups, 15 present exclusively in patients and 11 only in controls. The labelling efficiency was 98% and the confidence level of identification was determined as 'high', based in a qualitative scale. **Discussion:** The main classes of proteins identified were: structural, translational and serum proteins, such as hemoglobin subunits, GFAP, actin, ribosomal proteins, tubulins, among others. Moreover, the main enriched pathways found were: neuronal inflammation, neurofilaments and immune response to injury. Although we were able to detect proteins differently expressed in patients and in controls, we did not have sufficient material to identify all the differentially expressed proteins. **Conclusion:** Surgical human tissue offers a unique opportunity to identify the molecular mechanisms underlying disease without the bias of using animal models, however, they are obtained in limited amounts, especially when using laser-microdissection to isolate specific cell populations. Therefore, the use of multiplexing technologies, and improved protocols are very advantageous. We have shown that we can obtain enough material for proteomic studies. We are currently working to optimize our protocol allowing the quantification of all differentially expressed proteins in neuronal cells of the DG of patients with MTLE in comparison with controls.

References: [1] Blumck I et al., Epilepsia 54(7): 1315-1329, 2013; [2] Arrey TN et al., ASMS poster, 2017.

DETECTION OF METHYLATED CIRCULATING DNA AS A NON-INVASIVE BIOMARKER FOR THE IDENTIFICATION OF PATIENTS WITH EPILEPSY AND STROKE

D.C.F. Bruno[1], M. Martim[1], A. Donatti[1], W. Souza[1], S.H. Avansini[1], D.B. Dogini[1], M. Alvim[2], C.L. Yasuda[2], B.S. Carvalho[3], F. Cendes[2], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, [2]Department of Neurology, School of Medical Sciences, (FCM), [3]Department of Statistics Institute of Mathematics, Statistics and Scientific Computing (IMECC), University of Campinas,(UNICAMP), Campinas, SP, Brazil.

Introduction and Hypothesis: Currently, the diagnosis of patients with stroke and epilepsy is still a great challenge, since it is based on subjective clinical signs and symptoms. Therefore, the identification of biomarkers for the diagnosis and for the establishment of prognosis becomes essential. Methylated cell free DNAs (cfDNAs) have recently emerged as candidates for biomarkers [1,2], since they can be easily analyzed and quantified noninvasively. In addition, disease-specific DNA methylation patterns may undergo changes in response to treatment,

increasing the possibility that biomarkers based on DNA methylation are used for monitoring treatment efficacy. **Objective:** The main objective of this project is to investigate whether differentially methylated cfDNA can be used to aid in the diagnosis, in the establishment of prognosis and in the prediction of treatment response in epilepsy and stroke. Therefore, we initially propose (1) to isolate and quantify the cfDNA present in plasma of patients with epilepsy, stroke and controls; (2) to sequence cfDNA isolated from patients and controls by whole genome sequencing of bisulphite-treated (WGBS) genomic DNA; (3) to identify in the sequencing data candidate targets to be used as biomarkers applying advanced bioinformatic analysis; and (4) to customize panels with differentially methylated regions/genes to be used in an expanded sample of patients with stroke and epilepsy to validate the previously identified candidate biomarkers. **Methods:** We will study 100 patients with epilepsy, 100 with stroke, and 100 control subjects. All patients included in the study are prospectively followed at the UNICAMP university hospital according to a detailed research protocol that includes extensive clinical and neuroimaging evaluation. All phenotypic information is included in a database built especially for research projects. Determination of overall methylation of cfDNA will be performed by WGBS plasma free DNA. After identifying differentially methylated regions (DMRs), using Bismark [3], Bowtie2 [4] and BSmooth [5] it will customized a specific panel with the candidate genes and/or regions and applied this to a larger number of plasma samples cfDNA from patients with epilepsy and stroke. Subsequently, patients will be sub-divided into groups according to response to treatment and prognosis. **Relevance:** The diagnosis of epilepsy and stroke is based on neurological history, electroencephalogram and neuroimaging findings [6]. However, there is still a great challenge in diagnosis, since it still requires a certain degree of clinical experience for the appropriated interpretation of these findings. In this context, it is evident that the identification of non-invasive diagnosis methods such as the use of biomarkers is urgently needed. Furthermore, the comparison of the methylation pattern of cfDNA between these two neurological conditions is of interest in the study of mechanisms of brain damage and plasticity.

References: [1] Levenson VV and Melnikov AA, Pharm. Basel Switz. 5, 94–113, 2012; [2] Cheuk IWY et al., J. Breast Cancer 20, 12–19, 2017; [3] Krueger F et al., Bioinformatics, v. 27, n. 11, p. 1571-1572, 2011; [4] Langmead B and Salzberg SL. Nature Methods. 9:357-359, 2012; [5] Hansen KD et al., Genome Biol. 13, R83, 2012; [6] Engel, Epilepsia 52, 1195-1197; discussion 1205-1209, 2011.

DISTRIBUTION OF LOCAL ANCESTRY AND EVIDENCE OF POSITIVE SELECTION IN BRAZILIAN INDIVIDUALS

R. Secolin[1], A. Mas[2], L.R. Araúna[2], F.R. Torres[1], T.K. Araujo[1], M.L. Santos[1], C.S. Rocha[1], B.S. Carvalho[3], F. Cendes[4], I. Lopes-Cendes[1], D. Comas[2]

[1]Department of Medical Genetics, School of Medical Sciences, University of Campinas - UNICAMP, SP, Brazil; [2]Departament de Ciències Experimentals i de la Salut, Institute of Evolutionary Biology (CSIC-UPF), Universitat Pompeu Fabra, Barcelona, Spain; [3]Department of Statistics, Institute of Mathematics, Statistics and Scientific Computing, UNICAMP, SP, Brazil; [4]Department of Neurology, School of Medical Sciences, UNICAMP, SP, Brazil; and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: In genome-wide association studies, admixed populations have the advantage of increase the probability to identify causal variants due to creation of local ancestry tracts across the genome. Local ancestry has been inferred in admixed populations, but poorly studied in Brazilian individuals. Therefore, our main goals were to describe the distribution of local ancestry and to identify deviations across the genome in a Brazilian sample. **Materials and Methods:** We evaluated 264 individuals obtained within the scope of the Brazilian Initiative on Precision Medicine, and compared with data from the 1000 Genome Project and to additional 43 Native American samples from previous studies. Genotyping calling was performed by Genome-Wide Human SNP Array 6.0 platform. Individual and genotype filtering was performed by PLINK 1.9 software, which was also used to evaluate population structure by principal component analysis. Global and local ancestry was estimated by ADMIXTURE and RFMIX algorithm, respectively. **Results:** As expected, Brazilian sample presented high proportion of South European ancestry, followed by West African and Native American ancestries. However, local ancestry revealed a decreased European ancestry proportion followed by an excess of Native American on chromosome (ch) 8p23.1. **Discussion:** We showed that this deviation is due to haplotypes created by inversion events. In addition, Brazilian non-inverted haplotypes were found to be more similar to Native Americans than European haplotypes, different than what was found for other admixed populations (Puerto Rican and Colombian samples). We also found signals of recent positive selection on ch 8p23.1, and one gene (*PPP1R3B*) located within the target region is related with diet and have already been associated with type 2 diabetes and obesity, which strength the positive selection hypothesis. **Conclusions:** Our results add an important local ancestry information for both Brazilian and other admixed populations. In addition, our finding is also relevant for precision medicine, since it shows that a result derived from a strict population study may also have implications for medicine.

INVESTIGATING THE GENETIC COMPONENT OF DRUG RESISTANCE IN MESIAL TEMPORAL LOBE EPILEPSY: AN INTERNATIONAL MULTICENTER STUDY

M. C. Molck[1], R. Secolin[1], F. Rossi[1], M. Alvim[2], C. L. Yasuda[2], B. S. Carvalho[3], F. Cendes[2], I. Lopes-Cendes[1]

[1] Department of Medical Genetics; [2] Department of Neurology, School of Medical Sciences; [3] Department of Statistics, Institute of Mathematics, Statistics and Computer Sciences; University of Campinas, UNICAMP, Campinas, SP, Brazil.

Introduction and Hypothesis: Mesial temporal lobe epilepsy (MTLE) is the most common form of focal epilepsy in the adult population, and many of these patients have epileptic seizures refractory to treatment with antiepileptic drugs (AEDs). Due to the numerous tests with different combinations of AEDs, the indication of epilepsy surgery to control seizures may take many years. Based on this context, our group reported a prediction algorithm model for drug-response in patients with MTLE [1]. This model includes 56 SNPs in candidate genes and the presence of hippocampal sclerosis, leading to an accuracy of 0.8177 to predict which patient with MTLE will likely to be refractory to AED treatment. The present project aims to validate and expand the previous work by evaluating patients from multiple clinical centers in several countries, and accessing outcome (drug response) prospectively. **Objective:** Our proposal is a study carried out in two phases: i) the first phase of this study is a cross-sectional designed and aims to genotype the ten most statistically significant SNPs previously reported by Silva-Alves et al. [1] in an independent MTLE cohort including at least 300 patients (divided into two groups: responsive and refractory). ii) the second phase will be a prospective study, including at least 500 MTLE patients divided into the same two groups. These patients will be genotyped for the same SNPs that were used in the first phase of the study. In addition, all patients from phases 1 and 2 will be submitted for GWAS to detect new SNPs with potential to predict response to AEDs. **Methods:** TaqMan™ real time PCR system (Applied Biosystems, Foster City, CA, USA) and Gene Chip Genome-Wide Human SNP Array 6.0 (Affymetrix, Santa Clara, CA, USA) will be used for genotyping the ten most significant SNPs and perform GWAS, respectively, from patients of phases I and II. The patients from phase II will be followed for at least 2 years to determine if they are responsive or refractory to AEDs. **Relevance:** The algorithm we reported was the first evidence presented in the literature indicating that genetic information combined with clinical variables may help predict drug response in patients with MTLE. In this follow-up study we will be able to validate the algorithm for AED response, helping to determine which patients should be submitted to epilepsy surgery sooner.

References: [1] Silva-Alves M. S. et al. PLoS ONE, 12(1): e01692142017, 2017.

SURGICAL TREATMENT OF LONG-TERM EPILEPSY-ASSOCIATED GLIONEURAL TUMORS - EPIDEMIOLOGY, SURGICAL RESULTS AND PATHOLOGY

Giglio MV[1], Ghizoni E[1], Joaquim AF[1], Tedeschi H[1], Cendes F[1].

[1]Division of Neurosurgery, Department of Neurology, University of Campinas – UNICAMP.

Introduction and Hypothesis: Epilepsy is a debilitating condition causing distress and adversely affecting the quality of life. The long-term use of anti-epileptic drugs per se also carries a risk of wide-ranging adverse effects.[6] Brain tumors can lead to seizures in more than a half of cases. Thirty percent of these patients presenting epilepsy associated with tumors are drug-resistant[8]. Luyken at al. described a wide group of low-grade glial and glioneural tumors associated with early onset, chronic and drug-resistant focal epilepsy named LEATs - "long-term epilepsy-associated tumors"[1,2,4,7]. Surgery is the main treatment for such tumors and it is associated with good outcomes, a decrease in the use of anti-epileptic drugs and related adverse effects, and improvement in the quality of life. The optimal surgical approach and best-time to surgery,

however, are still not clear[3,5,6]. **Objective:** The objective of this study will be to establish whether different surgical approaches, duration of epilepsy before surgery, and findings of pathology may impact the final outcome. We will evaluate the population of patients submitted to surgery in University of Campinas (UNICAMP) and Centro Infantil Boldrini between 2.002 and 2.016 presenting epilepsy and a histologically confirmed diagnosis of LEATs. **Methods:** We will do a retrospective evaluation of medical reports of patients with epilepsy and a histologically confirmed diagnosis of LEATs that underwent surgery by the Division of Neurosurgery of both services. The analyzed variables will be sex, the age at the beginning of seizures and how long the patients were assisted up to surgery, tumor localization, surgical approach, histopathologic diagnostic, the presence of associated cortical dysplasias and the outcome according to Engle's classification. Pearson's Chi-square test, Fisher's exact test, Student's *t*-test, and logistic regression will be employed in the statistic analysis. The level of statistical significance will be set at p value < 0,05. **Relevance:** The outcomes of the present study will define the epidemiologic pattern of the patients with the diagnosis of long-term epilepsy-associated tumors assisted in both centers. Also, we may determine the prognostic factors that may be incorporated in the optimal treatment of such pathology.

References: [1] Blumcke I et al, Acta Neuropathol 128(1): 1-3, 2014; [2] Blumcke I et al, Acta Neuropathol 128(1): 39-54, 2014; [3] Giulioni M et al., J Neurosurg 111(6):1275-1282, 2009; [4] Luyken C et al., Epilepsia 44(6): 822-830, 2003; [5] Radhakrishnan A et al., Clin Neurol Neurosurg 141: 98-105, 2016; [6] Ranger A et al., Childs Nerv Syst 31(6): 847-855, 2015; [7] Thom M at el., Brain Pathol 22(3): 350-379, 2012; [8] van Breemen MS et al, Lancet Neurol 6(5): 421-430, 2007.

MILES FORWARD, BUT ONE STEP BACK: THE IMPACT OF METHODOLOGICAL DIFFERENCES IN WHOLE EXOME SEQUENCING CENTERS ON THE DEPTH OF COVERAGE OF CODING VARIANTS WITH KNOWN CLINICAL IMPACT

Murilo G Borges[1,2], Vera N Solferini[3], Benilton S Carvalho[2,4] and Iscia Lopes-Cendes[1,2]

[1]University of Campinas, School of Medical Sciences, Department of Medical Genetics. [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN). [3]University of Campinas, Institute of Biology, Department of Genetics, Evolution and Bioagents. [4]University of Campinas, Institute of Mathematics, Statistics and Computing Science, Department of Statistics.

Introduction: The coding region of the human genome corresponds to less than 2% of its entirety and it is known as exome. This portion of the human genome concentrates most of the pathologic variations, which are known to cause disease in humans. For a better interpretation of these variants, evidence-based databases, such as ClinVar, compiles data on the presumed relationships between DNA variants and phenotypes. In the present work, we aim to investigate the pattern of base-specific depth in variants present in ClinVar, within the exome definition, in subjects who had the exome captured by different approaches in different sequencing centers by the 1000 Genomes Project. **Materials and Methods:** We used public data from the 1000 Genomes Project Consortium [1] to investigate the depth of coverage variations in 1112 whole exome sequenced (WES) samples from sequencing phase 3. We extracted 282,453 variants from ClinVar (built 20170801, GRCh37.p13) and performed variant annotation using the Ensembl Variant Effect Predictor (VEP version 84). 4,543 of the total number of variants were exonic and had any impact on transcription as well (121 were classified as high, 2,166 as moderate, 1,641 as low and 615 as modifier). We used "samtools depth" (version 1.0) to estimate the base-by-base depth of the 4,543 considered variants. We conducted all further analyses using the R statistical environment (version 3.3.2). We tested the assumption of no difference among the density of depths for each sequencing center with a pairwise Wilcoxon Test with a subsequent Bonferroni correction. We also applied multidimensional scaling (MDS) to compare the groups, addressing the data high-dimensionality issue and obtained a low-dimensional representation of the data. **Results:** Depth distribution varies significantly ($p < 0.001$ among each sequencing center), with an average of 82.8±67.6 for BCM, 123.0±85.6 for BGI, 86.6±79.2 for BI and 49.4±33.8 for WUGSC. Multidimensional scaling analysis confirmed that samples depth patterns clusters according to the center they were sequenced in, with 69.0% of the explained variance for the first two principal components. This signals that protocol advancement and intrinsic methodological differences in each one of the sequencing centers directly affect the patterns of coverage in the set of variants analyzed. Through the depth distribution of the 450 variants with higher variance, we could correctly assign 96.9% of the samples to their sequencing centers when considering 5 clusters to the dendrogram branches. **Discussion:** The originality of the present study lies in the fact that this study compared samples only based on their depth of coverage. The present work shows for the first time that it is possible to distinguish samples based only on their depth patterns, showing that the capture reaction differences in whole exome sequencing directly reflect on final analysis results. Technical integration is challenging while trying to link genetic variations to disease, mainly for federated sequencing initiatives [2,3]. **Conclusion:** We conclude that WES depth in samples from different sequencing centers is liable to technical differences. Our results are not unexpected given that the initial step for a WES experiment is the capture of the target regions to be subsequently enriched and sequenced.

References: [1]. Consortium, 1000 Genomes Project *et al.* A global reference for human genetic variation. *Nature* 526, 68–74 (2015)/ [2]. Louie, B., Mork, P., Martin-Sanchez, F., Halevy, A. & Tarczy-Hornoch, P. Data integration and genomic medicine. *Journal of Biomedical Informatics* 40, 5–16 (2007)/ [3]. Ginsburg, G. S. & Willard, H. F. Genomic and personalized medicine: foundations and applications. *Translational Research* 154, 277–287 (2009).

REPRODUCIBLE WORKFLOWS FOR GENOMICS DATA ANALYSES

W. Souza[1], B. Carvalho[2], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, School of Medical Sciences, [2]Department of Statistics, Institute of Mathematics, Statistics and Computer Science; University of Campinas, UNICAMP, Campinas, SP, Brazil and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: New sequencing technologies have improved our abilities to collect biological information for large scale population studies. The availability of public datasets and the rise of federated genomic databases have allowed researches to find rare genomic variants. An increasing computing power is required to produce meaningful scientific contributions from high-dimensional genomic data. Cloud services have become affordable and popular among bioinformatics groups for computational-intensive tasks [1]. The combination of large scale datasets and cloud environments has resulted in new challenges to make genomic research more reproducible, which means the ability of other researchers to achieve the same results of the original analysis [2]. Task-specific bundles of software called containers have been used to guarantee that tools will always give the same results regardless of the computing environment. Domain-specific languages for describing tools and workflows have helped documentation and automation of bioinformatics data analysis protocols. To make our own genomic data analyses more reproducible, we have changed the methods we used to describe bioinformatics tools and workflows, and how we execute large scale data processing tasks. **Materials and Methods:** We created several Docker container images for bioinformatics tools. We also wrote description files for those tools using the Workflow Description Language (CWL), which is platform-independent and follows open standards. Docker images and CWL files were submitted to Dockstore, a web service that provides bioinformatics tools and workflows. Described tools and workflows have been used by our Biostatistics and Computational Biology Laboratory (BCBLab) for performing RNA-seq, small RNA-seq, whole-genome bisulfite sequencing and exome sequencing data analyses. **Results:** Validation tests showed that our workflows always generate the same results when executed in different computing environments. All tools and workflows are reusable reducing the effort to perform new analyses. Processing time was reduced since the entire analysis is performed automatically using optimized software executors capable of dynamically manage available computing resources. Disk space required to store genomic data was minimized because intermediary analysis files can be removed after execution and recovered whenever they are required. **Discussion:** Improvements in bioinformatics workflows have contributed to increase reproducibility and reusability of genomic data analyses. There are opportunities to develop new tools that facilitate utilization of description files and container images through application programming interfaces and user-friendly graphical interfaces. **Conclusion:** The use of software containers and definitions of tools and workflows allowed us to make our genomic research fully reproducible. We have plans to apply our methods on future large scale genomic data analyses using cloud computing services.

References: [1] Langmead B & Nellore A. Nature Reviews Genetics. 2018; [2] Wilkinson MD et al., Scientific Data, 3, 160018, 2016.

Supported: FAPESP.

EFFECT OF KINESIO TAPING IN THE FUNCTIONAL BRAIN OF CEREBRAL PALSY PATIENTS

F. B. Basilio[1], S. L. Novi[2], A. Quiroga[2], R. C. Mesquita[2], A. C. Coan[1]

[1]Child Neurology Discipline, Department of Neurology, FCM,UNICAMP; [2]Neurophysics Group, IFGW, UNICAMP.

Introduction and Hypothesis: Cerebral palsy (CP) is a group of permanent non-progressive posture and movement disorders that are caused by injuries in the developing brains. [1] In developed countries, CP is the most common cause of childhood disability with an incidence of 2.5 out of one thousand births. Among different cerebral lesions, those in the sensory motor cortex and in the corticospinal tract can cause changes in tone, reflex exacerbation, loss of selective motor control, muscular co-contraction and reciprocal inhibition, affecting negatively motor skills. Therapeutic approaches such as pharmacotherapy, orthopedic surgeries, physiotherapy and occupational therapy are usually employed in order to improve the development of motor skills. In this context, Kinesio Taping (KT) appears as an alternative, promising and effective method for motor rehabilitation. KT aims to facilitate or inhibit muscle functions, stabilize joints, reduce pain and maintain body alignment. [2] Even though such technique has been continuously used in the clinic, its fundamental mechanisms are still not fully understood by the physiological and neuroscience community. In the present work, we aim to deeply investigate the effects of KT in the cerebral cortex. Our hypothesis is that the benefits of KT are associated with changes at the cortical level. We are inclined to believe that the characterization of clinical and neuroimaging differences will further elucidate several opened questions regarding the fundamental mechanisms behind the KT. **Objective:** The main goal of this project is to investigate whether the use of KT is able to induce cerebral functional changes. **Methods:** For investigating the impact of KT in the cerebral cortex, we will perform a controlled clinical trial. For the group of patients, we will recruit patients with cerebral palsy with ages between 13 and 40 years old. Each patient will be evaluated with the Fugl-Meyer functional scale, and each one of them will have a paired control with the same age. To investigate the cerebral functional changes, we will perform near-infrared spectroscopy measurements, during motor block-designed experiments. The experiment is composed by 10 blocks of left and right motor activity (total of 20 blocks) in which all volunteers need to open and close one of their hands. Each experimental block presents 10 seconds of activity followed by 30 seconds of rest. All subjects will perform two runs. In the first run, volunteers will perform the task with free hands (without the tapping). The KT will be applied to one of their hands before the second run. Although our optical probe presents a high density of light sources and detectors over the cerebral motor regions, which is our focus, the probe also covers the whole head, allowing us to have access to the hemodynamic response of the entire brain. **Relevance:** KT is a low-cost intervention that uses a few resources, easily adapts to the body and can be used for several days without the need of specific maintenance. Compared to other treatments, KT is much more accepted by patients. However, despite the popularity of this technique since 1980 among physiotherapists and physical educators, the scientific community lacks scientific studies to support the use or not of KT. This lack of understanding is already in itself an important clinical and theoretical deficit, but it is additionally highlighted by the fact that KT treatments present huge benefits to cerebral palsy patients. So far, we have already studied one single cerebral palsy patient. We have seen that the use of KT highly changed the hemodynamic response of the patient. For example, in the first run (without KT), we observed that the patient had a contralateral hemodynamic response to the stimulus as expected. However, the application of KT induced a response to the ipsilateral hemisphere.

References: [1] Rosenbaum P et al., Dev Med Child Neurol 58(2): 492-501, 2007; [2] Chitaria SB et al., Crit Rev Phys Reahbil Med 27(1): 41-50, 2015.

EXPERIMENTATION WITH NATURALISTIC STIMULI: INVESTIGATING THE ASSOCIATIONS BETWEEN FNIRS SIGNALS AND BEHAVIORAL RESPONSES

C.S.F.Barreto[1], P.M.Vanzella[2], J.R.Sato[1,2]

[1] Center of Mathematics Computing and Cognition, Universidade Federal do ABC; [2] Interdisciplinary Unit for Applied Neuroscience, Universidade Federal do ABC.

Introduction: The current fNIRS data analysis methods are based on the application of the general linear model (GLM) in the observed hemodynamic signals and the expected response function of the individual. [1] Therefore, fNIRS data analysis of experiments with an ecological environment and naturalistic stimuli are limited and new methods for analysing this data are required. In that way, we propose a novel method to analyse fNIRS signals from experiments within the above-mentioned context. [1] We search for correlations between fNIRS signals of different individuals when they are submitted to the same stimulus and associate those correlations to behavioral responses. The methodology can be described in three main steps: (I) We apply the Inter Subject Correlation (ISC) analysis by measuring the similarity between brain hemodynamic signals for each pair of subjects, who were submitted to the same stimuli. [2] (II) We compute the distance between behavioral responses for each pair of subjects. (III) Finally, we compute the test for associations between the ISC and behavioral responses similarities. The statistical significance of these associations is assessed using the Multivariate Distance Matrix Regressor (MDMR). [3] As an illustration, we performed an emotional music induced experiment and applied our methodology to the data from this experiment. **Materials and Methods:** We collected fNIRS signals of 33 subjects submitted to the following protocol: 30 s in resting + 60 s listening to a music excerpt + time to answer the SAM +30s resting. The protocol was repeated eight times as we had eight music excerpts, which were previously classified as positive/negative valences, and high/low arousal. [4] The fNIRS signals were acquired using a NIRS Sport 8x8 NIRSx Medical Technologies, with 8 LED sources (750 e 860 nm) modulated by frequency and 8 detectors. The acquisition occurred with sample rate of 7.91 Hz. The 8 sources and 8 detectors were positioned at the prefrontal cortex based on the 10-20 EEG international system, resulting in 20 channels with 3 cm distance between source and detectors. **Results:** We found a positive statistical significant correlation ($r=0.139$, p-value < 0.05) between the ICS measure and behavioral response similarities for the most negative excerpt. Our findings suggest that subjects with similar emotional responses to the music stimuli presented more similar brain activation trajectories. Furthermore, more than half of the subjects reported responses in agreement with the characterization previously made by Andrade et al., considering only musicological features. **Discussion:** The main advantage of the proposed method is that the experimental protocol may not be restricted to a block or event related design. It requires only two conditions i) fNIRS data of multiple subjects submitted to the same stimuli; ii) behavioural data (e.g., questionnaires, etc) related to those stimuli. However, some limitations must be considered. First, systemic artifacts may cause spurious signal correlations leading to biased results, which might be more related to the vascular responses than the neural ones. Second, since the vascular system is different between children, adults and elderly, it is fundamental to work with participants in the same age span. **Conclusion:** We believe that this methodology is promising when considering fNIRS experimental designs with more ecological validity, in which block and event-related designs are not suitable.

References: [1] doi:10.1016/j.neuroimage.2013.06.016./ [2] doi:10.1126/science.1089506./ [3] doi:10.1016/j.neuroimage.2014.02.024./ [4] doi:10.1177/0305735616678056.

THE BRAINN EPILEPTIC ENCEPHALOPATHY GENETIC VARIANT DATABASE

C. S. Rocha[1]*,M. C. Gonsales[1], B. S. Carvalho[2]*, I. Lopes-Cendes[1]*

* for the BIPMed Collaborative Group

[1.] Department of Medical Genetics, School of Medical Sciences, [2.] Department of Statistics, Institute of Mathematics, Statistics and Scientific Computing; University of Campinas – UNICAMP and the Brazilian Institute of Neuroscience and Neurotechnology, Campinas, SP, Brasil.

Introduction: The Brazilian Initiative on Precision Medicine (BIPMed, www.bipmed.org) is an initiative of five Research Innovation and Dissemination Centers established in the state of São Paulo, Brazil, the Brazilian Research Institute for Neuroscience and Neurotechnology (BRAINN), Center for Computational Science and Engineering (CCES); Center for Research in Cell Therapy (CTC); Obesity and Comorbidities Research Center (OCRC); and Center for Research on Inflammatory Diseases (CRID). Aiming to help implement precision medicine through several projects, one of which is the establishment of public genomic databases. The design of these databases follows the recommendations of the Human Genome Variation Society and the principals and guidelines of the Global Alliance for Genomics and Health (GA4GH) for the ethical and responsible sharing of genomic and clinical information. Recently, the database for epileptic encephalopathies was made public, reporting all variants identified

in the SCN1A gene of patients with Dravet syndrome (DS), which have been studies by the molecular genetics team of the BRAINN. DS is a rare epileptic encephalopathy marked by early onset febrile clonic convulsions in a previously developmentally normal infant, followed by psychomotor delay and neurologic deficits, and highly resistant to treatment with antiepileptic drugs. The SCN1A gene, which encodes the pore-forming α1-subunit of the neuronal voltage-gated sodium channel Nav1.1, is considered one of the most relevant epilepsy-related genes in the clinical setting, with most mutation found in DS patients. **Materials and Methods:** SCN1A mutation screening was performed in 21 patients with DS from our outpatient epilepsy clinic. Sequence variants were described according to the conventional nomenclature based on the full-length SCN1A isoform (GenBank AB093548) and deposited in the public BIPMed database at http://bipmed.iqm.unicamp.br/epileptic-encephalopathy/ **Results:** Potentially deleterious SCN1A changes were identified in 81% of patients with DS. **Discussion and Conclusion**: The database was created from the need to have genetic information from the Brazilian population and make this information public. This information can be used by any researcher now, which wants to focus on additional studies to correlate genetic information with medical records. In addition, it is useful for clinicians interested in the better interpretation of diagnostic tests in the clinical setting. We believe that our work helps to launch the next era of medicine, which depends on large-scale comparisons of data. In conclusion, with this new platform we can easily integrate data, and make it accessible to researchers and clinicians.

SEARCHING FOR BLOOD BIOMARKERS TO IMPROVE THE DIAGNOSIS AND THE MANAGEMENT OF PATIENTS WITH EPILEPSY

M. Martin[1], S. H. Avansini[1], A.S. Vieira[1], R. Secolin[1], M.L. Santos[1], F. R. Torres[1], F. Rogério[3], A. C Coan[2], M.K.M Alvim[2], M. E. Morita[2], C. L. Yasuda[2], R. Barbosa[2], F. Cendes[2] I. Lopes-Cendes[1]

[1]Department of Medical Genetics, [2]Neurology and [3]Anatomical Pathology School of Medical Sciences, University of Campinas (UNICAMP), Campinas, SP, Brazil and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction and Hypothesis: The diagnosis of epilepsy it is still challenging. It is estimated that misdiagnosis of epilepsy occurs in about 25% of cases [1]; therefore, the development of innovative biomarkers to assist in the diagnosis of epilepsy is a priority. In addition, one third of patients with epilepsy do not have seizure remission despite appropriate therapy with anti-epileptic-drugs (AED). Major causes of drug resistant epilepsy (DRE) are mesial temporal lobe epilepsy (MTLE) and focal cortical dysplasia (FCD). Therefore, the identification of biomarkers for AED response could potentially speed-up the diagnosis of medically refractory seizures, which in turn would lead to an earlier indication of an effective alternative treatment [2,3]. One potential candidate for biomarkers are circulating microRNAs; these are small noncoding RNAs present in extracellular human body fluids including plasma or serum. It is well known that induced changes of microRNAs levels are stable in plasma and can be strongly associated with specific disease states and it is noninvasively and easily quantifiable technique [4]. **Objective:** The aims of this study are: i) to determine whether robust and non-invasive molecular signatures of circulating microRNAs could help to improve diagnosis and or management of patients with epilepsy, including MTLE, FCD and genetic generalized epilepsies (GGE) and ii) to identify and validate whether these molecular signatures could be also associated with response to AEDs. **Methods:** Next-generation sequencing technology (RNA-seq) will be used to measure plasma levels of microRNAs in two phases of the study: an initial discovery phase with 10 patients with MTLE who are responsive to AED treatment, 10 patients with MTLE who are AED pharmacoresistant, 10 patients with FCD type II, 10 patients with GGE and 10 control individuals. In the subsequent validation phase, we will enroll an additional independent cohort of at least 100 patients with MTLE using the same diagnostic criteria as previously described and assay the most significant microRNAs found in phase 1 using RT-qPCR. We will also recruit an additional 200 healthy individuals without epilepsy as a control group. **Results/Discussion and Conclusion:** To date, we have successfully completed the recruitment of patients and have performed experiments in order to improve mRNA isolation and RNA-seq experiments in order to improve the protocols.

References: [1] Ferrie C D. Arch Dis Child 91(3): 206–209, 2006 [2] Engel J, Pitkänen A, Loeb JA, et al. Epilepsia 54(4): 61-69, 2013; [3] Mathern GW. Epilepsia.50 (9):45-50, 2009; [4] Mitchell PS, Parkin RK, Kroh EM, et al. Proc Natl AcadSci USA. 105:10513-10518, 2008.

Supported: CEPID-FAPESP.

CHARACTERIZATION OF GUT MICROBIOME IN PATIENTS WITH DIFFERENT FORMS OF EPILEPSY AND AUTOIMMUNE ENCEPHALITIS THROUGH METAGENOMIC ANALYSIS

D. Mejía-Granados D[1], B.S. Carvalho[2], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, School of Medical Sciences, [2]Department of Statistics, Institute of Mathematics, Statistics and Computer Science; University of Campinas, UNICAMP, Campinas, SP, BRAZIL and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction and Hypothesis: Over time, man and microorganisms have co-evolved simultaneously to integrate a complex ecosystem. This symbiotic relationship is responsible for the regulation of physiological processes related to nutrition and metabolism and are essential for the correct function and development of immune system [1]. The intestine is considered the largest reservoir of these microorganisms, and the colon reaches the maximum density of germs [2]. Studies have shown that enteric microbiota may play a key role not only in proper digestion of food and maintenance of homeostasis, but also in the progression of diseases mediated by autoimmune mechanisms [3]. Such bidirectional communication is achieved through different pathways that includes neuroanatomic, circulatory, endocrine and immune system pathways [4]. In this context, the main objective of this work is to apply next-generation sequencing techniques of faecal samples to characterize the intestinal microbiome composition in individuals with different forms of epilepsy, autoimmune encephalitis as well as healthy controls [5]. Results obtained could reveal the potential impact in the onset, phenotypic variability and activity of different types of neurological diseases. It could also contribute to the development of new therapeutic targets [6]. **Objective:** To determine if there are differences in gut microbiota composition between patients with different forms of epilepsy and autoimmune encephalitis in regard to healthy controls. **Methods:** Total faecal human DNA will be extract and purified using the QIAmp DNA stool Mini Kit (Quiagen) from a cohort of 90 individuals classified as follows: 30 patients diagnosed with mesial temporal lobe epilepsy; 30 patients with genetic generalized epilepsy and 30 patients affected with autoimmune encephalitis. All of them will be sex and age matched. DNA libraries will be sequenced via Illumina HiSeq 2500 platform. The reads of individual libraries will be paired and assembled into contigs using different algorithms (IDBA-UD, MIRA and MetaVelvet). Taxonomic classification, phylogenetic and functional analysis will be done applying tools like MEGAN and MG-RAST. Prediction gene will be perform using MetaGene approach. Final results will be statistically validated and shared. **Relevance:** The identification of new microbial communities capable of modulating and regulating different physiological processes related to the gut-brain axis will allow the development of alternative therapeutic strategies for the treatment of specific neurological conditions such as managing difficult epilepsies and autoimmune encephalitis. The data generated in our study will constitute the first gene catalogue of normal gut microbiota in Brazilian population. This data will be also banked/stored in a public database (www.bipmed.org) and therefore, used by any national or international research group interested in studying the intestinal microbiota and Brazilian individuals.

References: [1] doi:10.1016/j.chom.2015.04.011; [2] doi: 10.4103/0366-6999.190667; [3] doi: 10.1038/nn.4476; [4] doi: 10.1002/ana.24901; [5] doi: 10.4137/BBI.S12462 [6] doi: 10.1038/nature11209

INVESTIGATION OF HUMAN PLASMA DEPLETOME FROM SCHIZOPHRENIA PATIENTS

L. C. Silva-Costa[1], S. Garcia-Rosa[1], P. Baldasso[1], J. Steiner[2], D. Martins-de-Souza[1]

[1]Laboratory of Neuroproteomics, UNICAMP, Brazil; [2]University of Magdeburg, Germany.

Introduction: The proteome of blood plasma is an interesting source of biomarkers and a potential way to improve treatment outcomes in psychiatric disorders. But its wide dynamic concentration range makes reducing its complexity necessary. Thus, in proteomic studies, a few of the most abundant proteins are depleted and normally discarded. This high-abundance fraction, called the depletome, however, is a source of potential biomarkers due to nonspecific bindings with low abundance proteins[1,2]. In this work, we aimed to characterize the high-abundance fraction using a shotgun mass spectrometry approach. **Materials and Methods:** The depletome from 20 antipsychotic-free schizophrenia patients were obtained by a MARS-14 immunodepletion system and digested to peptides by trypsin. The peptides were injected into a

2D-RP/RP Acquity UPLC M-Class System coupled to a Synapt G2-Si Mass Spectrometer using ion mobility. Data independent analysis (DIA) was used and fragmentation spectra were obtained by MS/MS analysis. Identification of proteins was executed by Progenesis software against the Uniprot Human Proteome Database. Finally, systems biology analyses were performed *in silico* to characterize proteins and correlate their molecular function and biological processes: HPRD was used to characterize identified proteins and DAVID Bioinformatic Database was applied to perform Gene Ontology functional annotation and enrichment test. **Results:** 83 proteins were identified in the plasma depletome, besides the 20 highly abundant depleted proteins. Of these 83 proteins, most of them have unknown biological processes and molecular functions, and 2 proteins exhibit experimental evidence at the transcript level in the HPRD Database. Results from the DAVID functional annotation chart, an enrichment analysis tool (p-value<0.01), reported 25 main biological processes such as receptor-mediated endocytosis, complement activation and regulation of immune response, along with 13 different molecular functions like antigen, heme, and hemoglobulin binding. **Discussion:** Proteins associated to the regulation of immune response and transport processes were identified in the depletome, which may be linked to the response and distribution of medication in the body. The immune system plays an important role in the etiology of psychiatric diseases. Patients with schizophrenia may present increased levels of inflammatory markers, which may affect the functioning of neurotransmitters through hypothalamic axes. Some antipsychotic medications may be associated with an immunomodulatory role [3,4]. Some of these proteins act in the transport of high density lipoproteins and are generally upregulated in patients with schizophrenia [5]. **Conclusion:** Depletome characterization from schizophrenia patients demonstrates the importance of investigating this fraction, considering the intrinsic potential of plasma to participate in and exhibit changes related to endogenous and exogenous stimuli. Furthermore, the high-abundance fraction of human blood plasma, usually neglected, carries proteins involved in the most diverse biological processes, making this material a potential source of diagnosis and response to medication biomarkers in psychiatric disorders.

References:[1]T. A. Koutroukides et al., *J. Sep. Sci.*, vol. 34, no. 13, pp. 1621–1626, Jul. 2011. [2]J. A. J. Jaros et al. *Methods Mol. Biol.*, vol. 1002, pp. 1–11, 2013. [3]S. M. Gibney and H. A. Drexhage, *J. Neuroimmune Pharmacol.*, vol. 8, no. 4, pp. 900–920, 2013. [4]Y. Li, et al., *Mol. Biosyst.*, vol. 8, no. 10, p. 2664, 2012. [5]K. A. McGhee, et al., *Schizophr. Res.*, vol. 76, no. 2–3, pp. 231–238, 2005.

ASSESSING THE PRESENCE OF DRAVET SYNDROME-RELATED *SCN1A* MISSENSE MUTATIONS IN DATABASES OF INDIVIDUALS FROM DIVERSE POPULATIONS

M. C. Gonsales[1], M. A. Montenegro[2], P. Preto[2], M. M. Guerreiro[2], I. Lopes-Cendes[1]

Departments of [1]Medical Genetics and [2]Neurology, School of Medical Sciences, University of Campinas, UNICAMP.

Introduction: Even with major technical advances in sequencing analysis, interpreting the clinical significance of genetic variants found in molecular tests can be challenging. This is particularly problematic for variants of unknown significance (VUS), which comprises mostly missense mutations and variants located within splice sites. Recent studies have postulated that one of the most reliable considerations in the interpretation of VUS is establishing its frequency in control populations [1]. In the present study, we carried out a comprehensive meta-analysis of previously described *SCN1A* mutations in Dravet syndrome (DS) patients, along with ones found in our cohort, and assessed the presence of missense mutations in databases of different populations. **Materials and Methods:** To expand our data on *SCN1A* mutations in DS patients for further analysis, we performed an updated meta-analysis of published studies. Literature search was performed on Pubmed (https://www.ncbi.nlm.nih.gov/pubmed/) up to December 2017. We conducted a systematic review of *SCN1A* mutations that were publicly available. We interrogated four different databases of individuals from diverse populations to measure the allele frequency of the *SCN1A* missense mutations reported in DS patients: BipMed (http://bipmed.org/), NHLBI Exome Sequencing Project (ESP) (http://evs.gs.washington.edu/EVS/), gnomAD (http://gnomad.broadinstitute.org/) and 1000 Genomes (http://www.internationalgenome.org/). **Results:** The compilation of *SCN1A* mutations reported in the literature, in addition to those identified in our laboratory, revealed a total of 910 potentially deleterious nucleotide variants in patients with DS. Of these, 45.9% (418/910) are missense mutations. We identified 28 of the 418 *SCN1A* missense mutations in the databases of individuals from different populations. Two variants (c.1811G>A and c.5782C>G) are present in all four databases, and they are the only DS-related variants that have allele frequencies higher than 1% in any of the populations investigated. Both are also the only variants found in the Brazilian population database (BipMed), with allele frequencies of approximately 0.5%. **Discussion:** We observed that few *SCN1A* missense mutations reported in DS patients are present in population databases, thus showing that the mutations in *SCN1A* associated with DS are extremely rare in the general populations. Only two of them have allele frequencies higher than 1% in at least one population and they are present in all four population databases. In addition, a recent study critically re-evaluated these variants regarding their pathogenicity and considered them benign [2]. Therefore, one cannot rule out the possibility of non-pathogenic *SCN1A* variants erroneously reported as associated with DS. We also noticed that populations of non-European ancestry are still underrepresented in the databases, affecting the interpretation of variants present in individuals from not well represented ethnicities. **Conclusion:** In our meta-analysis, we observed many VUS among the changes described in patients with DS, highlighting the necessity of using complementary tools for analysis such as population database investigation to better characterize these variants. However, we observed that some ethnicities remain underrepresented in population databases. Therefore, initiatives as the BipMed are important to enhance genomic data available from different ancestry groups.

References: [1] Richter S et al., Ann Oncol. 24 (Suppl 8):viii69-viii74, 2013;[2] Lal D et al., PLoS One 11(3):e0150426, 2016.

ANXIETY AND DEPRESSION SYMPTOMS DISRUPT RESTING STATE CONNECTIVITY IN PATIENTS WITH GENERALIZED EPILEPSIES

D.S. Garcia[1], M.K.M. Alvim[1] , M. Polydoro[1], A. Ishikawa[1], T. Zanão[1], M.H. Nogueira[1], J.C.V. Moreira[1], B.M. Campos[1], M.E. Morita[1], L.E. Betting[2], D. Gross[3], F. Cendes[1], C.L. Yasuda[1]

[1]Neuroimaging Laboratory, UNICAMP, [2]Botucatu Medical School- UNESP, [3]University of Alberta.

Introduction: Idiopathic Generalized Epilepsies (IGE) have been associated with good response to antiepileptic drugs (AEDs), normal intelligence, unremarkable MRI (on visual inspection) and genetic predisposition. However, some studies have described variable proportions of poor response to AEDs (20 -90%)[1,2], focal abnormalities on quantitative MRI analyses (functional and structural)[3,4] associated with both psychiatric[5,6] and cognitive alterations[3,7]. Our objective is to investigated the impact of symptoms of anxiety and depression on brain functional connectivity in IGE patients and evaluate the AED response. **Materials and Methods:** We evaluated 74 IGE patients (ILAE criteria), older than 16 years-old, with at least 2 years of follow up . Subjects were classified in three groups: Seizure-free (SF, n=12), Pharmacoresistant (PhR, n=14) and Fluctuating (FL, n=48). Third-eight patients performed a 3T Resting-state functional/structural MRI, answered the Beck Depression and Beck Anxiety inventories (BAI/BDI). Therefore, patients were classified in: ANX-DEP-group: 13 patients who presented symptoms of depression and anxiety (BDI or BAI score>20 and the other >=12) and ASYMPTOMATIC-MILD-group: 25 patients (both scores<12). For control group, 38 healthy volunteers (paired by age and gender). Functional connectivity (FC) analysis was performed with MATLAB2014/spm12/UF2C-TOOLBOX to compare alterations in 12 Resting State Networks between each group of patients and controls. Results of FC analyses were reported with P<0.05, corrected with false-discovery-rate for multiple comparisons. **Results:** PhR-group presented higher levels of both BAI and BDI; however, significant differences were observed exclusively for BAI scores as PhR-group presented higher values than SF-group (p=0.008). Patients with concurrent anxiety and depression symptoms were 7.7 times more likely to exhibit refractory seizures than those without concurrent symptoms (95% CI 1.57-37.4). In neuroimagin analysis, connectivity was reduced between Dorsal DMN (Default Mode Network) and both Visuospatial network/Dorsal Attention; similarly, there were decreases between Ventral DMN and Left Executive Control Network (LECN). However, only the ANX-DEPR-group displayed reduced correlation within the Visuospatial network/ Dorsal Attention. Moreover, ANX-DEPR-group exhibited opposite connectivity between Ventral DMN and LECN and demonstrated increased connectivity between the Ventral DMN and LECN. **Discussion:** Most IGE patients presents a fluc-

tuating pattern of seizure control through long-term follow-up. Patients with pharmacoresistance are more likely to present depressive/anxiety symptoms than those seizure-free. Patients with concurrent symptoms of anxiety and depression may have different functional connectivity than asymptomatic patients. **Conclusion:** Our results indicate that IGE patients with concurrent symptoms of anxiety and depression may have more disrupted FC than asymptomatic ones. Further studies with larger sample may explore the interaction with psychosocial outcomes.

References: [1]von Podewils F, et al. , Epilepsy research;108:1221-1227, 2014; [2]Martinez-Juarez IE, et al. Brain : a journal of neurology;129:1269-1280, 2006; [3]O'Muircheartaigh J, et al. Brain : a journal of neurology;135:3635-3644, 2012; [4]Wandschneider B, et al. Epilepsia;53:2091-2098, 2012. [5]Akanuma N, et al. Epilepsy & behavior; 13:248-2512008; [6]de Araujo Filho GM, et al. Epilepsy & behavior : E&B;27:385-392, 2013; [7]Sarkis RA, et al. Epilepsy & behavior;28:370-373, 2013.

EFFECT OF THE NON-PERIODIC ELECTRICAL STIMULATION OF THE BASOLATERAL AMYGDALA ON PATHOLOGICAL ANXIETY

L. A. Réboli[1], J. C. Oliveira[1], R. M. Maciel[1], C. Q. Tilelli[2], L. C. M. Damázio[3], V. R. Cota[1*]

[1]Laboratório Interdisciplinar de Neuroengenharia e Neurociências (LINNce), *Departamento de Engenharia Elétrica (DEPEL), Universidade Federal de São João Del-Rei (UFSJ), São João Del-Rei, Minas Gerais, Brazil [2]Docente, UFSJ/ Campus Centro-Oeste Dona Lindu (CCO), [3]Docente, UFSJ/ Campus Dom Bosco (CDB).

Introduction: Previous research of our group demonstrated that non-periodic electrical stimulation (NPS) with randomized inter-pulse intervals, even if low frequency on average (four pulses per second), applied to the basolateral amygdala (BLA) is capable of suppressing both acute and chronic spontaneous seizures in animal models [1,2]. In addition to its relation with epilepsy [3], connections of the BLA with other brain structures have roles in several neural functions [4] and pathologies [5], such as anxiety [6]. In this work, we tested whether NPS of the BLA would be therapeutic for pathological anxiety in animal models of stress induced by chronic restraint [7]. Anxiety levels were assessed through the elevated plus maze (EPM) and open field (OF) tests [8]. **Materials and Methods:** A total of 41 males Wistar rats (250 to 350 g) were randomly assigned to four groups: control (CTRL: EPM, n = 14; OF, n = 13); stressed control (CTRL_est, n = 10); stressed surgical control (SHAM_est, n = 9); and stressed / stimulated with NPS (NPS_est, n = 8) (protocols 025/2015 and 023/2016 of the Ethics Committee for Animal Research of our university). In a first experiment aimed at validating the stress model, animals of the CTRL_est group were submitted to the sub-chronic stress protocol induced by four consecutive 1-hour daily sessions of physical restraint and their anxiety levels were compared to control animals. A second experiment evaluated the anxiolytic effect of NPS by comparing animals of the SHAM_est and NPS_est groups, both of which underwent a surgical procedure for implantation of deep bipolar stimulation electrodes in the BLA bilaterally, to stressed animals. NPS_est group was stimulated during behavioral tests. Exploration time of each arm in the EPM was counted, as well as the time of permanence in the center and in the periphery and the crossings / locomotion in the OF. Electrode position was confirmed histologically. Data were considered statistically significant at $p < 0.05$. **Results:** In the first experiment, animals of the CTRL_est group remained longer periods in the closed arm of the EPM in relation to CTRL group ($p < 0.0001$, *t* test). CTRL group presented a greater number of crossings than CTRL_est in both the center ($p < 0.05$, *t* test) and in the periphery ($P < 0.01$, *t* test) of the OF. In the second experiment, NPS_est group remained in the closed arm of the EPM for less time when compared to CTRL_est group ($p < 0.05$, post hoc Tukey test). Moreover, the NPS_est group explored more the center of the OF when compared to CTRL_est group ($p < 0.05$, post hoc Tukey test). **Discussion:** Anxious animals tend to remain for longer periods of time in the closed arm of the EPM, to explore more peripheral sectors, and to present a smaller number of crossing in the OF [8]. Thus, results of the first experiment indicated a higher level of anxiety in the CTRL_est group, validating the stress model. By the same token, results of the second experiment show that NPS_est group exhibited lower levels of anxiety, suggesting NPS has an anxiolytic effect. **Conclusion:** The present work confirmed that physical restraint induces stress in animals and suggests that the NPS may have a therapeutic effect on pathological anxiety.

References: [1] doi: 10.1016/j.yebeh.2014.05.005; [2] doi: 10.1002/jnr.23741; [3] doi: 10.1016/j.eplepsyres.2006.08.008; [4] doi: 10.1146/annurev.ne.15.030192.002033; [5] doi: 10.1523/JNEUROSCI.1285-06.2006; [6] doi: 10.1016/j.biopsycho.2006.01.008; [7] doi: 10.1016/j.physbeh.2005.12.007; [8] Buccafusco JJ, Methods of behavior analysis in neuroscience, 2nd ed., 2009.

COGNITIVE ASSESSMENT OF PATIENTS WITH ATRIAL FIBRILLATION

B. G. Caseli[1], L. F. L. Pegoraro[2], D. S. Silva[3], A. C. Coan[3]

[1]Neurovascular Group, Department of Neurology, UNICAMP; [2]Department of Medical Psychology and Psychiatry, UNICAMP, Campinas, SP, Brazil; [3]Neuroimaging Laboratory, UNICAMP.

Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia and is one of the most important and emerging cardiovascular disease due to its impact on both mortality and morbidity [1]. The prevalence of AF ranges from 0.1% in patients up to 55 years to more than 9% for the ones over 85 years old [2]. AF may be an important factor of cognitive and functional decline, even in the absence of stroke [3, 4]. Authors argue that patients with AF, even without apparent functional or cognitive impairment, should be submitted to assessment for cognitive decline annually due to their higher prevalence and prognostic importance [4]. However, most studies of cognitive decline in patients with AF published so far have primarily focused on general cognitive screening batteries. The aim of this study was to analyze the cognitive performance of patients with AFwithout stroke using a broad neuropsychological battery. **Materials and Methods:** Twenty patients with AF were selected from the Cardiology Ambulatory of the Clinical Hospital of UNICAMP and age, sex and level of schooling-matched twentycontrols were selected from different ambulatories of the Clinical Hospital of UNICAMP. Patients and controls were also paired according to cardiovascular risk factors other than AF. All individuals signed an Informed Consent prior to the study enrollment. The data were collected in the period from March to October of 2017. After accepting to join the study, the subjects were submitted to a neurologicalevaluation conducted by a neurologist and magneticressonance imaging to exclude silent strokes. Individuals with clinical or neuroimaging suspicious of stroke were excluded. Individual were then submittedto the neuropsychological assessment. The neuropsychological assessment included the evaluation of awareness, executive functions, memory processes, praxys, language and visuoconstructive abilities. The battery was performed in a single session of 60 minutes. Individuals with severe clinical conditions, mental disorders or severe cognitive deficiency were excluded. The performance of the tests between the two groups was compared through Mann-Whitney test [5]. **Results:** We observed significant differences in patients with AF compared to the control group mainly in executive functions,such as cognitive flexibility, planning, operational memory, visuospatial abilities and inhibitory control. **Discussion:**AF has been associated with changes in hemostasis, endothelial injury, platelet dysfunction, low cardiac output, increased rates of silent lacunar infarction and microembolization [6]. All these mechanisms may secondarily affect cognition. Our data suggest that, in the absence of clinical and neuroimaging evidence of stroke, these or other mechanisms may lead to brain damage,manifestedas cognitive dysfunction, particularly in executive functions. Therefore, AF may lead to impairments in functionality and compromise the quality of life of these patients. **Conclusion:** Patients with AF without stroke can present cognitive abnormalities, particularly in executive functions.

References: [1] doi.org/10.1161/CIR.0b013e3182456d46;[2] Wajngarten, M. et al., PROCLIM (1): 9-46, 2008;[3] doi: 10.1503/cmaj.111173. Epub 2012 Feb 27; [4] doi: 10.1016/j.ahj.2014.12.015. Epub 2015 Jan 13; [5] Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. Ann MathStat. 1947;18:50–60;[6] doi: 10.1093/eurheartj/ehn341. Epub 2008 Jul 29

USING WGCNA AND NERI ALGORITHMS FOR THE IDENTIFICATION OF BIOLOGICAL PATHWAYS ASSOCIATED TO SCHIZOPHRENIA

A.S. Feltrin[1], A.C. Tahira[2], S.N. Simões[3], H. Brentani[2], D.C. Martins-Jr [1]

[1]CMCC - Universidade Federal do ABC, [2]IPq-HCFMUSP-USP, [3]Instituto Federal do Espírito Santo.

Introduction: Using two gene expression databases related to schizophrenia (BAHN and KATO), we propose a new approach consisting of combining the results of two network analysis algorithms: Weighted Gene Correlation Network Analysis (WGCNA) [1] and Network-Medicine Relative Importance (NERI) [2]. Considering the differences between the two methods, our hypothesis is that both are capable of producing compelling results related to different aspects of schizophrenia's biological pathways; therefore, are complementary to each other. For that, we used replication and enrichment analysis using public databases. **Materials and Methods:** WGCNA uses gene expression from two groups to build co-expression pairwise correlation matrices, using connectivity parameters for evaluation of the network. NERI also uses expression data, but its network construction is based on the integration of PPI (protein-protein

interaction) databases, gene expression, and a previously chosen seed genes list. The network analyses are based on shortest ranking path and relative importance calculation. We conducted an enrichment analysis using DAVID 6.8 (Database for Annotation, Visualization and Integrated Discovery) [3] for the identification of partial biological function of each result as well the SuperExactTest (*R* Package) [4] to calculate the intersection of the gene lists of WGCNA and NERI results. The Modular Single Set Enrichment Test (MSET) [5] analysis for GWAS, transcriptome, methylation and *de novo* mutation databases related to schizophrenia was applied to evaluate the replication and accuracy of our new approach when compared with each method in separate. **Results:** The WGCNA module represents a final network of 435 and 300 genes on BAHN and KATO expression data. The enrichment analysis (DAVID 6.8) of this group using PPI modules leads to 88 genes across 10 hyper-represented human modules (Bonferroni adj.p<0.05), mostly involving immunological and inflammatory processes. By using NERI, the final gene list was 150 genes for both BAHN and KATO with the enrichment analysis leading to modules related to glutamate receptor signaling, MAP Kinase, apoptotic processes and neurotrophin pathways. **Discussion:** Both methods achieved statistical relevant replication results (p<0.05, SuperExactTest), but only with one gene shared between WGCNA and NERI. In the MSET analysis, NERI was capable of achieving meaningful results for the methylation and *de novo* mutation databases; while our proposal of combining both results achieved better results for these two databases and additionally, for transcriptome (also increasing the number of candidate genes for each list). **Conclusion:** Our study suggests that using both methods in combination could be a promising approach for establishing a group of modules and pathways related to schizophrenia (or any complex disease). Combining both methods results provided a meaningful outcome, resulting on genes related to different aspects of schizophrenia, such as immunological activity, glutamate and neurotrophin pathways.

References: [1] Langfelder P. et al. BMC Bioinformatics, 9:559, 2008; [2] Simões, SN. et al. BMC Bioinformatics, 16 Suppl. 19:S9, 2015; [3] Huang, DW. et al. Genome Biol. 8(9): R183, 2007; [4]; Wang, M. et al. Sci. Rep. 5: 16923, 2015; [5] Eisinger, BE. et al. BMC Neurosci. 14: 147, 2013.

KINDLING EFFECTS DURING ZEBRAFISH BRAIN DEVELOPMENT

[1]T.G. Parolari, [1]V.C. Fais, [2]N. Peixoto [1]C.V. Maurer-Morelli

[1]Zebrafish Laboratory, Department of Medical Genetics, FCM, UNICAMP, 2Electrical and Computer Engineering Department - George Mason University, Fairfax, VA.

Introduction: In the last decade, *Danio rerio*, popularly known as zebrafish, has been used as a model for acute seizures[1]. Even so, there is no indication in the literature that the zebrafish can become chronically epileptic. In order to understand the epileptogenic process, electrical or chemical kindling have been used in animal models, mainly in rodents. Given the advantages of zebrafish for genetic, cellular, and drug screening studies, it is important to investigate whether zebrafish is able to become chronically epileptic. The main aim of this study is to investigate the effect of sub-convulsive doses of pentylenetetrazole on molecular, behavioural, and eletrophisiological patterns during brain development in the zebrafish larvae. **Materials and Methods:** This study was approved by the Ethics Committee on Animal Use (CEUA) of UNICAMP #4426-1, #4660-1 . Wild-type zebrafish larvae at 5 days post-fertilization (dpf) were divided in Control Group (CG) and Kindling Group (KG). Animals from KG were exposed to sub-convulsive doses of pentylenetetrazole (PTZ) at 7.5 mM for 2 minutes over four weeks (once a day, Monday to Friday). Behaviour and molecular profiles were assessed immediately after the first exposure to PTZ (5 dpf) and later at 9, 16 and 23 dpf (n = 25, each group). Animals from CG were handled in the same way but in PTZ-free water. Behavioural analysis were recorded by the Danio Vision equipment and analysed with EthoVision software for quantification of velocity and distance traveled. Real-time PCR were applied to assess the brain mRNA expression of *il1b, bdnf*, *kalrn, fosb* and c-*fos* genes using TaqMan™ system (Applied Biosystems, Foster City, CA, USA). For the electrophysiological analysis we immersed larvae in water with 30 mM PTZ for 30 minutes; for control larvae the same condition was applied but animals were immersed in PTZ-free water. The electrode was lowered through a triaxial micro manipulator until just touching the optical tectum. Signals were pre-amplified by 10 and filtered from 1 to 1,000 Hz. Amplification was performed by an Intan RHD2000 by 100, to a final total amplification of 1,000. Most of the seizure activity presented signals of amplitudes from 100 to 500 uV. All larvae were previously anesthetized in 0.002% tricaine, 10 uM D-tubocurarine, and immobilized in 1.2% low-melting agarose. **Results:** Daily treatment significantly increased distance traveled and velocity ($p \leq 0{,}001$) in the KG at 5, 9, and 16 dpf. The 23 dpf KG was not evaluated here. Regarding the transcript profile from candidate genes, we did not identify statistically significance between groups and analyzed genes; however, we notice an increased in transcript pattern for *cfos* and *fosb* genes in the KG at 16 and 23 dpf in comparison to the CG at the same age. Besides, we also observed an increased transcript pattern for *bdnf* and *kalrn* in the KG at 16 dpf in comparison to the CG. The electrophysiological parameters were successfully recorded in this study to confirm the ictal finding in the different ages of neuronal development using a cost-effective setup. **Discussion:** Although no seizures were observed during the kindling protocol, we found an increase in the quantitative behavior (distance and velocity) in all ages tested. Gene expression profile showed no statistical difference when both groups and ages were compared; however, there is a tendency to increase during the treatment. **Conclusion:** Zebrafish as a kindling model will be a valuable platform to study the neurobiological processes that underlie the epileptogenic process; however, additional studies are underway in order to investigate if the zebrafish larvae brain is prone to be chronically epileptic.

References: [1] Baraban, S. C. et al., Neuroscience, v. 131, n. 3, p.759–768, 2005.

TRANSCRIPTOMIC ANALYSIS OF SUBICULUM REGION IN ANIMAL MODEL OF MESIAL TEMPORAL LOBE EPILEPSY (MTLE) INDUCED BY PILOCARPINE

B. B. Aoyama[2], A. M. Canto[1], A. H. B. Matos [1], B. S. Carvalho[3], I. Lopes-Cendes[1], A. S. Vieira[2]

[1]Department of Medical Genetics, School of Medical Sciences, [2]Department of Structural and Functional Biology, Institute of Biology,[3]Department of Statistics, Institute of Mathematics, Statistics and Computer Sciences; University of Campinas (UNICAMP); and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: Temporal lobe epilepsy (TLE) is the most frequent type of epilepsy in adults and these patients usually are resistant to treatment. Among the different types of TLE, mesial temporal lobe epilepsy (MTLE) is the most frequent and it is characterized by damage in the mesial temporal structures, such as the hippocampus formation. Other structures belonging to the hippocampus formation, such as subiculum, dentate gyrus and enthorrinal cortex, are also altered in MTLE. The subiculum is an important structure because it forms the transition that connects the hippocampus with the enthorrinal cortex, which allows for high amplification and modulation of the neuronal response, and it is involved in the recovered short-term memory and spatial memory codification. This study aims to understand the molecular role of the subiculum in MTLE in the classical model of pilocarpine induced epilepsy. **Materials and Methods:** We used 4 sham-control and 4 pilocarpine treated rats (CEMIB-UNICAMP) and performed LCM (Zeiss). We extracted the subiculum from the brain tissue using a surgical microscope (Zeiss). Then we extracted RNA using 1 ml Trizol, and we separate the organic (proteins) and aqueous (RNA) phases using 0.5 ml Chloroform and 0.5 ml Isopropanol to precipitate RNA in solution. Then we wash pellets with 70% alcohol and resuspend them with water. Thereafter, we made RNA library's using Truseq (Illumina) library preparation kit according to manufacturer instructios. The quantifications of RNA library's were made with real time PCR. For this purpose, we used laser capture microdissection (LCM) to isolate cells from the subiculum, which were subsequently used transcriptomics studies. **Results:** Quantifications of dorsal subiculum control libraries were: (SDC) 12 nM (SDC2), 4.3 nM (SDC3), 8.6 nM (SDC4), 28.5 nM (SDC5) and ventral subiculum control (SVC) 59 nM (SVC2), 230 Nm (SVC3), 10.2 nM (SVC4) and 87.2 (SVC5). Quantifications of dorsal subiculum pilocarpine treatment libraries (SDP) were 0.5 nM (SDP2), 3.1 nM (SDP3), 18.6 nM (SDP4), 32.6 nM (SDP5) and the ventral subiculum treatment (SVP) are 120 nM (SVP2), 0.17 nM (SVP3), 6.7 nM (SVP4), 98.6 nM (SVP5). **Discussion:** These quantification shows that RNA extracted after microdissection were able to produce adequate amounts of sequencing libraries. After the quantification, we will submit libraries from control dorsal and ventral, and them respective treatment by pilocarpine to high throughput sequencing using Illumina Hiseq platform. **Conclusion:** This present work pretends to show the importance of molecular mechanisms in epileptogenesis process in MLTE.

Support: FAPESP, CNpQ.

INVESTIGATION OF NEURAL DESYNCHRONIZATION AS A MECHANISM OF SEIZURE SUPPRESSION BY NONPERIODIC ELECTRICAL STIMULATION

J.C. Oliveira[1], S.M.A.F. Rodrigues[1], R.M. Maciel[1], L.A. Réboli[1], L.C.M. Damázio[2], V.R. Cota[1,3]

[1]Laboratório Interdisciplinar de Neuroengenharia e Neurociências (LINNce) / UFSJ [2]Departamento de Medicina (DEMED), Universidade Federal de São João del-Rei (UFSJ) [3]Departamento de Engenharia Elétrica (DEPEL), Universidade Federal de São João del-Rei (UFSJ).

Introduction: In the animal model of seizures induced by pentylenetetrazole (PTZ), electrical stimulation (ES) applied with a random interpulse interval (nonperiodic stimulation - NPS) to the amygdala has anticonvulsant properties [1-3]. According to the notion that seizures are episodes of neural hypersynchronism [4,5], our hypothesis is that NPS may wield its effect by desynchronizing neural networks involved in the ictogenic process. One way to measure neural synchronism would be through the interaction of neural oscillations in different frequency bands. There has been particular interest in the modulation of the amplitude of high frequency oscillations by the phase of low-frequency oscillations (phase-amplitude coupling - PAC), which can be measured by the modulation index (MI) [6]. In this sense, the aim of this study is to investigate - by means of behavioral and electrophysiological assessments - the hypothesis that NPS suppresses seizures by desynchronizing neural oscillators responsible for ictogenesis. **Materials and Methods:** Electrophysiological recordings from cortex (CX), hippocampus (HP), and thalamus (TH) were performed and NPS was applied to the bilateral amygdala (AMY) in animals subjected to the PTZ continuous infusion model (10 mg/ml/min). Seven groups were evaluated according to the thresholds (t) of convulsant insult and the use or not of NPS until the onset of forelimb clonus (FC) or generalized tonic-clonic seizures (GTCS): CTRL-GTCS (n=15), CTRL-FC (n=14), NPS-GTCS (n=16), NPS-FC (n=12), NPS-FCt (n=7), NPS-GTCSt (n=13), NPScont-GTCSt (n=14). Threshold of PTZ required to trigger FC and GTCS behaviors were calculated. The MI technique used to evaluate PAC between different frequency bands (phase frequencies: 0-2 Hz, 2-6 Hz, and amplitude frequencies: 8-14, 14-30, 30-60, 60-100, 100-200, 200-300 Hz) in electrographic recordings is described elsewhere [6] (ethical protocol 31/2014). **Results:** The PTZ threshold to FC and GTCS were significantly increased in NPS-FC and NPS-GTCS when compared to control groups. Survival time of all NPS groups was statistically greater than that of control groups. NPS-GTCSt and NPScont-GTCSt groups had a lower number of convulsive behavior occurrence and deaths. For the analysis of the coupling between frequencies, the CTRL-GTCS and NPS-GTCS groups were compared. Analyses are related to the following five electrographic periods: 30 seconds (s) of PTZ infusion onset, 30 s preceding the FC, during FC, tonic phase, and clonic phase. For 0-2 Hz phase frequency, MI was significantly higher for CTRL-GTCS in the last 30 s preceding the FC in the amplitude frequencies of 8-14 Hz (in HP), 14-30 Hz (in HP and TH), and 30-60 Hz (in CX, HP and TH). It was also significantly higher in the tonic phase in the range of 30-60 Hz (in HP and TH), and in the clonic phase in the range 30-60 Hz (in TH). For the phase frequency of 2-6 Hz, MI was significantly higher for the CTRL-GTCS in the last 30 s preceding FC in the 8-14 Hz amplitude frequency range (in CX and HP), and in the tonic phase in the amplitude frequencies bands 8-14 Hz (in HP) and 14-30 Hz (in HP and TH). **Discussion and Conclusion:** Our results corroborate previous studies relating epilepsy to hypersynchronism and the notion that NPS suppresses seizures by desynchronization of epileptogenic networks. Furthermore, additional behavioral findings of groups with different thresholds of convulsant insult suggest that NPS interferes with the levels of excitability / neural synchronism, generating variations in the behavioral responses, and survival time and rate. Finally, new findings from electrographic studies contributed to characterize a new form of desynchronization, considering that the use of NPS was able to promote substantial decrease of the PAC between specific pairs of frequencies in particular periods during seizure evolution.

References: [1]doi:10.1016/j.yebeh.2008.09.006;[2]doi:10.1016/j.yebeh.2014.05.005; [3] doi:10.1016/j.yebeh.2012.01.004;[4]doi:10.1016/j.neuron.2006.09.020; [5] doi:10.1016/j.yebeh.2013.12.034; [6] doi:10.1152/jn.00106.2010

TRANSCRIPTOME INVESTIGATION ON THE MECHANISMS INVOLVED IN HIPPOCAMPAL SCLEROSIS ASSOCIATED WITH MESIAL TEMPORAL LOBE EPILEPSY

G.G; Zanetti[1], E. V. Dias [1], I. Lopes-Cendes[2], A. Vieira[1]

[1]Department of Structural and Functional Biology, [2]Department of Medical Genetics, School of Medical Sciences, University of Campinas (UNICAMP); and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, BRAZIL. [4]Multidisciplinary Center for Biological Investigation (CEMIB); University of Campinas (UNICAMP), Campinas, SP, Brazil.

Introduction: Temporal Lobe Epilepsy (TLE) is the most common adult focal epilepsy, and Mesial Temporal Lobe Epilepsy (MTLE) is the most frequente TLE subtype. The most frequent neuroimage finding in MTLE patients is Mesial Temporal Sclerosis, that has hippocampal atrophy as one of its main components. The electrical stimulation of the perforant pathway for a period of 8 hours in awake rats reproduces hippocampal lesion with a morphology that resembles the human condition without the induction of an episode of status epilepticus (SE). In order for animals to survive such a long period of stimulation in this model it is necessary two days of 30 minutes preconditioning sessions by electrical stimulation of the perforant pathway. The preconditioning sessions probably result in an increase in inhibition, or a reduction in excitation in the hippocampus. It is possible that an intense induction of excitatory activity in this region concomitant with high inhibitory activity is a crucial factor for the extensive neural degeneration observed in this animal model. However, the molecular mechanisms, and even which components of the inhibitory or excitatory systems are changes by preconditioning are still unknown. Therefore, the objective of the present project is to explore the biological processes, and the respective molecular components involved in the preconditioning by electrical stimulation of the hippocampus employing transcriptomic analysis of different sub-regions from this tissue. These analyses would give new insights into the interrelations between molecular mechanisms and functional changes in the hippocampus that would be involved in hippocampal atrophy. Such data could point novel components and mechanisms relevant to the pathophysiology of human MTLE. **Materials and Methods:** We used 5 sham-control and 5 stimulated rats (CEMIB-UNICAMP) and performed the surgery to implant the electrodes. We are going to make the microdissection of hippocampus (CA1, CA2, CA3 and Dentate Gyrus) using the PALM system (Zeiss) using glass slides covered by a PEN membrane (life technologies) with the material stained with Cresyl. Subsequently, we are going to do transcriptome analysis by high performance sequencing using the TruSeq Stranded mRNA LT (Illumina), and a HiSeq platform. **Objective:** To investigate biological process and the respective molecular components, that are responsible for the plasticity induced by preconditioning in an experimental animal model of hippocampal sclerosis associated with mesial temporal lobe epilepsy. **Relevance:** This study will allow a better understanding of the molecular mechanisms at the hippocampus that may prevent neuronal death following long term electrical stimulation, being a study capable of showing new pathways and differential expression of several RNAs at the hippocampus.

INVESTIGATION OF BRAIN CHANGES DUE TO MOTOR REHABILITATION BASED ON VIRTUAL REALITY GAMES IN STROKE PATIENTS

J. A. Feitosa[1,4], A. Camargo[2,4], R. F. Casseb[3,4], B. R. Ballester[5], P. Omedas[5], P. Verschure[5], L. L. Min[2,4], G. Castellano[1,4]

[1]Neurophysics Group, IFGW, UNICAMP, Campinas, Brazil, [2]Neurology Dept., FCM, UNICAMP, Campinas, Brazil, [3]Calgary University, Calgary, Canada, [4]BRAINN, FAPESP, [5]SPECS, Universitat Pompeu Fabra, Barcelona, Spain.

Introduction and Hypothesis: The most commonly affected motor function in stroke sufferers is the upper limbs' motion. Functional deficit of the upper limbs has received special attention by rehabilitation teams because these members are related to the quality of life of the survivors. Several techniques have been used in the motor recovery process of the upper and lower limbs of stroke patients, where intensive and repeated task-specific training gives satisfactory results [1]. But it is still a challenge to implement such techniques in a real environment, such as in the rehabilitation clinics and health clinics of the Brazilian health system (SUS), and to overcome patients' loss of interest in repeated tasks. For this reason, rehabilitation programs based on Virtual Reality (VR) have been highlighted as alternative therapy for motor recovery [1]. In this line, [2] implemented a computer-based rehabilitation system to treat a group of stroke patients. Patients showed significant improvements in the speed of movement of the affected arm and in other clinical scales when compared to stroke patients who used other complementary therapies. However, there have been no studies yet showing the effect in patients' brains of the use of this

rehabilitation therapy. **Objective:** The main goal of this project is to evaluate possible brain changes, both structural and functional, of patients undergoing VR therapy using the system developed in [2]. Specifically, we aim to: 1) Evaluate the neuroplasticity of stroke patients due to the traditional therapy allied to VR therapy; 2) To create, for the purposes of this research, a rehabilitation environment using VR in the UNICAMP's hospital (HC-UNICAMP); 3) Verify if the fMRI technique is able to identify and validate changes in plasticity; 4) Characterize brain changes resulting from the complementary treatment (VR). **Methods:** Thirty chronic stroke patients with upper limb motor deficit will be recruited. Subjects will be randomly divided into two groups: the experimental group, that will receive the traditional physiotherapy treatment plus VR, and the control group, that will receive the traditional treatment only. All patients will perform 24 sessions, 1h each – for the experimental group the sessions will be divided in: 20 min of VR therapy, 20 min of traditional physiotherapy and, again, 20 min of VR. The participants will be scanned on a 3.0 T magnetic resonance imaging device (Philips Achieva) in three distinct moments: before the therapy, after 12 sessions and after 24 sessions. In addition, functional and neuropsychological evaluations will also be performed in the same three moments. The project was approved by the Ethics Committee of Unicamp, and all subjects will be asked to sign an informed consent form prior to data acquisition. **Relevance:** The participants of this research may benefit from the rehabilitation sessions that they will receive, which even in the control group, should potentiate their recovery and return to activities of daily living. Once the rehabilitation environment has been implemented, other patients in HC – UNICAMP will benefit from this treatment. The results of this research will be published in highly regarded journals and presented in national and international congresses, symposia and workshops, contributing to the dissemination of science, particularly in the areas of cerebral connectivity, human-computer interaction and stroke rehabilitation.

References: [1] doi: 10.1186/1743-0003-11-32; [2] doi: 10.1186/1743-0003-7-48.

ANALYSIS OF THE DISTRIBUTION OF ALLELES OF THE HUMAN LEUKOCYTE ANTIGEN (HLA) SYSTEM IN BRAZILIAN POPULATION

D. C. Rosa [1], T. K. de Araujo [2], F. Cendes [3], N. Watanabe [4], F. R. Torres [5], I. Lopes-Cendes [6]

[1] Laboratory of Molecular Genetics, FCM, UNICAMP, [2] Dept. of Medical Genetics, FCM, UNICAMP, [3] Dept. of Neurology, FCM, UNICAMP, [4] Dept. of Medical Genetics, FCM, UNICAMP, [5] Dept. of Medical Genetics, FCM, UNICAMP, [6] Dept. of Medical Genetics, FCM, Unicamp.

Introduction and Hypothesis: Genes of the Human Leukocyte Antigen (HLA) system are associated with infectious, autoimmune and psychiatric diseases and cancer susceptibility. These genes are highly polymorphic [1] and show allele variability among different populations. Furthermore, to identify and associate HLA alleles with specific phenotypes, it is necessary to compare with a reference database of control individuals with the same genetic background and geographical localization of patients studied [2]. As far as we know, there are no HLA-reference databases for the Brazilian population. **Objective:** Our aim is to determine the allele frequency of class I (HLA-A, -B and –C) and class II (DPA1, DPB1, DQA1, DRB and DQB1) HLA genes in control individuals from the Brazilian population. **Methods:** This project will include 300 Brazilian healthy subjects. DNA integrity and purity will be evaluated by electrophoresis and spectrophotometry, respectively. Libraries will be prepared using a HLA Trusight v2 Illumina Sequencing Panel, which generates HLA amplicons with adaptors and indexes i5 and i7. Samples will be submitted to genotyping in a Miseq sequencer (Illumina). The FASTA data generated will be analyzed using the HLA Trusight Assign Illumina software. **Relevance:** Our goal is to determine the genetic structure of HLA system in the Southeast Brazilian population. Knowledge about HLA alleles frequencies in healthy subjects will be useful for future studies that aims to better understand the reaction to drugs used in clinical treatment. Furthermore, this project will generate data that could be used to investigate autoimmune diseases whose HLA system association is yet unknown.

References: [1] Goldberg AC, Rizzo LV, Einstein 13(1): 153-156, 2015; [2] Okada Y. et al., Nature Genetics 47(7): 798-802, 2015.

STUDY OF THE TECHNIQUE OF MAGNETIC RESONANCE SPECTROSCOPIC IMAGING (MRSI) AND APPLICATION TO EVALUATION OF BRAIN METABOLITES OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

J. Horvath[1,4], D. R. Pereira[2,4], J. Fontolan[2,4], L. Rittner[2,4], S. Appenzeller[3], G. Castellano[1,4]

[1]Neurophysics Group, IFGW, UNICAMP, [2]Computer Engineering and Industrial Automation Dept., FEEC, UNICAMP, [3]Dept. of Medical Clinics, FCM, UNICAMP, [4]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: The major measurable metabolites in proton magnetic resonance spectra of the brain are N-acetylaspartate and N-acetylaspartylglutamate (NAA+NAAG), creatine and phosphocreatine (Cr+PCr), glycerolphosphorylcholine and phosphorylcholine (GPC+PCh). A study carried out by Appenzeller et al. [1] showed that patients with systemic lupus erythematosus (SLE) have a decrease in the ratio NAA+NAAG/Cr+PCr, and an increase in GPC+PCh/Cr+PCr, compared to healthy subjects. These findings were achieved using the magnetic resonance spectroscopy (MRS) technique, with a single-voxel acquisition. In this study, we used multivoxel spectroscopy (MRSI, magnetic resonance spectroscopy imaging) to evaluate metabolite levels in the corpus callosum of SLE patients and to compare them to those of healthy subjects. We also tested, for the first time, a software, developed by Pereira et al. [2], which automatically matches MRSI data to corresponding anatomical MR images, which is something that was previously only possible to perform at the scanner console. **Materials and Methods:** Spectra of 20 patients (mean age 38 ± 16 years) and of an equal number of healthy subjects (mean age 36 ± 11 years), all women, were analyzed. Initially, the MRSI/MRI matching software [2] was used to combine the MR images with the MRSI grids and thus enable the verification of the positioning of the spectra grids, which were, in this case, in the upper region of the corpus callosum, to avoid cerebrospinal fluid. After this, the software allowed the selection of spectra with predetermined percentages of white matter, in this case, 85, 90 and 95%. It was also possible to visualize through the software the spectra that had passed in the previous steps and to remove spectra containing insufficient signal-to-noise ratio (SNR). After this preprocessing of the data, the software generated an average spectrum and the software *LCModel* [3] was used to quantify this spectrum. The results obtained for the metabolite concentrations for each group (patients and healthy subjects) were compared and, in order to guarantee if the differences between the results of each group were significant, a statistical analysis was performed. **Results:** With the methodology used in the present study, it was possible to observe a 10% decrease in the NAA+NAAG/Cr+PCr ratio in patients with SLE in relation to healthy individuals. However, the only methodology tested in this study that found a statistically significant difference between the groups was the one that used 85% of white matter with the exclusion of noisy spectra. **Discussion:** The results may be explained by the fact that the use of a lower threshold of white matter (85%) for the inclusion of spectra in the average spectrum increases its SNR (since more spectra are included). In addition, the manual exclusion of noisy spectra probably contributed to improve the quality of the average spectrum, allowing a distinction between the groups. **Conclusion:** With this work, with a multivoxel technique, it was possible to corroborate one of the results presented in a previous study [1] which used a single voxel technique. Besides, the MRSI/MRI matching software was tested for the first time, and its usefulness was confirmed.

References: [1] Appenzeller S *et al*, *Arthritis Rheum.* 55(5):807-11, 2006; [2] Pereira, DR *et al. Metodologia para seleção de espectros de interesse em espectroscopia multivoxel por ressonância magnética.* XXV Congresso Brasileiro de Engenharia Biomédica – CBEB, Foz do Iguaçu-PR, 2016; [3] Provencher SW, *Magn Reson Med* 30: 672-679, 1993.

USING WHOLE EXOME SEQUENCING TO IDENTIFY THE GENETIC DEFECT IN PATIENTS WITH GENETIC EPILEPSY WITH FEBRILE SEIZURES PLUS (GEFS+)

E. Almendares-Bonilla[1], H. T. Moraes[1], M. C. Gonsales[1], C. Soler[1], H. Urquia-Osorio[2], I. Lopes-Cendes [1]

[1] Department of Medical Genetics, [2] Department of Neurology; School of Medical Sciences, University of Campinas (UNICAMP), Campinas, São Paulo, Brazil; and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas SP, Brazil.

Introduction and Hypothesis: GEFS+ is a familial epilepsy syndrome with complex inheritance pattern, phenotypic heterogeneity, incomplete penetrance and variable clinical prognosis. It is characterized mainly by seizures triggered by fever. GEFS+ includes a broad phenotypic spectrum with different degrees of clinical severity. Currently, several mutations in GEFS+ families have been

identified, especially in genes encoding sodium channel subunits and GABAA receptors; nevertheless, in the great majority of the cases the genetic alteration remains unknown. **Objective:** This study aims to characterize the genetic bases of GEFS+ using whole exome sequencing (WES). **Methods:** We will generate and analyze WES data from a retrospective cohort of 13 patients with GEFS+. Other patients from national and international epilepsy centers that meet the inclusion criteria may also be incorporated into the study. The preparation of the DNA libraries will follow the protocol recommended by SureSelectXT Target Enrichment System for Illumina Paired-End Sequencing Library kit (Agilent Technologies) and will be sequenced on a Illumina Hiseq 2500 equipment. We will use a bioinformatics pipeline development in our laboratory in order to filter the putative variant causing the disease in each patient. **Relevance:** The results of this study will allow the genetic characterization of patients with GEFS+ and its correlation with clinical data. In addition, we will compare our results with our own studies about epileptic encephalopathies in order to further explore the possible causes for the clinical variability in patients with childhood epilepsies.

References: [1] Yue-Hua Z et al., Neurology 389(12): 1210-1219, 2017; [2] Camfield P & Camfield C., Epileptic Disord 17(2): 124-133, 2015.

MICRORNA EXPRESSION IN PATIENTS WITH SYMPTOMATIC AND ASYMPTOMATIC CAROTID ARTERY STENOSIS

F. S. Oliveira[1], D. B. Dogini[1], A. Donatti[1], M. Santos[1], A. T. Guillaumon[2], W. M. Avelar[3], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, [2]Department of Surgery, [3]Department of Neurology; School of Medical Sciences, University of Campinas, and the *Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction and Hypothesis: Stroke, the current second most frequent cause of death in the world [1], can occur due to an embolic blood clot formed during an atherosclerotic plaque rupture [2]. Atherosclerosis begins with the subendothelial accumulation of lipoproteins, followed by in site migration of monocytes and lymphocytes type T, leading to a chronic inflammation clinically observed as stenosis, the thickening of the artery walls [3]. Common risk factors for stroke are diabetes, obesity, arterial hypertension and smoking [3]. However, patients at similar ages and comorbidities often show different degrees of stenosis, suggesting that for this condition there may be a genetic influence. Circulating microRNAs are non-coding RNAs which are involved in fine gene regulation and have been proposed as disease biomarkers for several conditions [4]. **Objective:** To analyze the pattern of microRNA expression in plasma samples obtained from patients with asymptomatic and symptomatic carotid stenosis. **Methods:** The study will be composed by a cohort of 120 patients: 30 with symptomatic stenosis, 30 with less than 50% asymptomatic stenosis, 30 with asymptomatic mild stenosis (50-70%) and 30 with asymptomatic severe stenosis (70-99%) or occlusion (100%). Peripheral blood will be collected at Hospital das Clínicas, in Campinas, and the plasma will be frozen at -80ºC for future use. Circulating MicroRNA will be extracted using the kit mirVanaTM ParisTM (Thermo Fisher Scientific Inc.), the cDNA library will be constructed using the kit Illumina® TruSeq® Small RNA Library Prep– RS-200-0048 (Illumina, Inc) and the samples will be sequenced using the platform HiSeq 2500 (Illumina,Inc). To conclude, the obtained reads will be aligned to a reference genome using the program miRDeep, the normalization and read count will be done using HTSeqcount and Feature counts, and the final analysis of differential expression will be done with DEseq2. **Relevance:** Conclusions from this study might aid the understanding of the genetic influence in atherosclerotic plaque formation, growth and rupture, as well as it may contribute for the future identification of patients more suitable to undergo cirurgy.

References:[1] World Health Organization. Available at: <http://www.who.int/mediacentre/factsheets/fs310/en/>. Access in September 29th, 2017.[2] Munshi, A., et. al. Gene 555.2, 250-259, 2015. [3] Krieger, J. E (Ed.). Vol. 1. Atheneu. 2008. [4] Igaz, P. (Ed.). Vol. 106. Springer. 2015.

IMPACT OF DIFFERENT DTI PIPELINES TO EVALUATE THE CORTICOSPINAL TRACT IN PATIENTS WITH STROKE

R. Luccas[1], A.B. Conforto[1]

[1]Neurology Division, ICHC, HCFMUSP.

Introduction and Hypothesis: Diffusion tensor imaging (DTI) provides indirect information about the corticospinal tract (CST) integrity and white matter pathways [1]. DTI analysis is challenging in patients with brain lesions such as stroke due to the lack of a gold standard to process imaging data in the presence of lesions that include the CST. We hypothesize that different analytical pipelines will yield significantly different absolute results for DTI metrics in subjects with stroke and that intra- and inter-rater reliabilities will be high for each single analytical pipeline. **Objective:** In this project, we will analyze the impact of different DTI analytical pipelines on CST metrics in patients in the chronic phase after stroke. We will also evaluate intra- and inter-rater reliability of drawing lesion masks with three different software packages. **Methods:** Data is acquired from a MRI scanner Achieva 3.0T (Philips, Netherlands) with the acquisition of DTI (field of view = 256x256 mm, matrix = 128x128, repetition time = 10200 ms, echo time = 103 ms, slice thickness = 2 mm, flip angle = 90º, number of averages = 1, voxel sizes = 2.0 x 2.0 x 2.0 mm^3 and 64 directions). These data will be analyzed in two main steps. The pre-processing step aims to prepare the image for the processing step by correcting for some artifacts as subject motion, Eddy current and other distortions, but also by preparing the image file to be more suitable to be processed. The same set of data will be pre-processed with two different software packages, using and not using top-up correction. The results of the pre-processing steps will undergo the processing step in FSL. During the processing step, lesion masks will be drawn by using three different softwares. In each software package, the masks will be drawn in the diffusion and T1-weighted image. Drawings of the same images will be made by two different researchers, blind to each other. The following comparisons will be made to DTI metrics (FA, MD, RD, AD, etc.) obtained by: 1. Pre-processing with FSL *versus* ExploreDTI without top-up correction + processing with FSL with lesion masks drawn by Researcher 1 with MRIcro; 2. Pre-processing with FSL *versus* ExploreDTI with top-up correction + processing with FSL with lesion masks drawn by Researcher 1 with MRIcro. The DTI metrics will be compared with analysis of variance with repeated measures with factors "software package" (FSL and ExploreDTI) and "top-up correction" (yes and no); 3. Masks drawn in diffusion images and T1 images by Researcher 1 using MRIcro, in two different days. Mask volumes and each metrics obtained by diffusion or T1 analyses will be compared with paired t-tests or Mann-Whitney tests; 4. Masks drawn by Researcher 1 and Research 2 with each software: MRIcro, FSLview and Mango. Intraclass correlation coefficients obtained by the two analyses, with each software package are expected to be >0.75. Confidence intervals will be calculated in order to compare whether the coefficients are significantly different; 5. Masks drawn by Researcher 1 in different days, with each software: MRIcro, FSLview and Mango. Intraclass correlation coefficients obtained by the two analyses are expected to be >0.75, for each software package. Confidence intervals will be calculated in order to compare whether the coefficients are significantly more reproducible than another; 6. An ROI placed on the cerebral peduncle by Researcher 1 versus an ROI from the posterior limb of the internal capsule to the middle pons. The data will be compared with paired t-tests or Mann-Whitney tests. **Relevance:** At the end of the project, the data analyzed should provide enough information to evaluate the impact of using different methods and define the most reproducible pipeline(s) by identifying the quality of each one for analysis of data from patients with stroke.

References: [1] DOI: 10.5847/wjem.j.1920-8642.2017.02.003.

ASSOCIATION OF VIDEO IMAGE AND NON-INVASIVE ELECTROPHYSIOLOGICAL RECORDING IN ZEBRAFISH LARVAE BRAIN DURING SEIZURES

J. A. A. Fernández[1], T. G Parolari[1], M. C. S. Nunes[1], V.C., Fais[1], N. Peixoto[2], C.V. Maurer-Morelli[1]

[1]Zebrafish Laboratory, UNICAMP, Department of Medical Genetics, FCM, UNICAMP, [2]Electrical and Computer Engineering Department - George Mason University, Fairfax, VA.

Introduction: Zebrafish (*Danio rerio*) is an important model organism for studying human diseases. This little fish has many advantages for genetic and developmental investigations such as: high fertility, optical transparency during embryogenesis, about 70% homology with human genome, and 84% of genes that are known to be associated with human diseases, including epilepsy [1, 2]. One issue when designing experiments with larvae is the throughput as well as availability of simultaneous electrical and video signals. When larvae are allowed to swim freely, no electrophysiology is performed. On the other hand, when they are immobilized, analysis of behavioral variables is affected. Our hypothesis is that there is a reasonable compromise for both analyses. In this work

we propose a novel method for zebrafish larvae immobilization and recording using an electrophysiological setup and video recording system. **Materials and Methods:** Wild-type zebrafish at 7 days post fertilization (dpf) were anesthetized with 10 μM d-tubocurarine and 0.002% tricaine. Animals were immobilized in 0.8% low-melting agarose. Seizures were elicited by applying pentylenetetrazole (PTZ) at 15 mM. Electrophysiology recordings were performed using a 316L medical grade stainless steel electrode of 125 μm diameter with a 10 μm polyimide insulation and exposed tip. The ground was a similar electrode with up to 3 mm of uninsulated length along the electrode shaft. Ground was immersed in the agarose solution during all times. The electrode was lowered through a triaxial micromanipulator until just touching the optical tectum, between the eyeballs of the larvae. Signals were pre-amplified by 10 and filtered from 1 to 1,000 Hz. Amplification was performed by using the Intan RHD2000 by 100, to a final total amplification of 1,000. Acquisition was performed by a single channel throughout the experiments at 10k samples per second. Files were saved every 10 minutes for up to 70 minutes (per animal). Noise level of the system was tested before each experiment and saved as baseline file. All experiments were approved by the Animal Ethics Committee/UNICAMP - CEUA 4660-1/2017. **Results:** On average, the noise level was around 20 uVrms (root mean square). Most of the seizure activity presented signals of amplitudes from 100 to 500 uV. All larvae showed seizure activity that was synchronized with the video. Larvae showed seizures at approximately 15±3 minutes after PTZ immersion. All larvae survived until the end of the test (70 minutes) which was verified by visual detection of a heartbeat or proxy thereof (e.g. bladder movement or blood flow). **Discussion:** We propose a cost-effective protocol and setup for zebrafish larvae electrophysiological acquisition in association with video recording, which can be considered an advantage since it is possible to observe ictal findings and behavior at the same time. However, because we recorded one larva per time, our next step will be to improve our setup for recording large number of larvae simultaneously. **Conclusion:** We present an effective protocol for measuring zebrafish seizure activity correlating electrical and behavioral data.

Support: FAPESP 2014/15640-8, CEPID-BRAINN 2013/07559-3 and CAPES.

References: [1] doi: 10.1016/j.neuroscience.2004.11.031; [2] doi: 10.3390/ijms18030596

GENETIC FACTORS INFLUENCE ON CONNECTOME FINGERPRINTS AND FUNCTIONAL NETWORKS

F. L. Ribeiro[1,2], W. H. L. Pinaya[2], C. E. Biazoli Jr[1]

[1]Laboratório Interdisciplinar de Neurociência do Desenvolvimento Afetivo e Social, CMCC, UFABC, [2]Laboratório de Neurociência Computacional, CMCC, UFABC.

Introduction: The current revolution in fMRI data analysis points toward the development of personalized medicine. Many studies have demonstrated that functional connectivity profiles are sufficient to identify an individual[1,2]. Importantly, the ability to discriminate between subjects seems to depend on the high intersubject variability and low intrasubject variability[3]. With this in mind, we investigated the contribution of highly distinctive networks among the individuals in twin pair identification, to possibly establish whether these networks variabilities rise from the genetic code. **Materials and Methods:** *Dataset:* The data used is provided by the Human Connectome Project (HCP). We used resting-state functional and structural MRI data of 246 monozygotic twins. The technical details of this dataset are available at http://protocols.humanconnectome.org/. *Preprocessing:* The HCP dataset was preprocessed by using the standard and conservative pipeline of the toolbox CONN[4]. *Parcellation:* We applied two parcellation schemas: Shen[5] and Gordon[6]. Importantly, both atlases attribute each node to a functional system, which allowed further analysis of the contribution of each network to individual and twin identification. *Individual identification analysis:* The identification analysis was based on previous work[1]. In summary, a dataset was created containing all the functional connectivity matrices for each run (rest1 and rest2). The individual identification was determined by computing the correlation between each individual connectivity matrix from one run and all the other connectivity matrices. The predicted identity was that with the maximal Pearson correlation score. Additionally, we also investigated the contribution of single networks to identification accuracy by sub-sectioning the functional connectivity matrices into sub-matrices of single networks. *Twins identification:* Twin pair identification algorithm was obtained by few alterations of the individual identification analysis. The second run of the target subject was removed, and if the chosen maximum correlation value belongs to their twin, the prediction was considered correct. **Results:** The individual identification accuracy obtained by comparing a target matrix (rest1) against all the other connectivity matrices from the database (rest2) was well above chance (1/246=0.4%) by using both parcellation schemas, Shen (97.6%) and Gordon (99.6%). Based on the networks' definition of Shen's schema, the medial frontal (93.1%) and frontoparietal (92.7%) were the most successful for individual identification. On the other hand, the dorsal attention (99.6%) and default mode (99.2%) networks based on Gordon's schema were the most distinctive networks. For the twin identification analyses, the whole-brain based identifications were similar (Shen, 60.8%; Gordon, 61.3%). Finally, the medial frontal (23.1%) and subcortical-cerebellum (32.1%) networks (Shen's schema), and the default (13.3%) and dorsal attention (13.9%) networks (Gordon's schema) were the most successful networks for twin pair prediction. **Discussion:** Our results are in agreement with previous studies[1-3], supporting the fact that individual's connectivity profile is a reliable individual's marker. The high accuracy, well above chance (0.4%), obtained on whole-brain based twin identification might point to the importance of genetic factors on functional connectome individualities, despite the lower accuracy on network-based identification. Nonetheless, highly discriminant networks for individual identification demonstrated to be the most similar functional networks between a pair of twins, reflecting the importance of genetic factors on these networks. **Conclusion:** Connectivity profiles are a promising source for further individual's genetic studies, as the distinctiveness of a functional network might also be determined by genetic factors.

References: [1] doi:10.1038/nn.4135; [2] doi:10.1371/journal.pone.0111048; [3] doi:10.3389/fnins.2017.00085; [4] doi:10.1089/brain.2012.0073; [5] doi:10.1016/j.neuroimage.2013.05.081; [6] doi:10.1093/cercor/bhu239.

EFFECTS OF VIRTUAL REALITY AS A THERAPEUTIC APPROACH FOR THE IMPROVEMENT OF COGNITION IN HEALTHY ELDERLY.

Radl, A.L.M.[1], Rodrigues, T.O.[2]

[1]Doctorate in Health Psychology, UMESP, [2]Graduating in Physiotherapy, UMESP.

Introduction: Evidence indicates an increase in the elderly population in the forthcoming decades. It is essential to emphasize that aging is a process that involves motor, cognitive and sensorial losses that altogether can lead to the functional dependence of this population. In this context, cognitive training through virtual reality has been proposed as a new possibility of approach [1], since it allows prevention and enhancement of cognitive functions through dual tasks in a multi-sensorial, challenging, ludic environment with a high degree of motivation and patient involvement [2,3]. This study aimed to verify the efficiency of training through the Nintendo Wii videogame on the cognitive performance of the elderly through the Wechsler Intelligence Scale for Adults (WAIS-III) and to correlate the performance obtained with their evolution. **Materials and Methods:** Twenty-eight healthy elderly people, of both genders, aged 60-89 years participated in the study. Thirty-six training sessions were held with the Nintendo Wii videogame, each lasting 45 minutes, totaling 12 weeks. A neuropsychological evaluation was performed by a psychologist before the beginning of the training and at the end of the 36 sessions, where the WAIS-III was applied in order to obtain information about the cognitive aspects stimulated. The training consisted of two games: Table Tilt, controlled by a platform with sensors of discharge of weight that captures and reproduces in the screen the body movements, demanding attention, concentration, perception, reasoning and quick response to visual stimuli, and a game of dance (Just Dance), that through a control sensitive to changes of direction and speed projects on the screen the movements generated by the participant, stimulating memory, learning, attention, visual and motor coordination. **Results:** The results obtained through WAIS-III indicated an improvement in verbal IQ that assesses acquired knowledge, formal education, attention to verbal materials, verbal reasoning, memory, comprehension and language and in the VCI (verbal comprehension index) related to comprehension (verbal reasoning) and the mental process needed to answer the questions. **Discussion:** The results demonstrated that sensorimotor stimulation provided through a virtual environment favored the information processing speed and may have allowed the strengthening of synaptic connections contributing to the recovery of information previously learned through the cognitive reserve, benefiting the working memory and the

ability to solve problems. It can be postulated that there was neuroplasticity, observed through learning and consequent improvement in performance during games, making the maintenance of cognitive abilities that tend to decline in old age possible. **Conclusion:** The present study suggests that the Nintendo Wii videogame is viable as a therapeutic approach for cognitive enhancement in healthy elderly, since through multisensory stimulation it allows the double task training, favoring the cerebral plasticity, which implies in improving functions like processing speed and work memory, the main skills that decline with aging, resulting in an improvement in the quality of life and autonomy of this population.

References: [1] de Bruin E.D. et al., Z Gerontol Geriatr. 43(4): 229-234, 2010; [2] Batista J.S. et al. RBCEH, 9(2): 293-299, 2012; [3] Zimmermann R. et al., Neurology 82(14):1219-1226, 2014.

FUNCTIONAL ORGANIZATION OF INFORMATION PROCESSING IN TASK-BASED FMRI: A GRAPH THEORY APPROACH

P. H. R. da Silva[1], R. F. Leoni[1]

[1]Department of Physics, FFCLRP, USP.

Introduction: *Graph theoretical* analysis of resting-state functional *MRI (fMRI)* data *has established* that large-scale functional connectivity networks in the human brain display properties such as high clustering coefficient, as in a small--world topology[1]. In contrast, despite its increasing application, graph analysis of task-based fMRI suffers from restricted validity and of how much its conclusions can be generalized [2]. Therefore, the aim of this study was to examine if the topological structure in functional brain network organization during the performance of an MRI-adapted version of the Symbol Digit Modalities Test (SDMT), an international gold standard for screening the Information Processing Speed (IPS), presents small-world topology. **Materials and Methods:** Sixteen healthy controls were recruited and underwent a cognitive evaluation with an oral version of the SDMT before image acquisition. MRI was acquired in a 3T system. Functional MRI based on BOLD contrast was acquired with a 2D EPI sequence, and an experimental design adapted from a previous work [3]. We assessed the information processing network using 12 anatomical templates from Talairach Daemon database[4] in a region-to-region functional connectivity analysis in CONN Toolbox[5], from which the connectivity matrix was used to get graph theory measures (cost (K), local and global efficiencies) using a long range of cut-off threshold approach[2].
Results: In the interval between $0.34<\text{cost}(K)<0.5$ the experimental network (in red) presented global efficiency greater than a regular network (blue) with the same number of vertices, but smaller than a random network (green) (Figure 1a). In addition, it presented lower local efficiency than a regular network with the same number of vertices, but greater than a random one (Figure 1.b). Shaded gray area is a representation of the standard deviation between all subjects. **Discussion:** Our experimental network presented characteristics of a small world network, that is, high local and global efficiencies. It reflects highly clustered networks with a small feature path length, allowing rapid communication between any two regions in the network. Small-world are considered features of healthy networks.

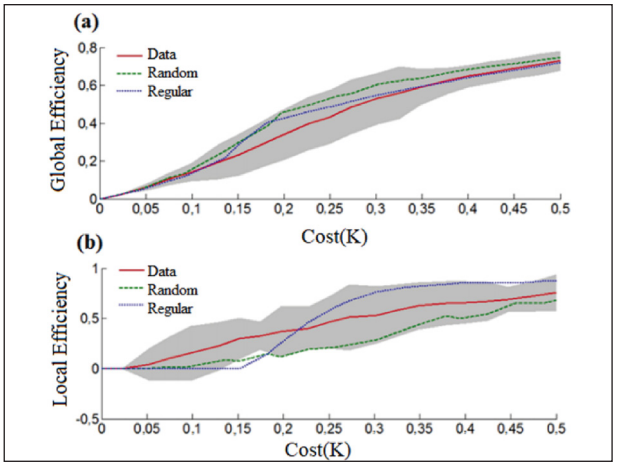


Figure 1. (a) Global and (b) local efficiency versus cost(K).

Conclusion: This study revealed that the topological structure in functional brain network organization during the performance of an MRI-adapted version of SDMT presents small-world topology. Therefore, the graph theory approach in the quantification of the topological structure of the network can be used as a tool in future studies to find biomarkers between healthy and clinical groups in both rest and task-based fMRI.

References: [1] doi: 10.1177/1073858406293182; [2] doi: 10.1371/journal.pone.0137020; [3] doi: 10.1016/j.bandc.2013.04.003; [4] doi: https://doi.org/10.1016/j.msard.2018.01.014; [5] doi: 10.1089/brain.2012.0073.

NETWORK AND PATHWAY ANALYSES IN ZEBRAFISH IMMATURE BRAIN AFTER SEIZURES

M. C. S. Nunes[1], J. F. de Vasconcellos[2], V. H. S. Zago[1], A. S. Vieira[3], A. H. B. Matos[3], C. S. Rocha[3], B. S. Carvalho[4], I. Lopes-Cendes[3], C. V. Maurer-Morelli[1]

[1]Zebrafish Laboratory, Department of Medical Genetics, School of Medical Sciences – UNICAMP, Campinas, SP- Brazil; [2]Genetics of Development and Disease Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; [3]Molecular Genetics Laboratory, Department of Medical Genetics, School of Medical Sciences – UNICAMP, Campinas, SP- Brazil; [4]Department of Statistics, Institute of Mathematics, Statistics and Scientific Computing, UNICAMP, Campinas, SP-Brazil.

Introduction: To investigate the molecular mechanisms underlying seizures, we analyzed the response of different seizure-induced protocols in the zebrafish brain by transcriptome analysis. For a comprehensive understanding of the biological mechanisms affected by the transcripts that were counter-regulated by the treatments, interactive networks and pathways analyses were performed using a systems biology approach. **Materials and Methods:** Wild-type zebrafish larvae at 7dpf were separated into three groups: control (CG, n=3), acute seizure (AS, n=2) and status epilepticus-like (SE, n=3). Larvae from groups AS and SE were exposed to PTZ 15mM for 20 minutes and 3 hours, respectively. Messenger RNA libraries were achieved after using Illumina's Sample Prep Kit and validated libraries were sequenced in the Illumina HiSeq 2500 System. Gene interactions and correlation networks were identified with the Ingenuity Pathway Analysis (IPA) software content version March/2017 (Ingenuity Systems, Mountain View, CA). The fold change threshold was >3 or ≤ -3 and the signaling pathways were considered statistically significant with a $p<0.05$. All IPA available databases at the time of the analysis were used in this study. **Results:** The most activated signaling pathway for AS vs. CG and SE vs. CG was the AMPK Signaling, but in opposite directions, since in the SE it was activated (positive z-score), and in the AS inhibited (negative z-score). However, comparisons between AS vs. SE showed that RhoGDI Signaling ($p=1.06E-07$) and Signaling by Rho Family of GTPases ($p=1.20E-07$) are the top-pathways inhibited (negative z-score) and activated (positive z-score), respectively, in the SE group. **Discussion:** Transcriptome studies followed by signaling pathway analysis showed that AS and SE have distinct molecular responses. The AMPK signaling pathway is responsible for coordinating several intracellular processes, like cell growth and metabolism reprograming, and is activated when intracellular ATP reach lower levels [1]. This signaling pathway was also reported in epilepsy as acting on epileptogenesis and synaptic plasticity regulation [2]. The RhoGDI family of genes regulate signaling through RhoGTPases by inhibiting the disassociation of Rho members from GDP, thus keeping these factors in an inactivated state [3]. We found that RhoGDI pathway is downregulated and the Rho Family of GTPases is up-regulated in the SE compared to AS group. It is known that the Rho family of GTPases have an important role in the morphogenesis of the dendritic spines of neurons [4] and contribute to the synaptic plasticity [5] that is observed in epilepsy. **Conclusion:** This study emphasizes the relevance of the zebrafish as a model for investigating seizures.

Support:FAPESP 2014/15640-8, CEPID-BRAINN 2013/07559-3 and CNPq.

References: [1] Mihaylova M.M. et al., *Nature cell biology* 13.9: 1016-1023 (2011); [2] Potter, W. B., et al. *PloS one* 5.2 (2010); [3] Garcia-Mata, R. *Nature reviews Molecular cell biology* 12.8: 493-504 (2011); [4] Elia, L. P. et al., Neuron 51.1: 43-56 (2006); [5] Negishi, M. et al., The Neuroscientist 11.3: 187-191 (2005).

A GENERIC CLASSIFIER FOR BRAIN-COMPUTER INTERFACES BASED ON STEADY STATE VISUALLY EVOKED POTENTIALS

R. C. Ferreira[1], H. M. A. Leite[1], T. B. S. Costa[2], G. F. G. Yared[1], R. Attux[2], S. N. Carvalho[1]

[1]Federal University of Ouro Preto (UFOP) – Brazil, [2]University of Campinas (UNICAMP), Brazil.

Introduction: Brain-Computer Interfaces (BCI) allow a direct interaction between a subject and a computer through the interpretation of brain signals. Before starting an online BCI based on Steady State Visually Evoked Potential (SSVEP), a common user is presented to visual stimuli not to control an application, but simply to train the system classifier. This stage is essential for the proper functioning of the BCI at online mode, although it can be tiring or tedious for the subject. In order to reduce the training stage, in this study we have analyzed the use of data from other subjects in the design of the BCI classifier to verify the possibility of conceiving a generic BCI-SSVEP, which does not require a priori knowledge of the brain signals of the subject who manages it. **Materials and Methods:** In this study, the brain signals of six health subjects of database described in [1] were used. There are 8 trials of 12 s for each subject, considering four visual stimuli flickering at 6, 10, 12 and 15 Hz, with a total of 32 trials per subject. The signals were acquired by electroencephalography with 16 dry electrodes and sampled at a rate of 256 Hz. Each trial of 12 s was windowed in 6 segments of 2 s and filtered by Common Average Reference. The feature extraction used the Welch method to estimate the Power Spectral Density around the evoked frequencies. The BCI employed a linear classifier based on least mean squares to discriminate between the four classes. For the training and validation of the classifier, three scenarios were considered: Scenario I - only the own data of the subject were used, 50% of the samples randomly selected were used for training and the remaining 50% of the samples were used for validation. We created 1000 random partitions of database. Scenario II - data from five subjects were used to train the classifier and the system was validated with data from a sixth subject. Scenario III - data from the five subjects and 50% of samples of the own subject were used to train the classifier and the remaining 50% of samples of the own subject was used to validate the system; also 1000 random partitions of database of subject were performed. **Results:** Table 1 show the average hit rate for the six subjects in the three scenarios.

Table 1. BCI-SSVEP performance for three classifier training scenarios.

Subject	1	2	3	4	5	6	Average	Variance
Scenario I	80.95	86.05	91.80	88.33	87.58	58.53	82.20	1.47
Scenario II	59.90	59.38	62.50	55.21	67.19	40.63	57.47	0.84
Scenario III	67.77	71.90	74.30	75.14	74.42	69.72	72.21	0.09

Discussion: The best performance of BCI is achieved when more training samples of the subject that validates the system are employed (Scenario I). However, the results indicate that it is possible to use data from other subjects to train the system, reducing the collection time for BCI-SSVEP training stage by 50%, with a performance reduction of about 10% (Scenario III).When no signals of the subject were used for training, the hit rate is around 57% (to discriminate four classes – Scenario II). **Conclusion:** Results suggest that is possible to build a BCI-SSVEP system by reducing the number of samples of the own subject to train the classification system, since the hit rate is greater than 25% (random case with 4 classes). Future works include a greater database to generalize the classifier in order to improve the system accuracy.

Support: CNPq, FAPESP, FINEP and UFOP.

Reference: [1] Leite, H. M. A. (2018). Design de interação para interfaces cérebro-computador baseadas em potenciais visualmente evocados.

BIOMETRICS SYSTEM USING EEG SIGNALS: PRELIMINARY RESULTS

P. T. Barbosa[1], H. M. A. Leite[1], G. F. G.Yared[1], T. B. S. Costa[2], R. Attux[2], S. N. Carvalho[1]
[1]Federal University of Ouro Preto (UFOP) – Brazil, [2]University of Campinas (UNICAMP), Brazil.

Introduction: Nowadays, systems capable of guaranteeing security and confidentiality in data access are important. Biometric systems employ physical or behavioral characteristics of living beings under the premise that each individual is unique and has distinct characteristics that allow identification. In this study, brain signals collected by electroencephalography (EEG) were used to design a biometric system. **Methods and Materials:** The database used to conceive the preliminary biometric system contained brain signals from 10 volunteers, while they were exposed to a scintillating visual stimulus at 10 Hz. The recording of the brain activity was performed with 16 dry electrodes by electroencephalography. Eight repetitions were conducted for each individual with 12 s of duration each. The biometry system was tested in two configurations, considering 12 s and 3 s windowing of signal. The identification system consisted of the following steps [2]: (1) the signals were filtered by the common average reference (CAR) technique; (2) the power spectral density was estimated in the frequency range from 9 Hz to 11 Hz, with a 50% overlap, using the Welch periodogram method; (3) a linear classifier based on the least squares method was applied. The system used 80% of the subject base to train the classifier and was validated with the rest of the data in a scheme of 120-cross validation. **Results:** Table 1 shows the average accuracy of the preliminary biometric systems for each subject, considering the two scenarios of signal duration (12 and 3 s).

Table 1. Average accuracy of the biometric systems.

Time/ Subject	Average Accuracy (%)										
	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Total Average
12 s	96.7	75.0	76.7	97.9	70.0	100	75.4	96.3	50.4	74.2	82.0
3 s	88.8	61.4	80.8	90.7	43.6	95.7	40.6	100	13.6	67.7	68.3

Discussion: Results show that our preliminary biometry system is able to perform a correct validation in 82% of the cases using 12 s of signal and in 68% with only 3 s of the signal. However, we can note that, for some subjects, such as S5, S7 and S9, the system becomes very fragile with the reduction of the analysis time, while for others the system remains robust. Particularly, for the subject S9, the system is not efficient, even with the 12 s windowing: probably his signals have a low signal-to-noise ratio and need to be better processed. **Conclusion:** The use of CAR, Welch method and linear classifier allowed the development of a biometric system capable of identifying individuals through EEG signals, mainly using a larger time window. To improve the system, features selection techniques will be tested and the database will be expanded.

Support: UFOP, CNPq, FINEP and FAPESP.

References: [1] Leite, H. M. A. (2018). Design de interação para interfaces cérebro-computador baseadas em potenciais visualmente evocados. [2] Theodoridis S., et al. Pattern recognition, 2003.

BCI-SSVEP: PRELIMINARY ANALYSIS OF FEATURE EXTRACTORS AND CLASSIFIERS

V. M. Barbosa[1], H. M. A. Leite[1], G. F. G.Yared[1], T. B. S. Costa[2], R. Attux[2], S. N. Carvalho[1]
[1]Federal University of Ouro Preto (UFOP) – Brazil, [2]University of Campinas (UNICAMP), Brazil.

Introduction: Brain-Computer Interface (BCI) allows converting brain signals into control commands. A usual approach of BCI is based on Steady State Visually Evoked Potentials (SSVEP), which explores the increase in brain activity that emerges in the visual cortex of a subject exposed to a scintillating visual stimulus at a specific frequency. In this study, we compare the performance of a BCI-SSVEP in four scenarios, combining two feature extractors –Welch's Method and Fast Fourier Transform (FFT) – and two classifiers – a linear classifier based on least squares and a feedforward artificial neural network (ANN). **Materials and Methods:** In this study, we have used the brain signals acquired of two healthy volunteers [1]. The brain activity was registered at 256 Hz, by electroencephalography, using 16 dry electrodes. The visual stimuli blinked on a monitor at four frequencies: 6, 10, 12 and 15 Hz. The database used was composed of 8 instances of 12 s for each frequency, totaling 32 trials per volunteer. The signal processing was performed in three stages: preprocessing, feature extraction and classification. In the preprocessing, the signal of 12 s was windowed in 3 s and filtered by the Common Average Reference technique, in order to eliminate noises and artifacts. In sequence, the feature extraction was operated by two techniques: (1) FFT: the features were considered the FFT magnitude of signal at the evoked frequencies, (2) Welch: the features were the power spectral density (PSD) of signal estimated around 0.1 Hz of evoked frequencies – the values were normalized by the sum of the PSD of the four bands. In the last stage, the classifiers (linear and the ANN) were trained with 78% of the samples, randomly selected, and validated with the remaining 22%, this process was repeated 20 times for each scenario. **Results:** Table 1 presents the average accuracy obtained for each scenario.

Table 1. Comparison of performance of BCI-SSVEP applying different classifiers and feature extractors.

			Average Accuracy (%)				
Volunteer	Classifier	Extractor	6 Hz	10 Hz	12 Hz	15 Hz	average ± standard deviation
1	Linear	FFT	77.14	69.29	77.86	79.29	75.90 ± 4.49
		Welch	75.71	85.71	79.29	83.57	81.07 ± 4.46
	ANN	FFT	80.00	75.00	76.42	81.42	78.21 ± 3.00
		Welch	80.71	97.14	77.14	97.14	88.03 ± 10.62
2	Linear	FFT	73.57	73.57	72.14	66.42	71.43 ± 3.40
		Welch	73.57	87.14	83.57	87.14	82.86 ± 6.41
	ANN	FFT	83.57	75.71	72.14	75.00	76.61 ± 4.89
		Welch	78.57	96.43	77.86	95.00	86.97 ± 10.12

Discussion: The results show that the feature extraction by the Welch's method provides better attributes than by FFT, with difference of accuracy of about 10%. The ANN has slightly higher results than those obtained by the linear classifier; however, this difference remained within the margin of the standard deviation. The performance among the frequencies was closed, not revealing a clear polarity for either of the two volunteers. Nonetheless, the accuracy for 10 and 15 Hz were slightly better using Welch. **Conclusion:** All scenarios evaluated are adequate for the implementation of a BCI-SSVEP, presenting a hit rate higher than 70% to discriminate four classes. For both volunteers, the best performance was obtained with the combination of Welch's method and ANN. However, the simplicity of implementation and the low computational cost of the linear classifier may justify its use, since it provides practically the same accuracy.

Support: CNPq, FAPESP, FINEP and UFOP.

Reference: [1] Leite, H. M. A. (2018). Design de interação para interfaces cérebro-computador baseadas em potenciais visualmente evocados.

INVESTIGATION OF EEG SIGNALS GENERATED BY MOTOR IMAGERY FOR APPLICATION IN BCIS: PRELIMINARY RESULTS

C. M. Mendes[1,2], A. C. Buzzi[1], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN (FAPESP), UNICAMP.

Introduction: A brain-computer interface (BCI) is a system that measures brain activity in order to translate it into commands that operate an application. Electroencephalography (EEG) has been the most used technique in BCI systems to record brain activity. One of the strategies to generate the signals captured by EEG is motor imagery (MI), that may be seen as the mental rehearsal of a motor task without its execution, allowing, in principle, the control of a BCI device [1]. In this study, we sought to investigate how the brain response of users during MI happens, by analyzing a database of EEG signals in which healthy subjects were asked to imagine the movement of their right and left hands. Our goal has been to recognize patterns associated with this task, through a spectral evaluation of different segments of the signal. **Materials and Methods:** Sixteen channel EEG data of six healthy volunteers were provided by a previous database collected by our group. It consists of MI-based acquisitions for right and left hands, with blocks of rest in between. A single task or rest block lasted 10 s, within a set of nine rest blocks and four blocks of each type of imagination per trial (totalizing 170 s each *run*). All the electrodes were distributed on the scalp in a 10/10 positioning system, near to sensorimotor regions of the brain: C1, C2, C3, C4, C5, C6, Cz, FCz, FC3, FC4, FC5, FC6, CP3, CP4, CP5 and CP6. A standard preprocessing procedure was used for the datasets: bandpass filtering (0.5 to 50 Hz), identification and removal of bad channels (channels with a low recording signal-to-noise ratio), exclusion of artifactual portions of the data, and common average reference (CAR) filter. The criteria for these removals were, mainly, visual inspection of extreme amplitudes and/or lack of correlation with other channels. An estimate of the power spectral density (PSD) of the signal was calculated per second; the values corresponding to the μ and β bands (8 to 30 Hz) were summed and the result was plotted for visual analysis. Currently, only one trial per subject has been investigated. **Results:** Figure 1 shows the power sum of μ and β bands for C3 and C4 channels from one subject. **Discussion:** We expected to find, during left hand MI, a decrease in the power sum at even channels (event-related desynchronization), followed by an increase in resting state (event-related synchronization). In right hand MI, the drop was expected at odd channels. Unfortunately, as demonstrated in Figure 1, these findings did not occur frequently in any subject. Furthermore, we couldn't discriminate a pattern associated with the MI task. **Conclusion:** Although our preliminary results were unsatisfactory, only 6 out of 60 *runs* of the database have been evaluated. Besides, another MI-based EEG database, with 64 channels, will be soon explored. In general, we found that the data investigated so far were very noisy, requiring a great deal of effort in preprocessing, so that data removals may have impaired the analysis.

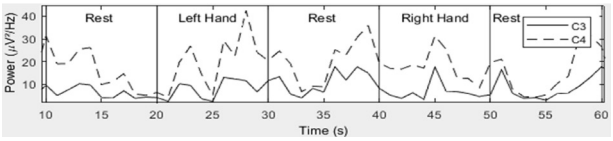


Figure 1. Power sum curves in the μ and β range recorded over left and right sensorimotor cortex during motor imagery. Only two channels and five blocks are shown to exemplify the results. Deflections represent band power increase (synchronization) or decrease (desynchronization). Vertical lines delimit the rest/task blocks.

References: [1] Pfurtscheller G et al., Proceedings of the IEEE 89(7): 1123–1134, 2001.

ASSESSMENT OF PATIENTS DIAGNOSED WITH CAROTID ATHEROSCLEROSIS DISEASE BY NIRS METHODS

A. Quiroga[1,2], S. Novi[1,2], A.A.V. Oliveira e Sousa[2,4], W.M. Avelar[2, 4], T.N.S. Goncalves[2,3], A. T. Guillaumon[2,3], R. C. Mesquita[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, SP, Brazil [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil, [3] Department of Surgery, School of Medical Sciences, UNICAMP, SP, Brazil [4] Department of Neurology, School of Medical Sciences, UNICAMP, SP, Brazil.

Introduction: Carotid atherosclerosis disease (CASD) causes at least 15-20% of all ischemic stroke. It is estimated that 5-10% of elderly (over 50 years of age) has asymptomatic carotid stenosis (ACS) [1], that is, without stroke events recently. Establishing whether patients with ACS need surgical intervention to avoid a stroke is a challenge for neuro-vascular physicians due to lack of accurate cerebral biomarkers. Our hypothesis is that the brain hemodynamics is directly affected by the presence of carotid plaque leading to a state of chronic hypoperfusion and potential neuronal damage [2], [3]. In this situation, the microvasculature would regulate itself by presenting a permanent vasodilatory response to meet metabolic requirements. However, available information from current clinical methods (Vascular Doppler, Angiography imaging and Tomography Imaging) derives from macrovasculature only. Near infrared spectroscopy (NIRS) is able to probe brain hemodynamics at the microvascular level, which makes it a potential tool for assessing the cortical consequences of CASD. NIRS is based on absorption and scattering of infrared light, and it is sensitive to variations of oxy- () and deoxy- () hemoglobin concentrations in tissue [4]. **Objective:** The main goal of the current project is to translate NIRS for clinical monitoring of patients with CASD by identifying biomarkers from the brain that relate to the level of stenosis of patients. **Methods:** In the first stage of this project, we enrolled forty patients with years old. Patients were recruited after being diagnosed with CASD at the Hospital of UNICAMP. From all patients, 25% of the cases were ACS. Vascular Doppler imaging, cranial CT and angiography imaging were employed to establish both the stenosis level and the affected artery. The comorbidities information was obtained from clinical history. Brain hemodynamics was assessed by a commercial NIRS system (NIRScout, NIRx Medical Systems) with 16 sources and 32 detectors arranged in a head cap designed to cover the whole head. All patients were measured during their ambulatory visit at the hospital. Each patient was performed a vasodilatory task based on breath holding for a minimum of 10 seconds followed by 30 seconds of rest. This protocol was repeated six times per patient. For data analysis, we will compare the hemodynamic response between the ipsilesional hemisphere and the contralesional hemisphere as function of stenosis level, and will try to correlate our results with the comorbidities to better understand the dynamics of stenosis at the microvasculature level. **Relevance:** Evidence suggests that an alteration in cerebral hemodynamic function may play a relevant role in the occurrence of stroke in patients with carotid artery disease [2]. In this work, we offer a novel, low-cost, noninvasive and portable method that can be used to clinical monitor brain hemodynamics in patients with potential to study brain diseases.

References: [1] M. M. Mughal., *Expert Rev. Cardiovasc. Ther. (2011);* [2] W. M. Avelar *et al.*, Int. J. Stroke Off. J. Int. Stroke Soc. (2015); [3] E. J. Forero *et al.*, Med. Res. Arch., (2017); [4] R. C. Mesquita *et al.*, Biomed. Opt. Express, (2010).

INTER AND INTRA-RATER ANALYSIS OF HEMIPARETIC SHOULDER THROUGH THE PHYSIOPLAY: A RANGE OF MOTION ASSESSMENT SOFTWARE.

Ferreira, D.M[1], Oliveira,V.A[1], Lima, C.R[2], Bassi, M.L[3], Carvalho,L.C[4], Reis,L.M[4]

[1]Neurophysics Group, Graduate student in Rehabilitation Sciences, UNIFAL-MG, [2]Department of Kinesiology, Recreation and Sports, Indiana State University, [3]Coordinator at the Unifeg School Clinic,UNIFEG-MG, [4]Professor and Researcher at the Graduate Program in Rehabilitation Sciences, UNIFAL.

Introduction: The cerebrovascular accident (CVA), also known as stroke, is one of the main causes of death and limitations in adults.[1] Motor, sensory and cognitive impairments are observed[2]. An important somatosensory subsystem involves the proprioception which if impaired may alter the *feedback* and the therapy progress, negatively impacting the range of motion (ROM). [1] The most common instrument used to assess ROM is the universal goniometer. Its usage requires experience from the therapist in order to reduce measurement errors. The data is manually recorded which makes it even more difficult to process the information and furthermore, it gives little to non-*feedback* to the patient. With the invention of movement sensor equipment, such as *Kinect*, *exergames* have been developed, which are games that consist in the physical interaction of the players with the virtual environment. Therefore, the purpose of the study was to evaluate the reliability of the inter and intra measurement-raters of the shoulder abduction ROM in post-stroke patients, through the *exergame PhisioPlay,* which is a software developed by the UNIFAL-MG that gives a visual *biofeedback* to the patient allowing the interaction between patient and virtual reality to happen through the performance of movements lead by stimuli generated on the screen. **Materials and Methods:** 13 volunteers diagnosed as chronic post-stroke patients, participated in this study, age range of 58,23±9,96 (male and female).The evaluation was conducted by two physical therapists where goniometry of the shoulder and the *exergame PhisioPlay* were done. The collected data were obtained through a report that was generated at the end of each session, showing all the angles captured during the game. After one week the follow-up test was done. The *Statistical Package for the Social Science* (SPSS, v. 20.0) for *Windows* was used for statistical analysis. The agreement of the intra and inter-rater results for the use of the *PhisioPlay* software was analyzed using the Intraclass Correlation Coefficient - $Type_{1,1}$ and $Type_{1,2}$ – (CCI). *Shapiro Wilk* test was used for the maximal measurements found in the goniometry and in the *PhisioPlay,* the calculated variables were correlated using the *Pearson*'s Correlation. The alpha level (α) was set at 0,05. **Results:** The analyses demonstrated that the inter-rater and intra-rater reliability through the CCI was high (r>0,90) for all the obtained variables (p<0,05). The *Pearson's* Correlation results for the maximal goniometry and *Phisioplay* measurements showed a high correlation (r>0.90). **Discussion:** As stated by the previous literature, the *Kinect* shows to be an accurate and precise tool to assess the human movement in general, as well as in the upper extremity, proving to be an important tool to assess ROM[3]. In this study, the ROM dynamic evaluation done through the *Phisioplay*, was able to record the active movements performed by the patient from the beginning to their maximal efforts, supporting the efficacy of this software when compared to the universal goniometry. The exergame through *Physioplay* allow the evaluation process to be more dynamic due to the set goals offered by the game and due to the visual biofeedback which also helps with achieving the correct movement performance. **Conclusion:** In conclusion, the Kinect in association with the *exergame Phisioplay* is a reliable tool in assessing the ROM in a fast, simple, cost beneficial manner, with minimal variation in the data collection.

References: [1] doi.org/10.1371/journal.pone.0170368; [2] Cavalcante, T.F et al., Rev Esc Enferm USP 2011; 45(6):1495-1500; [3]doi.org/10.1016/j.gaitpost.2016.04.004.

MACHINE LEARNING METHODS FOR CLASSIFICATION OF DISEASE OUTCOMES BASED ON MOLECULAR SIGNATURES IN CASE-CONTROL STUDIES

M. R. Rodrigues[2], B. Henning[2], I. Lopes-Cendes[2], B. S. Carvalho[1]

[1]Department of Statistics, IMECC, UNICAMP, [2]Department of Medical Genetics, FCM, UNICAMP.

Introduction: Machine learning methods are capable of learning from data and generate a model that, in turn, can be used to classify new data. Their use in precision medicine is being strongly advocated and presents promising results. However, disease prediction based on genomic data is still a challenge due to the size and complexity of these kind of data, and to the proportion of the disease that is explained by genetic factors. Here we apply machine learning methods to model case-control data composed of Single Nucleotide Polymorphisms (SNPs) of control subjects and epilepsy patients. Our main goals are first to test the prediction power of genomic data in the case of epilepsy and second, to look for possible candidate SNPs associated with the outcome for further investigation. **Materials and Methods:** We used a dataset with ~100,000 SNPs from 402 samples (203 epilepsy patients and 199 controls). This data was used to train a number of supervised machine learning models with different configurations. Since literature shows that there is no single best machine learning method for every application and data type, we tested different methods (both linear and non-linear) to find the best fit to our genomic dataset. These include Support Vector Machines (SVMs), Penalized logistic regression, Random Forests (RF), lasso and Elastic Net. They were selected based on their capacity to handle high-dimensional data. Best practices, such as partitioning the dataset in train and test sets, 5-fold cross-validation and parameter tuning with 100 iterations, were applied to avoid overfitting the models and reduce bias and variance. We also applied feature selection strategy based on cui-squared analysis to reduce data dimensionality. Relevant biological information was included in the models from a brain-specific genome-wide functional interaction network (Greene et al., 2015). **Results:** In preliminary results three methods obtained an area under the ROC curve (AUC) of 0.66 on the test set: RF, linear SVM and Penalized logistic regression. These results were obtained with a reduced set of 27 SNPs selected by a feature selection strategy. From this, candidate variants can be identified through the feature importance list of the best performing methods. These are baseline results without the incorporation of brain-specific gene interactions. **Discussion:** We believe our result is promising, given the reduced number of learning samples used, and can be improved once a larger dataset is available. Also, an increase in performance is expected once relevant biological information contained in the brain-specific gene interaction network is incorporated, since it can help identifying the most relevant variants to be considered as predictors. **Conclusion:** The present work advances in the emerging area of machine learning methods for precision medicine. We investigate the role of genetic data alone and accompanied by functional information in the performance of disease prediction models in the context of case-control studies.

References: [1] Greene CS et al., Nature Genetics 47(6):569-579, 2015.

ANALYSIS OF CIRCULATING MICRORNAS IN PATIENTS IN THE ACUTE PHASE OF ISCHEMIC STROKE: PHENOTYPIC CHARACTERIZATION OF THE COHORT RECRUITED

A.Donatti[1], R.Secolin[1], F.S. Oliveira[1], M. Martin[1], A.Sousa[2], W.M. Avelar[2], I. Lopes-Cendes[1]

[1]Department of Medical Genetics,[2]Department of Neurology, School of Medical Science, University of Campinas, UNICAMP, and the Brazilian Institute of Neuroscience and Neurotechnology, Campinas, Brazil.

Introduction and Hypothesis: Stroke is one of the most common causes of death or disability worldwide. MicroRNAs are small noncoding RNAs molecules that have been described as potential biomarkers in several diseases, mainly due to their ability to regulate gene expression. Studies have demonstrated that altered pattern of microRNA expression could influence disease progression and prognosis. Considering that there are different pathophysiological pathways for brain damage and recovery in ischemic stroke we hypothesize that differential regulation of microRNA expression could be linked to the prognosis. **Objective:** The aim of this study is to determine plasma microRNAs expression in the acute and chronic phases of ischemic stroke and to correlate it with the prognosis of patients. **Methods:** This study will evaluate a total of 50 patients with ischemic stroke. Plasma samples were collected in two periods: up to 24 hours after the stroke ictus (acute phase) and 6 months after the ischemic event (chronic phase). MicroRNAs will be extracted from plasma samples using miRvana Paris kit (Illumina, Inc). Subsequently we will determine microRNA profile using small-RNA Sequence technique. Sequencing libraries will be prepared using TruSeq® Small RNA Library Prep kit – RS-200-0048 (Illumina, Inc) and sequenced in a MiSeq System (Illumina, Inc). Reads will be counted using HTSeqcount and Feature counts software. Then, we will analyze differential expression patterns using DEseq2 and mirDeep softwares. The relevant results will be compared with clinical data, neuroimaging evaluation, risk factors and ischemic stroke subtypes. **Results**: To date we have recruited patients, 51% are males, with average age of 65.8 years old (+/- 13 years). Their main risk

factors presented by the patients are hypertension (66%), diabetes (46%) and smoking (9%). **Relevance:** At the end of our study we hope to be able to identify circulating microRNAs that can be used as a non-invasive biomarker of prognosis in patients with ischemic stroke. These may help to better tailor treatment strategies in the acute phase of ischemic stroke in order to improve recovery rates.

References: [1] Sepramaniam, S et al, Int. J. Mol. Sci. 15: 1418-32,2014; [2] Vemuganti, R. Neurochemistry International 63: 438–449,2013; [3] Dobkin and Carmichael. Neurorehabilitation and Neural Repair. 30, 2015.

STUDY OF THE EPR (ELECTRON PARAMAGNETIC RESONANCE) SPECTRA OF IRON IONS IN CEREBRAL TISSUE

F. S. Otsuka[1], J. H. O. Barbosa[1], R. S. Lima[2], E. A Junior[2], M. C. G. Otaduy[2], C. E. G. Salmon[1]

[1]InBrain Lab, Department of Physics, FFLRP, USP, [2]Department of Radiology, HCFM, USP.

Introduction and Hypothesis: The *EPR (Electron Paramagnetic Resonance)* is an useful technique in quantifying the paramagnetic ions' concentrations in frozen samples because it can also tell its form and binding states. In the case of the Fe^{3+} on brain tissue, different peaks can be observed related to heme and nonheme metalloproteins [2-6]. Also, at different temperatures it was observed different peaks for the same sample [2,3] of purified neuromelanin, suggesting polynuclear (superparamagnetic and antiferromagnetic) aggregates of iron in neuromelanin. One other work [7] used the SQUID technique together with EPR as a means of getting a more detailed study about ferritin (magnetite/maghemite). **Objective:** Using the *EPR* (*Electron Paramagnetic Resonance*), this study aims to obtain spectra of the different ionic states of iron in the brain tissue and, eventually, at different temperatures to study the paramagnetic characteristics of the iron in the brain. **Methods:** The extraction of the basal ganglia tissues of one *postmortem* subject was performed at HCFM-USP and the EPR experiments will be made with a X-band spectrometer with freeze-dried samples at different magnetic field sweeping rates and, eventually at different temperatures in order to obtain different ionic states' spectra of iron in the brain. Simulated curves will help telling what the peaks observed represents. And the peak-to-peak amplitude will tell the quantity of that ion.

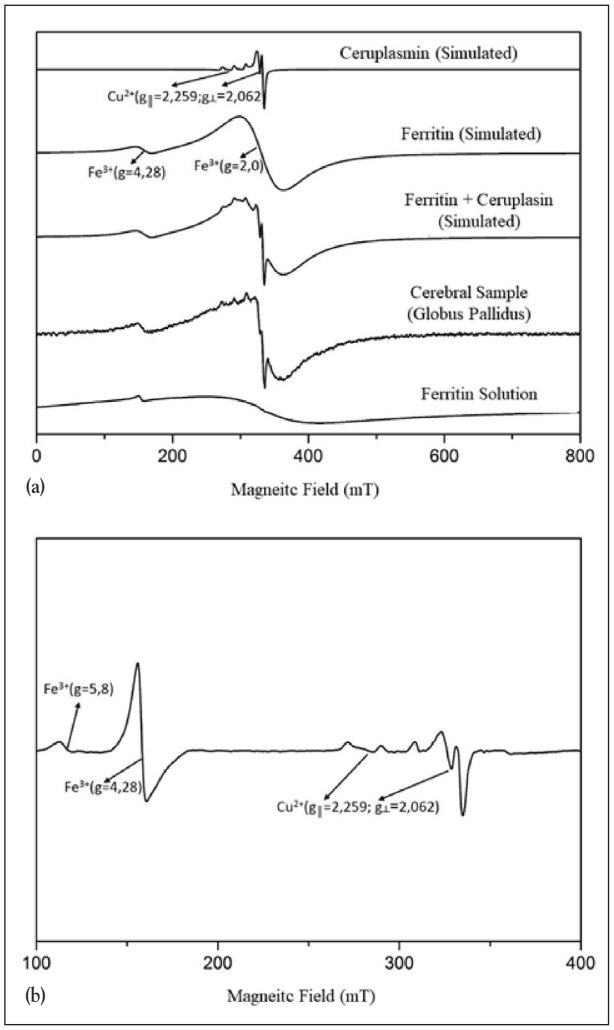


Figure 1. An EPR spectra at room temperature (a) and -196ºC (b). It is possible to see different peaks corresponding to the same ion but in different forms. Figure adapted from [1].

Relevance: Few studies have shown EPR spectra of the different ionic states of iron in the brain tissue. A more detailed study of these spectra will provide further information about the state and specific forms of iron in the brain and thus it will enable a more in-depth study of neurodegenerative diseases in the optic of the biochemistry and biophysics.

References: [1] Barbosa JHO et al., Tese de Doutorado, USP: 72, 2016; [2] Aime S et al., Biochimica et Biophysica Acta 1361(1): 49-58, 1997; [3] Lopiano L et al., Biochimica et Biophysica Acta 1500(3): 306-312, 2000; [4] Shima T et al., Free Radical Biology & Medicine 23(1): 110-119, 1997; [5] Zecca L et al., J Neural Transm 5: 203-213, 1993; [6] Weir MP et al., Biochimica et Biophysica Acta 828: 298-305, 1985. [7] Kumar P et al., Scientific Reports 6: 38916, 2016.

PHENOTYPIC CHARACTERIZATION AND PRELIMINARY GENETIC STUDIES OF A LARGE COHORT OF PATIENTS WITH CHILDHOOD EPILEPTIC ENCEPHALOPATHY (CEE).

HT Moraes[1], MC Gonsales[1], L Sauma[2], CV Soler[1], PAO Ribeiro[1], ML Santos[1], MM Guerreiro[2], MA Montenegro[2], AC Coan[2], BS Carvalho[3], I Lopes-Cendes[1]

[1]Department of Medical Genetics, [2]Department of Neurology; School of Medical Sciences; [3]Department of Statistics, Institute of Mathematics, Statistics and Computer Science; University of Campinas, UNICAMP, Campinas, SP, Brazil and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: CEEs is a heterogeneous group of rare and severe epilepsies characterized by different types of seizures with difficult control and high-risk of progressive neurological deterioration [1]. There are different clinical types of CEEs related with the age of onset including: Dravet syndrome, Doose syndrome, Ohtahara syndrome, early myoclonic encephalopathy, West syndrome, Lennox-Gastaut syndrome, epilepsy of infancy with migrating focal seizures, epileptic encephalopathy with continuous Spike-and-wave during sleep and Landau-Kleffner syndrome [2]. The diagnosis of CEE is based on clinical data and electroencephalogram results and the etiology remains unknown in most patients. Even with the progress of molecular studies and the identification of new mutations associated with CEE a significant number of the patients still do not have a major genetic variant identified, since only 1-2% of epilepsies are considered monogenic [3]. This highlights the need for additional studies using complex models of genetic inheritance. Therefore, the main objective of this study is to access a large cohort of patients and to characterize them in detail from the phenotypic and genetic aspects, including search for genetic variants which may cause CEE in a single gene or polygenic inheritance. In preparation for our genetic studies we describe here the results of the detailed clinical characterization of these patients as well as some preliminary genetic results. **Materials and Methods:** All patients with CEE diagnosis followed at our childhood epilepsy clinic from the year 2000 to today were invited to participate in this study. In addition, we received samples for the genetic study of patients from different centers in Brazil. Clinical data was collected following a standard protocol by the treating physicians. To date, we have accessed a total of 171 patients with different CEE syndromes. One hundred and thirty-three of whom have been tested for the presence of mutations in six candidate genes using Sanger sequencing and a next-generation sequencing panel. The results of the sequencing experiments were analyzed using different bioinformatics algorithms and compared to a panel of 200 normal individuals of the Brazilian population, data available at www.bipmed.org. **Results:** Of the 171 patients, 99 were male (57.9%) and 72 were female (42.1%). We obtained the birth date on 99 patients and age of onset of seizures on 99 different patients and determined that the current age ranged from 1 to 42 years old (mean 12.7 years) and the age of onset of seizures ranged from 0 (within the first month of life) to 132 months (mean 23.8 months). We also obtained DNA samples from 151 patients and tested 133 for the presence of mutations. Preliminary genetic studies showed 19 patients with mutations in the *SCN1A* gene (14.2%), one patient with a mutation in the *SCN2A* gene (0.7%), ten patients with mutations in the *SCN1B* gene (7.5%) and, most interesting, five patients with mutations in both *SCN1A* and *SCN1B* genes (3.8%). **Discussion:** Assuming a monogenic

inheritance we were able to make the diagnosis in only 26.2% of 133 patients with CEE. We believe that as our project progresses and we add new bioinformatics analysis, especially considering a polygenic inheritance, we will increase the yield of molecular diagnosis. **Conclusions:** We report preliminary results of clinical and genetic characterization of a large cohort of patients with CEE. To our knowledge, this is the largest study of this kind in Latin America and it is likely to significantly contribute to a better understanding and diagnosis of CEEs. We also aim to make public at www.bipmed.org all genetic data acquired in this study, contributing further to improve research in this field.

References: [1] doi: 10.1016/S1474-4422(15)00250-1; [2] doi: 10.1590/0004-282X20150122; [3] doi: 10.1111/j.1469-8749.2008.03058.x.

SEARCHING FOR SOMATIC MUTATIONS IN FOCAL CORTICAL DYSPLASIA USING NEXT GENERATION SEQUENCING

V.S. de Almeida[1], S.H. Avansini[1], M. Borges[1], F.R. Torres[1], F. Rogerio[2], B.S. Carvalho[3], F. Cendes[4], I. Lopes-Cendes[1]

[1]Department of Medical Genetics, School of Medical Sciences, [2]Department of Anatomical Pathology, School of Medical Sciences, [3]Department of Statistics, Institute of Mathematics, Statistics and Scientific Computing, IMECC,[4] Department of Neurology, School of Medical Sciences; University of Campinas, UNICAMP, Campinas, SP, Brazil and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, SP, Brazil.

Introduction: Malformations of cortical development (MCD), including focal cortical dysplasia (FCD), can cause epilepsy and are often associated with the occurrence of refractory seizures [1]. FCD is characterized by alterations in cytoarchitecture also observed in other MDCs, such as Tuberous Sclerosis (TS) and Hemimegaencephaly (HME) [2,3]. Recently, mosaic mutations were detected in TS, HME and FCD [4]; however, it is still unclear whether somatic mosaicism is indeed frequent in FCD [4]. **Materials and Methods:** Deep sequencing of the mTOR pathway genes was performed on genomic DNA extracted from brain tissue resected by surgery (BTRS) and blood samples of five patients with FCD type II. We performed capturing and enrichment with SeqCap EZ Choice Library (NimbleGen, Roche). Samples were sequenced following a 150bp paired-end protocol in a Miseq (Illumina), to achieve at least 600x of average coverage. We aligned sequences using BWA-MEM and performed realignment around SNPs and indels, quality recalibration and variant calling using the Genome Analysis Toolkit (GATK). We evaluated mosaicism using Mutect2. Variants were classified as mosaic mutations when less than 10% of reads are not aligned to human genome reference and are present only in BTRS. Variants were filtered prioritizing frameshift, missense, nonsense and splicing site mutations that were localized in coding regions or exon-intron boundaries. In addition, we also focused in variants not described previously or variants whose minor allele frequency (MAF) is < 0.01. Effect of variants was evaluated using Variant Effect Predictor (VEP). **Results:** We identified somatic mutations in 2/5 patients (40%). Patient P20 presents a *MTOR* somatic mutation c.4379T>C/p.Leu1460Pro (rs1057519779, NM_004958.3) with allele frequency of 9/503 reads (1.8%) in BTRS and 0/438 (0%) in blood. Patient G118 presents a *TSC2* somatic mutation c.3781G>A/p.Ala1261Thr (not reported previously; NM_000548.3) with allele frequency of 7/409 reads (1.7%) in BTRS and 0/373 reads (0%) in blood and an *AKT1* somatic mutation c.349_351del/ p.Glu117del (rs768025881, NM_005163.2) with allele frequency of 10/454 (2.2%) in BTRS and 1/350 reads (0.29%) in blood. These mutations were not found in the Exome Aggregation Consortium (ExAC) and in a Brazilian database of genomic variants (www.BIPMed.org). VEP classified all variants as probably damaging. In addition, is already reported in a patient with FCD. **Discussion/Conclusion:** Somatic mutations identified are potentially deleterious since they were found in genes previously associated with FCD. Furthermore, somatic mutations in mTOR genes seems to be common in patients with FCD. Additional deep sequencing experiments, including more patients with FCD, will be carried out in order to confirm our preliminary findings.

Supported: CEPID-FAPESP

References: [1] Kuzniecky RI. Epilepsia. 35 Suppl 6:S44-5 6, 1994. [2] Fauser S, Huppertz HJ, Bast T, et al., Brain 129:1907-16, 2006. [3] Mühlebner A, Coras R, Kobow K, et al., Acta Neuropathol 123:259-72, 2012. [4] Becker AJ, Urbach H, Scheffler B, et al., Ann Neurol 52:29-37, 2002.

IMPLEMENTATION OF A LATIN AMERICAN NETWORK FOR THE INVESTIGATION OF THE GENETIC LANDSCAPE OF CHILDHOOD EPILEPTIC ENCEPHALOPATHIES: REPORT OF PRELIMINARY RESULTS

H. Urquia-Osorio [1, 3], E. Almendares-Bonilla [2], M. T. Medina [3], R. Caraballo [4], F. Cendes [1], I. Lopes-Cendes [2]

[1] Department of Neurology, [2] Department of Medical Genetics; School of Medical Sciences, University of Campinas (UNICAMP); and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas SP, Brazil. [3] Faculty of Medical Sciences, National Autonomous University of Honduras (UNAH), Tegucigalpa, Honduras. [4] Hospital J P Garrahan, Neurology, Capital Federal, Buenos Aires, Argentina.

Introduction: Childhood epileptic encephalopathies (CEEs) are a heterogeneous group of epilepsies characterized by progressive development of psychomotor dysfunction associated with severe epilepsy. Recently, rare *de novo* mutations have been found in patients with CEEs. Since it is well known that allele frequency for rare variants may significantly vary across populations from different ethnic backgrounds, it is possible that the frequency of the mutations causing CEEs may also vary. In order to investigate the issue, we have established a Latin American research network for the investigating of the genetic landscape of CEEs. **Materials and Methods:** This is a project involving the BRAINN and the International League Against Epilepsy (ILAE). Neurology services from different countries in Latin America have been contacted over the past year. A common clinical protocol has been established which includes inclusion and exclusion criteria for patient enrolment. Data will be obtained from patients with all types of CEEs (West, Otahara, Lennox-Gastaut, Dosse, Dravet syndrome and others). DNA extraction will be performed in each country and samples will be shipped to the molecular genetics laboratory at UNICAMP for molecular testing performed by whole exome sequence. **Results:** From November 2016 to October 2017 we were able to directly contact 17 collaborative centers (CCs) from eight Latin American countries (Peru, Mexico, Argentina, Chile, Colombia, Honduras, Nicaragua and Dominican Republic). More than 80% (14/17) of the CCs were receptive to the proposal by answering to our messages, and around 70% (12/17) of the CCs remain in current active communication with us (3 CCs from Peru, 2 from Argentina, 4 from Chile, 1 from Colombia, 1 from Honduras, and 1 Dominican Republic). Six CCs are still waiting for institutional approval for international collaboration or to better explore local capacities for DNA extraction. Seven CCs already submitted the projects to the local ethics committee, of which until now, two were approved. Currently, around 20 patients with CEEs have already been selected for DNA extraction in the respective countries. In addition, we developed a program, including videos and on-site training, aiming to establish a centralized DNA extraction facility in Honduras (led by researchers from the UNAH) to centralize extraction in all Central America and Caribbean countries.

Discussion: The results obtained so far in the consolidation process of the regional research network have been successful. Mostly, the initiative has been well accepted; however, several factors have delayed the work, such as: i) few centers for the studies of epilepsies in Latin America; ii) difficulties to identify local capacities to perform DNA extractions mainly in Central America and Caribbean countries; iii) use of extraction methods different from the one required for next-generation sequencing; iv) significant delays in institutional and local ethics committees for approval of the project. Strategies to solve these problems have been implemented successfully in most cases. **Conclusion:** A systematic evaluation of CEEs has never been performed in Latin America, which have negative implications in the ability to make the diagnosis and manage these patients. On the research side, due to the high heterogeneity and population admixture, we are likely to identify additional mutations/candidate genes in the Latin American population, thus contributing to the ILAE global efforts to better understand and to offer better treatments to severe epilepsies worldwide.

References: [1] Gonsales MC et al., Arq Neuropsiquiatr 73(11): 946-958, 2015; [2] McTague A et al., Lancet Neurol 15(3): 304-316, 2016.

COMPARATIVE ANALYSIS OF DENTATE GYRUS FROM NAIVE WISTAR RATS AND HUMAN HIPPOCAMPUS USING MOLECULAR TOOLS.

A. B. Godoi[1], A. M. Canto[1], A. H. B. Matos[1], A. S. Vieira [2], I. Lopes-Cendes[1]

[1]Genetics Dept., FCM, UNICAMP.

Introduction and Hypothesis: Studies about the hippocampus have been performed throughout the years with the main purpose of understand its functioning and with that explain the various diseases which affects this structure. However, to understand the complexes mechanisms underlying these diseases we must understand other structures which compose the Hippocampus formation [1], not only the hippocampus itself. This set of structures are composed by the Dentate Gyrus, Subiculum and Entorhinal cortex and they are directly connect-

ed which makes the study of each one of them essential for the knowledge of the Hippocampal formation [HF] and its physiology. Among the components of the HF, the Dentate Gyrus [DG] is the structure responsible for preprocess the information coming from the entorhinal cortex, so that the stimuli originated in the cortex can reach the hippocampus CA3 [2]. Therefore, the use of some molecular tools such as proteomics and transcriptomics will allow us to generate data about the regulation of the gene expression in the DG of human tissues and rats. **Objective:** We propose to analyze the DG from naïve Wistar rats and human tissue coming from autopsy using proteomics and transcriptomics techniques to identify changes in molecular mechanisms between the two species, and with these data the Rat is a suitable animal model for Humans. **Methods:** Five brains from Wistar rats and five human hippocampus from autopsy will be used in this project. Therefore, the cellular populations of interest, dentate gyrus, will be isolated using laser-capture microdissection. The rat DG will also be divided into Dorsal and Ventral portions. After this processes, the tissues will be analyzed using proteomics (MS/MS – label-free) and transcriptomic (New generation sequencing) analyses. The proteomics starts with the extraction of the proteins using Urea 8M followed by trypsinization and dessalting with C18 columns. The proteins will be analyzed using a LTQ-Orbitrap from CeTICS/ Butantan and the bioinformatics analysis with MaxQuant e Perseus software. The transcriptomic analysis will be performed by sequencing the RNA using an Illumina Hiseq® platform. Sequences will be aligned and quantified with the TopHat/DESeq2 pipeline for total RNA. **Relevance:** This study is relevant because it will generate a multi-OMICs and multi-species database which has never been generated before. It will allow us to compare and validate the Rat as a good animal model to Humans in the neurobiological approach. Furthermore, the study of that structure itself, the Dentate Gyrus, might contribute to the comprehension of classic Neuroscience events, such as long-term memory and the special localization. Such data will give parameters for new researches aimed to understand diseases affecting the dentate gyrus, such as Epilepsy, Alzheimer's Disease, among others.

References: [1] doi: 10.1093/acprof:oso/9780195100273.003.0003; [2] doi: 10.3389/fncir.2013.00015.

WHY NEUROSCIENCES NEED NEUROETHICS? A FIRST APPROACH IN THE BRAZILIAN CONTEXT

Barbosa, S.Emerson[1,3]; Bertolucci, P. Henrique[1,2]; Nogueira, Maria Inês1[1,3];Russo, Marisa[1,3]

[1]Neuroethics Group CNPq- NEURO-I-SELF, UNIFESP ,[2]Neurology, UNIFESP. [3]Neuroanaomy, ICB-USP.

Introduction and Hypothesis: The neuroscience's field is within the context of the so-called emerging technologies, which are characterized by the use of sophisticated technology. Neurotechnology revolutionized the way we understand the brain, our feelings, cognitive abilities, decision-making and moral choices. These achievements have strongly impacted not only the clinical and experimental field related to the knowledge of the brain, butalsohave affected the various sectors of society, such as economic, education and law. Due to this strong social impact of neurosciences many institutions and scientific Brain consortiums have created discussion groups to reflect on neuroethics issues.Undergraduate neuroethic training has been proved to be fundamental to help the students to deal with ethical questions that are not necessarily raised bythe traditional bioethics. Neuroethic training would also increase the students' perceptions of a responsible science *vis-a-vis* of society. Some recent studies in other countries have shown that neuroethic training has a positive impact on neurosciences students. **Objective:** In Brazil the undergraduate neuroethics training is quite recent along with poorly understanding of various topics by students and teachers. The objective of this research is to depict this gap and reveal some recent data performed by the NEURO-I-SELF Group (CNPq). **Methods:** A preliminary survey has been carrying out to map the neuroethics courses at the main public Universities in Brazil. We will also identify the researchers teams dedicated to the neuroethics studies and training in Brazil. This will be done by analyzing the date of the main funding agencies in Brazil (such as CNPq, FAPESP and Capes).Our first step for the analyses is to determine the impact of neuroethics training course among the neurosciences students of UNIFESP and USP. In a second step, a questionnaire will be used to measure the changes in the student's perception between the neuroscience and society. **Relevance:** In spite of the relevance of the subject for science and society, there are few studies in Brazil approaching the teaching of neuroethic and their impact among neurosciences students. This study can help to improve neuroethics training courses in Brazil.

References: [1]Abu-Odeh D., J, JUNE, 13(2) :A110-A119, 2015; [2] Forlini, C, et al, Frontiers in Psy, 6,1-5, 2016;[3] Gini, A. et al., Neuroscience Neuroecomy, 4, 1-10, 2015; [4] Greely, H. et al., Neuron, 92,2,2016; [5] Sahakian, B.J. et al,, Phil.Trans. R.Soc.B 370, 20140214, 2015 ;[6]Sanakian,BJ ; Morein-Zammir,S., Science, 325, 147,2009 ;[7]Walther G, Neurotehics, 6,343-351, 2013 ;[8] Walther, G. Neuroethics, 6, 343-351,2013.

KINEMATIC ASSESSMENTS IN PATIENTS SUBMITTED TO ROBOTIC THERAPY AND TDCS

S.B.Reis[1], H.I.Krebs[2], A.B.Conforto[3]

[1]OT. Master degree student. Hospital das Clínicas/São Paulo University, Brazil, [2] MIT, Boston, MA, US, [3]Neurostimulation Laboratory, Hospital das Clínicas/São Paulo University, Brazil.

Introduction: Previous studies indicate that quantification of kinetics and kinematics contributes to understanding of the motor learning process [1]. The goal of this preliminary study is to perform kinematic assessments in patients submitted to robotic therapy (RT) and transcranial direct current stimulation (tDCS) at an early stage after stroke. **Materials and Methods:** Six patients, between 3 to 9 weeks post stroke with upper limb paresis (scores 7-56, Fugl--Meyer Motor Assessment, upper limb) were randomly assigned to RT and either active or sham cathodal tDCS (ctDCS). Patients received 18 sessions (one session per day, 3 days per week) of 20 min of ctDCS of the motor cortex of the unaffected hemisphere followed by 40 minutes of RT (InMotion Arm – 2 degrees of freedom), Adaptive Protocol. The movement smoothness (average of 16 trials) was assessed at the beginning of each session and after each of 1 to 3 blocks of training (320 movements per block). We performed an exploratory analysis with paired t-tests to compare the improvement in smoothness between the first and the last session of treatment in each group. We compared changes in smoothness between the two groups with the Mann-Whitney test. **Results:** There was a statistically significant improvement in smoothness in the active group ($p=0.01$) but not in the sham group ($p=0.23$). However, the difference in change in smoothness was not statistically significant between the groups ($p=0.32$). **Discussion:** These preliminary results suggest that RT preceded by ctDCS of the unaffected motor cortex may improve smoothness of movements in patients in the subacute stage after stroke, broadening results of a previous study that assessed smoothness of wrist movements after administration of anodal tDCS plus RT in patients in the chronic phase after stroke [2]. The lack of significant between-group differences may be due to the small sample size. **Conclusion:** These results should encourage further studies with a greater number of patients to confirm positive effects of ctDCS combined to RT, on kinematics of the upper limb in the subacute stage after stroke.

References: [1] Veerbeek JM et al., Neurorehabil Neural Repair 31(2):107-121, 2017; [2] Giacobbe V et al., NeuroRehabilitation 33: 49–56, 2013.

SIMULTANEOUS ASSESSMENT OF CBF AND BRAIN FUNCTION THROUGH DUAL-ECHO ARTERIAL SPIN LABELING

A. M. Paschoal[1], F. F. Paiva[2], R. F. Leoni[1]

[1]InBrain Lab, FFCLRP, USP, [2]CIERMag, IFSC, USP.

Introduction: Both Cerebral Blood Flow (CBF) and information about brain functions are important parameters for the evaluation of cerebrovascular diseases, such as vascular dementia. Arterial Spin Labeling (ASL) is an MRI perfusion--weighted method essentially developed to measure CBF non-invasively [1]. However, due to its intrinsic low SNR, it is necessary to acquire multiple volumes over the time to estimate CBF. Recently, the ASL time series has been used to infer functional information. The present study aims to assess CBF and brain function parameters in a single acquisition through a dual-echo readout approach of ASL (DE-ASL) [2] during a motor task condition. Materials and Methods: 20 participants were scanned on a 3T MRI scanner equipped with a 32-channel receive head coil. DE-ASL data were acquired using a 2D EPI readout and a pseudo-continuous (pCASL) labeling scheme with the following parameters: TR = 4000ms; TE1/TE2 = 9/28 ms; labeling duration/post-label delay = 1450/1550 ms, 20 slices, slice thickness = 5 mm, spatial resolution = 3.75 x 3.75 mm2, FOV = 240 x 240 mm2, flip angle = 90°. The experimental protocol was a block-designed paradigm alternating rest, and right hand finger tapping. Each block had duration of 32 seconds, totalizing four blocks of rest and four blocks of motor task. Results: In figure 1, we show the CBF map for the group for TE1.

For the functional analysis, we obtained a total of 5 networks for each TE through ICA. Specifically to motor network, we found that CBF time-series was better correlated to experimental design for TE1, and that CBF network seemed to be more spatially specific than concomitant BOLD (cc-BOLD) network (figure 2). **Discussion:** For CBF quantification, short TE is recommended since for long TE values there is an increase in BOLD contributions to the signal. Our results for short TE were consistent with the literature regarding the CBF values. For network identification using ICA, our results for long TE showed a high activation T-score, confirming the effects of BOLD contribution. The better correlation

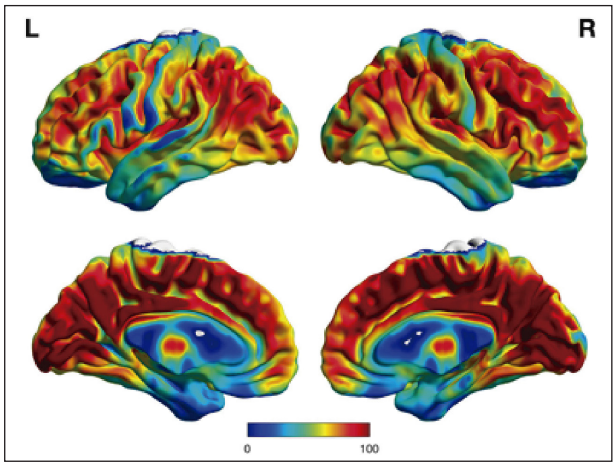


Figure 1. CBF maps.

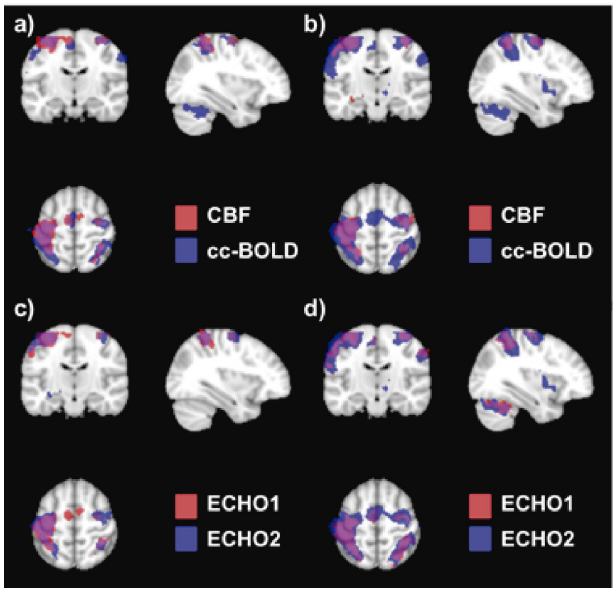


Figure 2. Motor network comparison between a) CBF and cc-BOLD for TE1, b) CBF and cc-BOLD for TE2, c) TE1 and TE2 for CBF networks and d) TE1 and TE2 for cc-BOLD networks.

between CBF time-series and experimental design for TE_1 is due to the reduced contribution of T2* effects on images acquired with shorter TE values, and consequently higher SNR when compared to images acquired using long TE values. Finally, the higher spatial specificity of CBF networks reflects effects that are measured directly in the activation site, while BOLD effect comes from an indirect measurement. **Conclusion:** Our study analyzed how CBF and functional fluctuations can be measured simultaneously through DE-ASL. We concluded that CBF maps should be extracted from short-TE images. For functional analysis, long TE values are recommended to identify general networks, while CBF networks acquired using short TE are better to find accurate spatial activation site.

References: [1] Detre JA et al., Magn Reson Med 23(1): 37-45, 1992; [2] Tak S et al., Neuroimage 84: 672-680, 2014.

DECREASED SHORT-INTERVAL INTRACORTICAL INHIBITION CORRELATES WITH BETTER PINCH STRENGTH IN PATIENTS WITH STROKE AND GOOD MOTOR RECOVERY

K.N.F. Andrade[1,2], A.B. Conforto[1,2,3]

[1]Neurostimulation Laboratory, Neurology Clinical Division, Hospital das Clínicas/ São Paulo University;[2] NAPNA-USP (Núcleo de Apoio à Pequisa em Neurociência Aplicada) São Paulo University, São Paulo, Brazil; [3]Hospital Israelita Albert Einstein, São Paulo, Brazil.

Introduction: Short-interval intracortical inhibition (SICI) evaluated through transcranial magnetic stimulation (TMS) reflects activation of inhibitory, $GABA_A$ergic cortical neurons in the primary motor cortex [1]. A meta-analysis concluded that SICI is decreased in the primary motor cortex of the affected hemisphere ($M1_{AH}$) early, but not in the chronic phase after stroke [2]. In this phase, in patients with moderate to severe upper limb impairments, deeper SICI correlates with better motor performance [3,4]. **Materials and Methods:** Twenty-two subjects were included in the study. SICI was measured with a paired-pulse paradigm. Thumb lateral pinch force was measured according to a standardized protocol [5]. Between-group comparisons were made with unpaired t tests or Mann-Whitney tests according to distribution of the data. The correlations between behavioral and TMS measures were evaluated with Spearman´s rho. P-values ≤ 0.05 were considered statistically significant. **Results:** There was a significant correlation (rho = 0.69, p = 0.014) between SICI and pinch strength in patients, but not in controls. SICI was significantly deeper in patients with greater hand weakness. **Discussion:** For the first time, we report a significant correlation between SICI in $M1_{AH}$ and pinch force in subjects with excellent motor recovery in the chronic phase after stroke. In line with results of a meta-analysis [2]. here were no significant differences in SICI between patients with stroke and controls. In controls, the absence of a significant correlation between pinch strength and SICI may be explained by a ceiling effect. In patients, SICI in $M1_{AH}$ was deeper in subjects with stroke and lower levels of pinch strength. This result contrasts with those reported in subjects with moderate to severe hand motor impairment in the chronic phase [3,4]. **Conclusion:** These preliminary findings suggest that decreased $GABA_A$ activity in $M1_{AH}$ correlates with better hand motor performance in well-recovered subjects with stroke in the chronic phase. It is possible that effects of up- or down-regulation of $GABA_A$ activity may lead to different outcomes, according to severity of motor impairments.

References: [1]. Talelli P et al., Clin Neurophysiol 59: 1641-59, 2006; [2] McDonnell MN et al, Brain Stimulation 10:721-734, 2017;[3] Marconi B et al., Neurorehabil Neural Repair 25:48-60, 2011; [4] Honaga K et al., Clin Neurophysiology 124:364-70, 2013; [5]. Mathiowetz V et al. Arch Phys Med Rehabil 66:69-74, 1985.

ATTITUDES OF TEACHERS TOWARDS EPILEPSY AND THEIR RELATION WITH KNOWLEDGE AND BELIEFS

T. P. Ferro[1], I. Assumpção[2], L. M. Li[1, 2]

[1]Brazilian Institute of Neuroscience and Neurotechnology, BRAINN, UNICAMP, [2]Assistence of patients with epilepsy, ASPE, UNICAMP.

Introduction: This study aims to evaluate the adequate knowledge and beliefs about epilepsy and association with different models of attitudes described by teachers towards students with epilepsy. Epilepsy is a chronic neurological disease that affects 1% of the population and about 50% of the cases are diagnosed in children. This condition is marked by stigma that affect the psychological, physical, social and schooling areas, revealing difficulties from childhood to adulthood. Identifying the influences and patterns of teachers' behavior in the face of epileptic seizures can help us design actions to reduce stigma. **Materials and Methods:** A cross-sectional study was conducted among public school teachers from 10 different schools in São Paulo State between May 2017 and November 2017. A self-report questionnaire with multiple choice and dissertations answers was given anonymously to each teacher and answered in the researcher presence. The questionnaire was focused on asking for information regarding the following areas: teachers' demographic information, knowledge about epilepsy, attitudes towards epilepsy and perceptions regarding this condition. The questionnaires were home designed after a deep review literature and developed following a standard process for elaboration and validation. The Qui-Square test was used to assess association between attitude and knowledge/belief and the p. value less than

0.05 was set as significant. **Results:** A total of 135 teachers from the public school system participated in this study (average of 43 years old and 75% female). Most teachers (72%) had more than 10 years of experience and more than half gave classes in Elementary School and High School. Overall, 52% of the participants demonstrated misconceptions about the scientific knowledge about epilepsy and 39% showed inadequate beliefs about this disease. Among them, 88% had heard about epilepsy, 24% had students with epilepsy and only 4% had some course about this topic. We found that teachers who demonstrated correct levels of knowledge about the causes and symptoms of epilepsy tend to have more appropriate attitudes towards students with epilepsy (p=0,01). The same is true for participants who have demonstrated adequate beliefs about epilepsy (p=0,003). However, a level of statistical significance was not found among participants who presented lack of knowledge (p=0,1) and beliefs (p=0,67) about epilepsy and their attitudes towards students with epilepsy. **Discussion:** The results found on the low level of knowledge of teachers about epilepsy corroborate with the literature, but different from other studies, the present study reveals qualitative data regarding the type of attitude of the participants in moments of epileptic seizure during classes, demonstrating that attitudes in the assistance during an epileptic seizure are associated with the level of scientific knowledge about this disease. Meanwhile, teachers' inadequate attitudes during students' seizures may be related not only to the level of knowledge and beliefs on the subject, but to other psychological and cognitive variables that control human behavior, such as levels of mental health, initiative, flexibility, empathy and own experience with epilepsy in other contexts. **Conclusion:** The present work confirms the relevance of the health area being closer to education, especially with the new reality of school inclusion. Many health issues are present in the school routine, especially neurological conditions that impact students' social learning and social interaction.

A FRIENDLY INTERFACE FOR FUNCTIONAL CONNECTIVITY ANALYSIS FOR EEG SIGNALS

D. M. Alves[1,2], G. S. Ueti[1], P. G. Rodrigues[1,2], A. K. Takahata[1], D. C. Soriano[1,2]

[1]Center for Engineering, Modeling and Applied Social Sciences (CECS), ABC Federal University (UFABC), [2]Brazilian Institute for Neuroscience and Neurotechnology (BRAINN).

Introduction: Graph theory has been well succeeded in representing relation between elements. Techniques based on functional connectivity evaluation and graph measures, in neurosciences, have contributed to pathologies diagnosis, such as Parkinson, Alzheimer, depression.[1] Electroencephalogram-based (EEG-based) Brain Computer Interfaces (BCIs) have been proposed using this framework, which raised the possibility to improve the understanding of functional organization of mental processes that are fundamental for this emerging assistive technology. **Objective:** This work aims to provide a friendly interface for evaluating functional connectivity and the underlying graph metrics from EEG signals collected by Open BCI hardware. **Methods:** We developed a Java-based interface that allows loading a text file from acquisitions performed by Open BCI or other BCI system. It allows users to apply a spatial common average reference (CAR) filter and to set updating graph rate, i.e., samples number for time window and overlapping samples number between consecutive windows. Functional Connectivity is evaluated with the use of Pearson's correlation between electrodes, that when greater than correlation threshold (defined by user) it establishes the edges between nodes, representing connections between brain regions. Four graph measures can be evaluated by our interface using the GraphStream toolbox [2]: node degree, clustering coefficient, eigenvector centrality and betweenness centrality. The results with desired metrics can be exported to a text file. Figure 1 shows a study case, exposing the parameters control panel (left) and the difference between functional connectivity pattern obtained under right (middle panel) and left feet movement (right panel). The graph layout reproduces the default electrode positions on scalp used in Open BCI software. Moreover, nodes colors and sizes are related to its respective degree. The experimental protocol was approved by ethics committee of UFABC (CAAE: 51005615.2.0000.5594).

Relevance: This work presents a friendly graphical interface for functional connectivity analysis and brain functional organization investigation. The interface was integrated with low cost Open BCI acquisition hardware and *GraphStream* toolbox, a computational efficient graph analysis environment with high potential application for online operation, which outlines a natural perspective of this work.

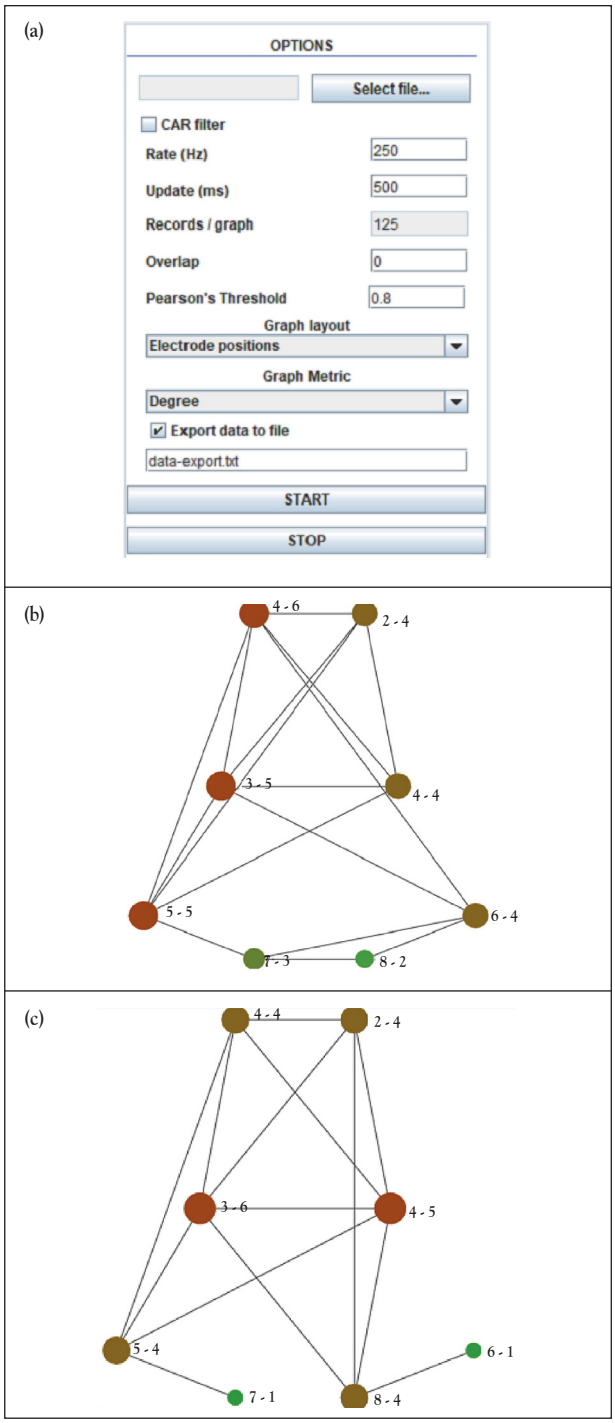


Figure 1. (a) Interface parameter control; (b) Functional Connectivity evaluated under right feet movement; (c) Functional Connectivity evaluated under left feet movement.

References: [1] Friston KJ, Brain Connectivity 1: 13-36, 2011; [2] Graph Stream Project., http://graphstream-project.org, 2016.

QUANTIFICATION OF BOLD-FMRI HEMODYNAMIC PARAMETERS IN PATIENTS WITH ASYMPTOMATIC CAROTID STENOSIS IN HYPERCAPNIA

K. F. Secchinato[1], P. H. R. Silva[1], A. P. A. Camargo[2], O. M. Pontes-Neto[2], R. F. Leoni[1]

[1]Inbrain Group, Department of Physics, FFLCRP, USP. [2]Department of Neuroscienses and Behavaioral Science, FMRP, USP.

Introduction and Hypothesis: Asymptomatic unilateral internal carotid stenosis is associated with cognitive performance impairment that can be explained by changes in cerebral hemodynamics [1]. However, quantitative hemodynamic parameters and their correlation with the subject's cognitive status are unknown. Therefore, our hypothesis is that the quantification of the hemodynamic response parameters, obtained with the blood oxygenation level dependent functional magnetic resonance imaging (BOLD-fMRI) in combination with a hypercapnia challenge [2], may provide useful information to assess brain alterations due to this pathology. **Objective:** To investigate and quantify the cerebral hemodynamic parameters in response to inhalation of CO_2 in patients with asymptomatic carotid stenosis. **Methods:** With the approval of the Research Ethics Committee, 10 patients with unilateral internal carotid artery and 10 age-matched healthy controls participated in this study. Experiments were performed on a 3T Philips System, using a 32-channel head coil for reception. For anatomic reference and volumetric analysis, images were acquired using a 3D T1-weighted GRE sequence (TR/TE = 6.7/3.1 ms, FA = 8°, FOV = 256 mm, 160 slices thickness 1mm). BOLD images were obtained with a GRE echo-planar imaging (EPI) sequence, covering both hemispheres using the following parameters: TR = 1000 ms, TE = 30 ms, flip angle = 90º, matrix = 128 x 128, FOV = 230 mm, slice number = 20, slice thickness = 1 mm. The vasodilator stimulus was composed of a mixture of CO_2 and medical air. A device designed by the collaborators was used to deliver the gas mixture to the subject. The paradigm design was composed by five intervals of hypercapnia (14 s each) intercalated by six intervals of rest (30 s each). All BOLD images were motion corrected, spatially normalized to the MNI template and spatially smoothed with a Gaussian filter (FWHM = 4 mm) using SPM12 software. Then, for each subject, the mean signal time curves of brain regions irrigated by the anterior (ACA), middle (MCA) and posterior (PCA) cerebral arteries of both hemispheres were obtained using a script developed in Matlab. The next steps will include: (1) temporal filtering of the hemodynamic signal to improve data quality and quantification accuracy, (2) quantification of the hemodynamic curve parameters (onset, amplitude, time-to-peak and width) and (3) statistical analysis to compare both groups. **Relevance:** The hemodynamic parameters may become potential biomarkers to explain why some asymptomatic individuals present a deficit of cognitive activity and have greater chances of a future ischemia [3]. Then those individuals can have an adequate clinical intervention. However, these parameters should be analyzed with caution, since it has been shown that BOLD responses vary in regions of the brain even in healthy individuals [4].

References: [1] Balucani, C. *et al.*, Neurology, v. 79, n. 17, p. 1788-1795, 2012; [2] Leoni, R.F. *et al.*, Neuroimage 41(4), 1192-1198, 2008; [3] Silvestrini, M. *et al.* JAMA, v. 283, n. 16, p. 2122-2127, 2000; [4] Liu, Y. J. *et al.*, American Journal of Neuroradiology, v. 28, n. 6, p. 1009-1014, 2007.

HIGH-FAT DIET-INDUCED OBESITY INCREASES CHRONIC PAIN SUSCEPTIBILITY: PRELIMINARY RESULTS FROM THE MESOCORTICOLIMBIC SYSTEM ROLE IN MICE

A. F. Brandao[1], I. J. M. Bonet[1], M. O. F. Pagliusi Junior[1], S. F. Magalhaes[1], C. R. Sartori[1]

[1]Laboratory of Pain Studies (Led), Institute of Biology, Department of Structural and Functional Biology of State University of Campinas, UNICAMP.

Introduction: Chronic pain and obesity are the two most prevalent health problems in the modern world and these chronic illnesses are likely to be deeply correlated. In fact, epidemiologic data have shown that patients with obesity have an increased chronic pain susceptibility [1], and some researchers propose that this is related to the increased body weight [2]. However, another hypothesis suggests that the neuroplasticity in the mesocorticolimbic system, particularly in the dopaminergic signaling between ventral tegmental area (VTA) and nucleus accumbens (NAc) [3,4], is underlying the chronic pain susceptibility. Thus, this study investigates how high-fat diet-induced obesity can promote neuroplasticity in the mesocorticolimbic system and, as a consequence, induce mechanical chronic pain susceptibility. **Materials and Methods:** Twenty (six-weeks-old) male C57BL/6JUnib mice were randomly and individually housed with *ad libitum* food and water. Mice were divided in two groups and, for eight weeks, fed with a standard chow diet (CD) (16% from fat) [5] or with a high-fat diet (HFD) (58% from fat) [6]. During all the study, weight was measured weekly. Epididymal, mesenteric and retroperitoneal fat tissues were extracted and weighted. The inflammatory chronic pain induction was adapted from Villarreal et al., in which 18μl of prostaglandin E2 (PGE) (90 ng) or 18μl of saline (0.9% NaCl) was administrated in the plantar surface of the right hind paw for seven consecutive days. Therefore, CD and HFD groups were subdivided in four groups: CD group that received saline (CD-SAL) or PGE (CD-PGE) and, HFD group that received saline (HFD-SAL) or PGE (HFD-PGE). The mechanical nociceptive threshold was assessed using an electronic von Frey apparatus adapted for mice paw [8] and was expressed by delta threshold in grams (g). Experimental procedures were approved by CEUA-UNICAMP, nº4243-1. **Results:** HFD group presented higher total body weight ($p<.05$ from the fifth week on) and fat tissue ($p<.001$) when compared to CD group. ANOVA revealed a diet*time interaction ($p=.01$) and *posthoc* analysis showed that PGE groups (HFD and CD) had higher mechanical nociception threshold 1 day after PGE administration when compared to CD-SAL ($p<.01$) but not HFD-SAL (vs HFD-PGE $p=.89$; vs CD-PGE $p=.99$). Seven and 14 days after PGE administration, only the HFD-PGE group showed a significant increase in the mechanical nociception threshold (7 days $p=.02$; 14 days $p=.01$) when compared to all other groups. Results did not alter when adjusted for total body weight. **Discussion:** Mice with high-fat diet-induced obesity have increased mechanical nociception threshold, even when adjusted for total body weight, as has been recently showed [9]. The neuroinflammation already linked to high-fat diet may be promoting several alterations in the central nervous system signaling, particularly dopamine, leptin and/or inflammatory cytokines' communication within the mesocorticolimbic system. **Conclusion:** High-fat diet increases the mechanical nociception threshold in mice and that is unrelated to total body weight. Future molecular approach is necessary to understand the neuroplasticity role underlying the chronic pain susceptibility promoted by the high-fat diet.

References: [1] McCarthy LH et al., J Am Geriatr Soc 57:115–9, 2009; [2] Grotle M et al., BMC Musculoskelet Disord 9:132, 2008; [3] Taylor AMW et al., J Neurosci 35:8442–50, 2015. [4] Kato T et al., Neurosci Lett 629:73–8, 2016; [5] Reeves PGG et al., J Nutr 123:1939–51, 1993; [6] Cintra DE et al., PLoS One 7:e30571, 2012; [7] Villarreal CF et al., Life Sci 85:822–9, 2009; [8] Martinov T et al., J Vis Exp e51212, 2013; [9] Song Z et al., Sci Rep 7:10350, 2017.

INVESTIGATION ON THE USE OF MULTISCALE ENTROPY ANALYSIS OF TMS MOTOR EVOKED POTENTIALS TO UNDERSTAND THE INFLUENCE OF TDCS

J. R. Camatti[1], A. P. A. G. Q. Carneiro[2], J. Z.Cavalcanti[2,3], I. O. Gomes[2], J. G. V. Miranda[2], A. F. Baptista[1,2,3]

[1]Federal University of ABC;[2]Federal University of Bahia; [3]Bahian School of Medicine and Public Health.

Introduction: Transcranial Magnetic Stimulation (TMS) allows the investigation of cortical activity characteristics through electromiographic (EMG) evoked activity in a target muscle – the Motor Evoked Potential (MEP) [1]. Here we propose Multiscale Entropy (MSE) [2] as a way to assess MEP changes due to transcranial Direct Current Stimulation (tDCS) of the motor cortex. Our hypothesis is that tDCS would induce an increase in the corticomotor system complexity. Materials and Methods: Cortical excitability was assessed through TMS (BiStim, Magstim, UK) on three different moments: 1) baseline; 2) immediately after anodal or cathodal tDCS over the motor cortex (20 minutes, 2 mA); 3) 15-minutes follow-up. A series of 20 single TMS pulses was delivered at each moment with real-time EMG recording (CED, UK) of the first dorsal interosseous of the hand. Participants were 23 healthy male volunteers allocated into three groups, anodal (n = 9), cathodal (n = 5),and sham stimulation (n = 9). For each evaluation a constructed time series was produced by 20 concatenated MEPs. A coarse- grained time series was constructed corresponding to the scale factor. In this work, we performed the analyses on scales one to 10. Entropy values obtained for each scale were averaged within groups for statistical analyzes. A two-way ANOVA was used to identify differences between and within groups at each assessment moment, with statistical significance set as $p < 0.05$. All statistical procedures were performed using OriginPro v. 8.5 (OriginLab, US). **Results:** The results showed no significant statistical differences between or within groups at any time point. Figure 1 shows the mean comparisons between groups at each assessment moment. Figure 2 shows a trend for escalation of entropy values across scales, especially for the anodal tDCS group, with continuous increase at the follow-up assessment.

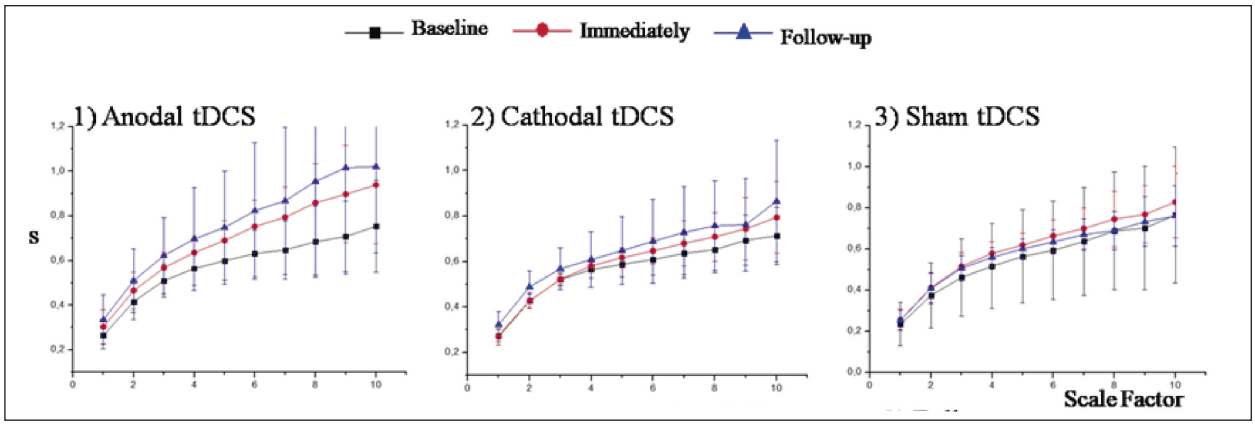


Figure 1. Shows the mean comparisons between groups at each assessment moment.

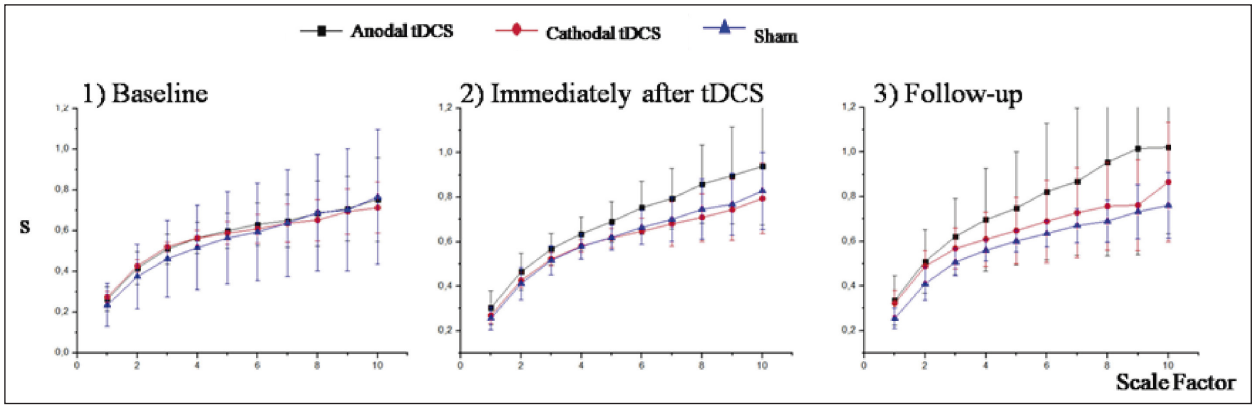


Figure 2. Shows a trend for escalation of entropy values across scales, especially for the anodal tDCS group, with continuous increase at the follow-up assessment.

Discussion: The differences on entropy values across assessment moments could only be noticed on higher scale values for the anodal tDCS group. Meanwhile no effect was shown for the sham group at any scale factor. The time scale influence on complexity analyzes has been previously stated in the literature by comparing healthy and pathological conditions using ECG recordings. Higher complexity across scales may suggest an adaptive capacity and better function of the system. This novel approach may be a potential resource to evaluate changes in motor excitability [2]. **Conclusion:** We found that MSE may be a worth technique to assess MEP changes in studies of cortical excitability.

References: [1]doi:10.1016/j.clinph.2012.01.010 [2] doi: 10.1103/PhysRevE.71.021906

DEVELOPMENT OF AN LED STIMULATION DEVICE FOR BCI-SSVEP

B. A. Navarro[1], M. M. Tiago[1], S. N. Carvalho[1]

[1]Federal University of Ouro Preto (UFOP), Institute of Exact and Applied Sciences (ICEA), Brazil.

Introduction and Hypothesis: Brain-computer interfaces (BCIs) are devices capable of creating a communication between the human brain and machines, one method to accomplish that is using electrical potentials generated by the brain cells. BCI based on selective attention needs a source of external stimulation to evoke a specific brain activity; this stimulation can be auditory, somatosensory or visual. A popular BCI approach is based on steady-state visually evoked potentials (BCI-SSVEP), which employs visual stimuli that flicker at different frequencies, increasing brain electrical activity at this same frequency in the visual cortex [1]. This brain activity can be successively monitored by electrodes positioned on the scalp, using electroencephalography (EEG). The visual stimulation normally is done by LEDs or images projected onto monitors. **Objective:** In this project, we intend to build a visual stimulation source using four LEDs to be integrated into a BCI-SSVEP system. The LED should flicker precisely at any set frequency, in the range of 1 to 100 Hz. The scintillation scheme should follow two behaviors, be chosen: sine wave or square wave. The frequency of each LED should be individually configurable, as well as the luminous intensity. The system should also be isolated electromagnetically, so as not to interfere in the brain signal acquisition and in the application devices. **Methods:** For the construction of the control circuit of the LEDs, we intend to use a microcontroller of low cost, probably one of the family 16F. At the moment, some initial tests were done using the signal generator of Tektronix AFG 3021B setting the voltage peak approximately to the LED forward voltage drop. The output signal was collected directed from the LED and compared with of a photodiode to study the reaction of the stimulus without the interference of the flickering circuit. An Arduino Mega, with 15 PWM (pulse-width modulation) output and 5 timers, was used as the LED feeder. The sine waves were generated mapping a sine function from the mathematic library and normalizing the PWM signal output that was filtered by an external low-pass filter before feeding the LED. The square wave needs only digital outputs, so it was generated only by changing the output state (high/low). A challenge is that the evoked frequency should be accurate for a correct functioning of BCI, due to the high sensitivity of the brain activity. Multiple LEDs will be fed at different frequencies and a variable resistor will control the LED bright intensity. Dry electrodes placed on the scalp of subjects will be used to collect the brain signal. The electrodes are very sensitive to electromagnetic interferences, so the electric circuit will be electromagnetically isolated, to avoid noises and interferences in the registered brain signal. **Relevance:** BCI systems can control various applications, and are especially interesting in the assistive area, to control automatic wheelchair and prosthesis, for example. The stimulation by LED allows BCI-SSVEP systems to be more portable since they do not require a monitor for stimulus projection. Also, LEDs can flicker precisely on larger frequency bands (generally, monitors are restricted at 30 Hz), which should reduce visual fatigue. In addition, in some applications, LEDs can be more easily integrated into a scenario of control. The source of stimulation that we are building, will allow research and analysis of the quality of the evoked potential considering several factors, such as light color, light intensity, and positioning of the stimuli. The generation of scintillation

controlled by square and sinusoidal waves will also allow to synchronize the data acquisition with the stimulation and to explore besides the recognition in frequency, the differentiation by phase.

Support: UFOP.

References: [1] Graimann, Allison, Pfurtscheller. Brain–Computer Interfaces: A Gentle Introduction, 2010.

DEEP-LEARNING NETWORKS APPLIED TO INTEGRATIVE ANALYSIS OF MOLECULAR DATA OBTAINED FROM PATIENTS WITH NEUROLOGICAL DISORDERS

B. Henning[1], M. P. Viana[2], I. Lopes-Cendes[1], B. S. Carvalho[3]

[1]Medical Genetics Dept., FCM, UNICAMP, [2]IBM Research Brazil, São Paulo, [3]Statistics Dept., IMECC, UNICAMP.

Introduction and Hypothesis: The physiopathology of most neurological disorders remains unexplained for most cases, leading to poor response to the current available treatments [1]. Identifying molecular signatures can be useful for diagnostic and prognostic purposes, particularly in the context of precision medicine, to increase treatment efficiency. Omics data, such as genomics, transcriptomics, proteomics, and metabolomics are being produced at an unprecedented rate [2]. Statistical tools were developed to analyze different omics data, but a single omic data alone is not sufficient to characterize the complexity of pathological changes [3]. The current demand is for statistical tools capable of learning how to detect meaningful associations among omics data. Such an integrative analysis is challenging due to the own nature of omics methods. They are high-throughput, data-driven, and holistic approaches based on top-down methods [3]. Also, these methodologies can have both discrete and continuous outputs, complex correlation structures, and nonlinear relationships [4]. **Objective:** Our goal is to apply an integrative analysis based on deep-learning networks to investigate the complex relationship between different types of omics data from neurological disorders studies. **Methods:** We will obtain omics data from previously published studies, public data repositories, and on data generated by our group on epilepsy and stroke. These data will be the input for an encoder-decoder deep network [5] that will learn how to map an individual type of omic data onto another type, e.g. its transcriptome onto its proteome (Figure 1). The encoding part of the network learns how to embed the transcriptomic response in a latent space with dimension much smaller than the real data. Next, the decoding part is responsible for recreating the proteome from its latent representation. Because the network links different types of omics data, we will be able to investigate intrinsic relationships between them by analyzing the trained network. This analysis could be based on different combinations of omics data to be the input and the predicted one.

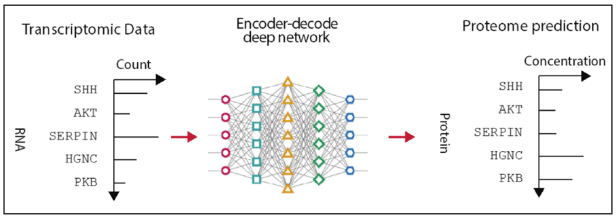


Figure 1. Example of analysis. The deep network receives as an input a type of omic data and learns how to predict another type of omic data from a given individual.

Relevance: We expect to predict the proteome of an individual from its transcriptome, or any other combination of omics data. In case-control studies, we expect to identify alterations in a type of omic data of affected individuals, compared to healthy ones, and how these alterations are dependent on variations on another type of omic data. Our findings will clarify complex relationships between omics data and improve the knowledge of the biological bases of neurological disorders.

References: [1] https://doi.org/10.1093/brain/awx341; [2] doi:10.1038/nbt.3790; [3] doi:10.1099/mic.0.034793-0;[4] https://doi.org/10.1101/081380; [5] doi: 10.1126/science.1127647

CORTICAL ATROPHY IN FIRST-DEGREE ASYMPTOMATIC RELATIVES OF TEMPORAL LOBE EPILEPSY PATIENTS

M. Katsurayama[1], V. Ferraz [1], T. Zanão[1], M. Nogueira[1], J.C. V. Moreira[1], M.K. Alvim[1], R. Barbosa [1], I. Lopes-Cendes[2], F. Cendes[1], C. L. Yasuda[1]

[1]Neuroimaging Laboratory; Department of Genetics[2], UNICAMP.

Introduction: It is already known that patients with Temporal Lobe Epilepsy (TLE) have cortical abnormalities related to hippocampal sclerosis. Newly, studies have aimed to investigate the heritability as an important factor in structural alterations in TLE patients[1]. There has been a search for a biomarker that proves the familial role in the TLE; therefore, quantitative MRI studies have been used to evaluate cortical alterations in their asymptomatic relatives[2]. **Materials and Methods:** Fifty-eight asymptomatic first-degree relatives of TLE patients from Unicamp's Epilepsy Service were invited; they were free from any neurologic disease, and have never presented seizures. For group comparisons, sixty-nine healthy controls were selected from an MRI bank of healthy volunteers. Images were acquired at Hospital de Clínicas (Unicamp) using a 3 Tesla Philips MRI scanner including 3D-T1 weighted images (WI) (isotropic voxels of 1 mm^3, acquired in the sagittal plane; 1 mm thick, flip angle=8°, TR= 7ms, TE 3,2ms, FOV= 240 x 240 x 180 mm^3). All images were segmented according to standard SPM12/CAT 12 protocol (http://www.neuro.uni-jena.de/cat/) (www.fil.ion.ucl.ac.uk), which included: spatial normalization [MNI-152], tissue segmentation and smoothing, Quality control of image segmentation was performed. Statistical analyses of images were performed with SPM12, while clinical information was compared with Social Sciences (SPSS 23). **Results:** Group of relatives and controls were balanced regarding gender (p= 0.9) and age (p=0.13). The Figure below shows significant reduction of cortical thickness on family members compared to healthy controls (p<0.01, uncorrected for multiple comparisons).

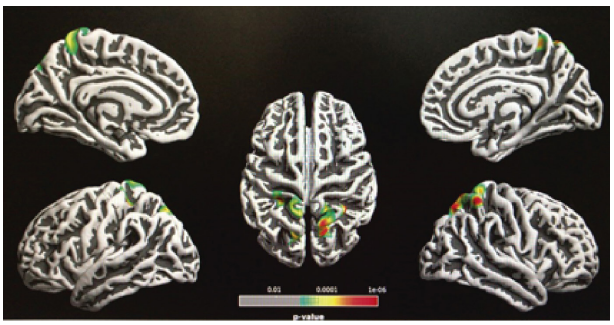


Figure 1. Atrophy was concentrated on left postcentral gyrus, bilateral parietal superior gyrus and precuneus.

Discussion: The morphologic changes observed in asymptomatic family suggest some degree of genetic influence over cortical thickness atrophy of TLE patients. It is possible that genetic determinants of neuronal migration during brain maturation (or early environmental factors) are somehow abnormally expressed in both patients and their relatives, resulting in alterations of surface area and cortical thickness [3,4,5,6]. **Conclusion:** Areas of atrophy identified in first-degree relatives of TLE patients strongly suggest a heritable condition/trait. Further studies of brain connectivity with fMRI (Functional MRI) and Diffusion images may reveal subtle alterations to corroborate this hypothesis.

References: [1] Whelan CD et al .Epilepsia56(10): 1551-1561, 2015; [2] Scanlon C et al. J Neuroimaging 23: 64-70, 2013. [3] Armstrong E et al. Cereb Cortex 5:56-63, 1995. [4] Panizzon MS et al. 19:2728-2735, 2009. [5] Berkovic SF, Scheffer IE. Curr Opin Neurol. 12:177-182, 1999. [6] Kobayashi E et al. Arch Neurol 59: 1891-1894, 2002.

ASSOCIATION BETWEEN NEUROCYSTICERCOSIS AND HYPOCAMP SCLEROSIS

J.M.C. Jama-António [1], F. Cendes[1], C. Yasuda[1]

[1]Department of Neurology, School of Medical Sciences, University of Campinas (UNICAMP); and the Brazilian Institute of Neuroscience and Terotechnology (BRAINN), Campinas SP, Brazil.

Introduction: This study aims to describe the existence of a possible association between neurocysticercosis NCC and hippocampal sclerosis. NCC is the most common helminth infection of the central nervous system (CNS) and a frequent cause of epilepsy worldwide. Hippocampal sclerosis (HS) is the most common structural lesion associated with mesial temporal lobe epilepsy (MTS) in adults. Some studies have shown evidence of a possible association between NCC and HS. However, the actual prevalence of this association is largely unknown. **Materials and Methods:** Approved by the ethics committee of FCM /

UNICAMP, Code: CAAE, 55942116.5.0000.5404. A retrospective case-control study involving individuals aged over 18 years, with brain CT scan showing lesions suggestive of NCC. Cases with calcifications of other etiologies were excluded. We evaluated a total of 181 individuals, of which 70 patients and 111 controls (healthy individuals), matched by sex and age. All magnetic resonance images (MRI) were acquired in a 3T scanner (Philips Achieva). An automatic volumetry of the hippocampus was performed by the Volbrain online program (http://volbrain.upv.es). Data analysis was performed using SPSS version 23 for mac. We analyzed the frequency of categorical data. Significance was identified as p<0,005. **Results:** We found a higher frequency of women (52.9%) among patients with NCC. There was a significant difference in hippocampal volumes in patients compared to controls (p<0,001; Mann-Whitney test). Forty-five of 70 patients (64.3%) presented HS on MRI. **Discussion:** Other studies have demonstrated a higher prevalence of NCC among females. There was a high frequency of HS in patients with NCC and hippocampal sclerosis in our series as suggested by other authors. The coexistence of hippocampal sclerosis and other epileptogenic brain injury is commonly referred to as dual pathology, which may be common in regions where NCC is endemic. It may occur only by chance. A prevalent hypothesis is that seizures due to NCC constitute an initial precipitating event, leading to the development of HS. Another hypothesis is that the occurrence of inflammation near the hippocampus results in clinical or electrographic seizures within the hippocampus, leading ultimately to the development of a lesion (HS). **Conclusion:** The present work confirmed a high frequency of HS in patients with NCC. Further studies are necessary to confirm the association between NCC and HS.

References: [1] Del Brutto HO et al., Am. J. Trop. Med. Hyg 92 (1): 64-68, 2015. [2] Oliveira MCB et al., Arq Neuropsiquiatr 72(7):510-516, 2014.

VISUAL EVALUATION OF CURVILINEAR REFORMATTING FOR PEELING OFF THE SKULLCAP IN MRI-T1 VOLUMES

[1]A.V.S. Lima, [1]W.S. Loos, [2]Enrico Ghizoni, [2]D. Oliveira, [2]C. L. Yasuda, [2]F. Cendes, [1]S.T. Wu,

[1]School of Electrical and Computer Engineering, [2]School of Medical Sciences University of Campinas.

Introduction: Due to the complexity of the brain's structure, the curvilinear multiplanar reformatting (CMPR) tool is more suitable than the conventional multiplanar reformatting (MPR) for exposing subtle cortical lesions. Since it re-slices the brain almost parallel to the dura-mater membrane, we hypothesize that the technique is also suitable for unveiling spatial relationships between the vascular and the cortical cerebral structures if the blood vessels are visible. In this work we present a series of tests we conducted with use of an in-house developed software VMTK [2] for evaluating this novel application of curvilinear reformatting. **Materials and Methods:** We used two groups of T1-weighted magnetic resonance imaging (T1wMRI) scans. The first group consists of 511 T1wMRI volumes of female and male subjects, without contrast, ranging from 11 to 80 years of age for assessing the slicing quality. And the second group of 6 T1-weighted fat-suppressed gadolinium-contrast enhanced magnetic resonance imaging (GAD-T1wMRI) volumes of operated patients for comparing the preoperative view of vascular and cortical spatial relations provided by the CMPR and the neurosurgeon's intraoperative view. All T1wMR sequences (voxel size = 1 x 1 x 1 mm^3, no gap, TR = 7 ms, TE = 3.2 ms, flip angle = 8, matrix = 240 x 240; FOV = 240 x 240; resolution = 180 x 240 x 240) were acquired in a 3T MRI scanner (Philips Medical Systems, Best, The Netherlands) in the Clinics Hospital. For evaluating the slicing quality, we visually checked the geometry of the slicing mesh with respect to the brain. For assessing its usefulness in surgery, we manually overlap the photos taken during surgery and the preoperative cropped volumes generated with VMTK. **Results:** For each T1wMR volume its intersection with the slicing mesh was drawn per coronal, sagittal and axial slice, as illustrated in Figure 1. Note that the slicing mesh keeps a certain distance from the cortical surface. The intraoperative photo and the image generated with VMTK shown in Figure 2 demonstrate that the anatomical structures around the cortex have not been removed with the VMTK's curvilinear slicing mesh.

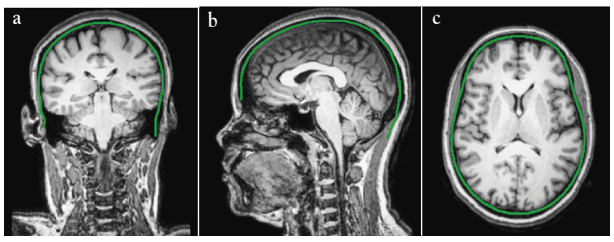


Figure 1. The intersection of the slicing mesh in green with: (a) coronal, (b) sagittal and (c) axial slices.

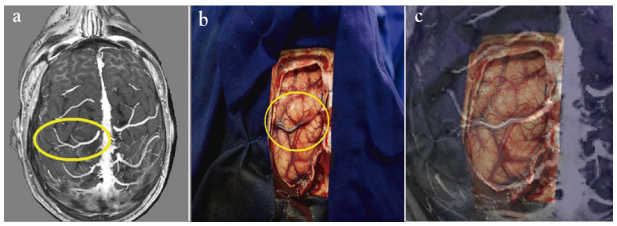


Figure 2. (a) Preoperative volume generated with VMTK, (b) intraoperative photo and (c) their overlay.

Discussion: Despite the shallow depression of temporal fossa, filled with temporalis muscle and fatty tissues, the CMPR implemented in VMTK provided a good visualization of cortical vascular anatomy. It showed to be invariant to gender and ages. **Conclusion:** The results showed that the CMPR implemented in VMTK can be applied both in the diagnosis of subtle cortical lesions and in the surgical planning.

References: [1] doi: 10.1007/978-3-319-67552-7_1. [2] VMTK: Visual Manipulation Toolkit for NeuroImages.http://www.dca.fee.unicamp.br/projects/mtk/wu_loos_voltoline_rubianes/index.html.

ASSESSMENT OF NEURAL SYNCHRONISM USING SPIKE MORPHOLOGY AND ICTAL COINCIDENCE IN ANIMAL MODELS OF EPILEPSY SUBMITTED TO NON-PERIODIC ELECTRICAL STIMULATION

S.M.A.F. Rodrigues[1,2], J.C. de Oliveira[2], L.C.M. Damázio[2,3], V.R. Cota[1,2]

[1]Programa de Pós-graduação em Engenharia Elétrica – Associação ampla UFSJ e CEFET-MG (PPGEL) / UFSJ. [2]Laboratório Interdisciplinar de Neuroengenharia e Neurociências (LINNce) / UFSJ. [3]Departamento de Medicina (DEMED) / Universidade Federal de São João del-Rei (UFSJ).

Introduction: A promising alternative to treat refractory epilepsy is the electrical stimulation of the nervous system [1-4]. Inspired by the fact that aberrant synchronism of neural oscillators may underlie the pathophysiology of epilepsy [5], our group successfully developed and tested desynchronizing non-periodic electrical stimulation (NPS), consisting of square pulses with randomized inter-pulse intervals, to suppress ictogenesis and epileptogenesis [3]. To objectively study the effect of NPS, we assessed neural synchronism during ictal activity by quantifying parameters of spike morphology and their coincidence between recorded channels; both of which are markers of neural synchronism [6]. **Materials and methods:** A total of 23 male Wistar rats divided in a control (CTRL; n = 9) and a stimulated (NPS; n = 14) groups were used in this study (Ethics Committee on Animal Research protocol #31/2014 / CEUA-UFSJ). Using an infusion pump, all animals were submitted to a controlled continuous intravenous infusion of convulsivant agent pentylenetetrazole (PTZ) until the onset of generalized tonic-clonic seizure (GTCS) as the experimental model of choice. NPS animals also received non-periodic stimulation in both amygdalae, asynchronously between hemispheres (distinct randomization for each side), and with biphasic square pulses of current (low frequency on average: 4 Hz). Local field potentials (LFP) were simultaneously recorded from the cortex (CX), hippocampus (HP), and thalamus (TH). LFP recordings were first band-pass filtered at 10 to 100 Hz in order to remove slow fluctuations and high frequency noise and, consequently, to highlight spikes. The occurrence of a spike was determined whenever two consecutive crossings (first up and second down) of a given threshold were detected. Time stamp of spikes were computed as the time instant of maximum value between crossings. Threshold levels varied and were set at 60% the local (1-sec periods) maxima in order to coup with highly variable amplitude of spikes. Ictal coincidence between two substrates was computed whenever there was a co-occurrence of spikes on both channels within a given time window of variable sizes (0.001 to 0.05 s). Ictal coincidence, expressed as a percentage

of total spike counting, was computed for all three possible pairs of channels. Finally, spike morphology parameters such as amplitude, duration, and firing ratio were also computed. **Results:** Parameters of spike morphology did not display any differences between groups, no matter the channel assessed. On the other hand, NPS group showed less coincidence between spikes than the CTRL group, using HP as a reference and CX as a comparison, for all temporal windows during forelimb clonus (time window of 0.0025: $p < 0.05$; time window of 0.005 s: $p < 0.05$). **Discussion:** The absence of difference in spike morphology suggests that NPS has no effect on the micro domain of small populations of neurons. Ictal temporal coincidence is related to the propagation of aberrant activity in ictogenic circuits. Therefore, present results suggest that NPS may have an decreasing effect on synchronism between substrates of the temporal lobe. **Conclusion:** This set of results indicate that the desynchronization of neural circuits involved in ictogenesis is a possible mechanism of NPS in the suppression of seizures.

References: [1] doi:10.1016/j.yebeh.2012.01.004; [2] doi:10.1016/j.yebeh.2008.09.006; [3] doi:10.1002/jnr.23741; [4] doi:10.1016/j.yebeh.2014.05.005; [5] doi:10.1016/j.jneumeth.2009.05.015; [6] ISBN 0-7817-5126-8.

PARTICIPATION OF THE CANNABINOID RECEPTOR CB1 IN THE ANALGESIA INDUCED BY LASER THERAPY IN THE PERIAQUEDUCTAL GRAY SUBSTANCE IN MICE TREATED BY LASER THERAPY AFTER CHRONIC CONSTRICTION OF THE SCIATIC NERVE: A RANDOMIZED CONTROLLED TRIAL

G. X. Santos [1], S. S. Lima [2], H. U. de Oliveira [3], R.S. dos Santos [4], C. Kosour [5], L. M. dos Reis [6].

[1] Academic of the Physiotherapy course of the Federal University of Alfenas - Department of Physical Therapy, Alfenas, MG, Brazil. [3] PhD in the Multicentric Program of Post-Graduation in Physiological Sciences of the Brazilian Society of Physiology (SBFis), Federal University of Alfenas - UNIFAL - MG, Brazil. [3] Faculty of Physical Therapy, Federal University of Alfenas - UNIFAL - Physiotherapy Department, Alfenas, MG, Brazil.

Introduction: The patients with neuropathic pain present spontaneous pain, allodynia and hyperalgesia, and usually do not respond well to a great variety of therapies. These patients often present comorbidities like depression, anxiety, psychological problems and sleep disturbance, which leads to a worsening of quality of life [1,2,3]. Aspects related to the cannabinoid receptor CB1 and the central processing structures in the transmission of neuropathic pain remains contradictory in the literature. The objective of this study was to identify the influence of the cannabinoid receptor CB1 in the periaqueductal gray (PAG) substance in mice treated with low level laser therapy (LLLT) after chronic constriction of the sciatic nerve (CCI). **Materials and Methods:** Male mice were submitted to the CCI [4] and cannula implant into PAG (AP= -4,1 L= -1,4 V= -2,3) [5]. Five days later, a cannabinoid CB1 receptor antagonist (AM251) or its vehicle was infused intra-PAG and the mice were treated with LLLT, with the intensities of 0 J/cm2 and 50 J/ cm^2 [6] in an acute condition. Thermal and mechanical hyperalgesia were evaluated by hot plate test and von Frey test, respectively. **Results:** After the CCI it was observed a significant reduction in the nociceptive threshold in all groups, evaluated by the mechanical hyperalgesia test ($p<0,001$) and thermal test ($p<0,001$). However, after the application of LLLT only in the CCI + Salina + LLLT 50 J/cm^2 group it was detected the antinociceptive effect through the hot plate test ($p<0,001$) and Von Frey test ($p>0,05$). Nonetheless, the groups CCI + AM251(N--(peperidina-1-il) -5-(4-iodofenil) -1-(2,4-diclorofenil) -4-metil-1Hpitazole--3-carboixamida) + LLLT 50J/cm^2 and CCI + AM251(N-(peperidina-1-il) -5-(4-iodofenil) -1-(2,4-diclorofenil) -4-metil-1Hpitazole-3-carboixamida) + LLLT 0J/cm^2 did not show any alterations to the mechanical nociceptive threshold ($p>0,05$) and thermal threshold ($p>0,05$). **Discussion:** [7] Andrade ALM et al. showed in their study that LLLT produces the increase of β-endorphin and reduces effectively the neuropathic pain, by using higher fluencies of 20 and 40 J/cm.[2] These findings corroborate with our studies, being that the LLLT produced the antinociceptive effect on the hot plate test on CCI + SALINA + TLBP50J/cm^2 group. The antinociceptive effect provided by the LLLT was reversed by the AM251, CB1 cannabinoid receptor antagonist infusion, suggesting that this antinociceptive effect provided by the LLLT is mediated by the cannabinoid CB1 receptor on PAGd.1. **Conclusion:** It is suggested the participation of CB1 receptors in the lateral back of the periaqueductal gray substance on lateral back, in the antinociceptive effect provided by gallium arsenide aluminium laser of wave-length of 830 nanometres, continuous and 10mW power and intensity of 50 J/cm^2 after chronic constriction of the sciatic nerve.

References: [1] Nishikawa N, Nomoto M., J Gen Fam Med 18(2): 56-60, 2017; [2] Inoue S et al., Eur J Pain 21(4): 727–737, 2017; [3] Benbouzid M et al., Eur J Pain 12(5): 591-9, 2008; [4] Bennett GJ, Xie YK., Pain 33: 87-107, 1988; (5) Franklin KB, Paxinos G., ed. Califórnia: Academic Press; 1997; (6) Neves LMS et al., Mol Neurobiol. 5: 792, 2017; (7) de Andrade ALM et al., Lasers Med Sc 32(4): 865-872, 2017.

METABOLITE CHANGES IN THE BRAIN DURING VISUAL STIMULATION USING FUNCTIONAL MAGNETIC RESONANCE SPECTROSCOPY WITH ^{31}P

E. Abelama Neto[1], T. B. S. Costa[2,3], R. C. G. Landim[4], E. L. Silva[3,5], G. Castellano[3,4]

[1]Undergratuate student, FCM, UNICAMP, [2]Digital Signal Processing and Communication Group, FEEC, UNICAMP, [3]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), [4]Neurophysics Group, IFGW, UNICAMP, [5]Physics Institute, UFMT.

Introduction and Hypothesis: Brain metabolic variations that underlie neuronal activation are still far from being well understood and quantified. One way to study these variations is using the technique of functional magnetic resonance spectroscopy (fMRS). MRS using the phosphorus nucleus (31P-MRS) is a non-invasive technique, which does not use ionizing radiation, and which allows the evaluation of some specific brain metabolites, in particular, the so-called high energy phosphates, such as phosphocreatine (PCr) and ATP [1]. The MRS data consist of a spectrum which is a mixture of signals from the different metabolites present in the sample. The quantification of these parameters is usually accomplished through computational techniques, so in this work we will use the AMARES method (Advanced Method for Accurate, Robust and Efficient Spectral fitting of quantization MRS data) [2]. In previous work [3], we performed an experiment where volunteers were alternately subjected to rest and visual stimulation periods, while 31P-MRS data were acquired. Visual stimuli were presented in three periods, each with a different flickering frequency. Our hypothesis is that the levels of several of the metabolites detected by 31P-MRS should correlate with the periods of stimulation and rest, and this should be differentiated according to the frequency of the stimulus. **Objective:** The main objective of this project is the analysis of the variation of high energy phosphates during a fMRS experiment with visual stimulation with different frequencies, performed in normal individuals, using 31P-MRS spectra, to see if the levels of these metabolites correlate with the periods of stimulation and rest of the functional experiment. **Methods:** The paradigm used for data acquisition consisted of the application of a visual stimulus in a scheme of 7 blocks lasting 4 min each (total duration of 28 min), 4 of rest and 3 of stimulus [3]. The visual stimulus consisted of a radial checkered pattern flashing at 4, 8, and 16 Hz and the rest blocks consisted of a dark screen with a fixing point [3]. For the acquisition of fMRS the ISIS 3D sequence was used, with the voxel positioned in the center of the occipital cortex, over the calcarine fissure [3]. The steps to be performed in the present work are: the fMRS data must go through two stages: 1) pre-processing, for cleaning of the signal; and 2) quantification, which consists in relating the measured signal to the concentrations of the metabolites that generated it. Both steps will be performed using the jMRUI software [4]. Step 2 will be performed using the AMARES method [2], which is implemented in jMRUI. **Relevance:** The use of MRS using the phosphorus nucleus in functional experiments is a relatively new area, with controversial results on metabolic variations associated with neuronal activation. We expect this work will shed light on whether high phosphate levels in the visual cortex change according to visual stimulation and rest periods.

References: [1] Graaf RA. In Vivo NMR Spectroscopy: Principles and Techniques. 2nd ed. John Wiley & Sons, West Sussex, 2007; [2] Vanhamme L et al. J Magn Res 129: 35–43, 1997. [3] Costa TBS et al., 18th OHBM Annual Meeting, 2012. [4] Stefan D et al., doi: 10.1088/0957-0233/20/10/104035.

CONTROL OF A ROBOTIC ARM BY BCI-SSVEP- A CASE STUDY

G. V. Vargas[1], R. Y. Takeda[1], H. M. A. Leite[1,3], T. B. S. Costa[2,3], R. Attux[2,3], S. N. Carvalho[1,3]

[1]Federal University of Ouro Preto (UFOP) – Brazil, [2]University of Campinas (UNICAMP) – Brazil, [3]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN).

Introduction: Disability is described as every structural or functional problem with the human body [1]. It is estimated that 6.2% of the Brazilians present some kind of disability, such as physical, visual, intellectual or/and hearing [2]. Assistive technologies can improve the quality of life and the inclusion in society of these individuals. Particularly, Brain Computer Interfaces based on Steady

State Visually Evoked Potential (BCI-SSVEP) are a modern technology that allows a direct interaction between the human brain and the computer, mapping brain signals onto commands for external devices [3]. Not requiring commands from the limbs, BCI-SSVEP is promising for control applications destined to the physically disabled, such as limb prostheses and wheelchairs. In this study, we briefly describe the integration of a BCI-SSVEP controlled robotic arm using four commands. **Materials and Methods:** In this study, the brain signals were acquired by electroencephalography (EEG) with 16 dry electrodes placed on the occipital, parietal and central zones [4]. The visual stimulation consisted of four squares that alternated the colors black and white on a monitor at the rates of 6, 10, 12 and 15 Hz. In order to eliminate artifacts from the brain signal, a Common Average Reference (CAR) filter was employed [5]. In the sequence, features were extracted using the Fast Fourier Transform (FFT) and selected by the Pearson's Correlation method. A linear classifier based on the least squares method was employed to discriminate between the four classes (frequencies). The classification system was trained with 8 trials of 12 s for each frequency. During the online operation, the system processed 6 s of signal and sent the identified command to the robotic arm through a serial connection. Each stimulation frequency was associated to an action to be performed by the robotic arm: rotation of 90 degrees in clockwise direction (6 Hz), rotation of 90 degrees in counterclockwise direction (10 Hz), claw opening and downward movement (12 Hz) and claw shutting and upward movement (15 Hz). The system was preliminarily tested with a healthy volunteer of 24 years, whose purpose was to move a foam cube from one point to another, using all the commands of the robotic arm. **Results:** The brain data acquired during the training indicated an average accuracy of the classification system around 70%, using a time window of 6 s, to discriminate between the four classes. The volunteer was able to move the cube from one point to another defined at the beginning of the experiment. The minimum execution time of the activity, if no error had occurred, was 24 s. However, the volunteer needed more than 1 minute to complete the task, in all performed tests. **Discussion/Conclusion:** We were able to successfully integrate the EEG signal acquisition system with the control of an automation application through an online BCI-SSVEP. The preliminary results indicate that the volunteer has been able to complete the requested task, which required performing all the movements of the robotic arm, despite the need for more time. The system will be enhanced with the inclusion of visual feedback, which will allow the user to visualize the movement of the robotic arm, complementing the sound feedback; this should improve the individual's concentration on the stimuli and, consequently, the BCI performance.

Support: UFOP, CNPq, FAPESP and FINEP.

References: [1] doi:10.1590/S1415-790X2005000200011; [2] Censo, IBGE (2010); [3] doi: 10.3389/fnins.2010.00161, Article 161; [4] Leite, H. M. A. (2018). Design de interação para interfaces cérebro-computador baseadas em potenciais visualmente evocados. [5] doi:10.1109/NER.2011.5910512.

INVESTIGATION OF THE EFFECTS OF ELECTRIC STIMULATION OF THE PERFORANT PATHWAY OVER OBJECT DISPLACEMENT RECOGNITION FUNCTION IN RATS

Pedroni, Breno[1], Dias, V. Elayne[1], Vieira S. André[2]

[1]Physiology and Biophysics Department, IB, UNICAMP, [2]Physiology and Biophysics Department, IB, UNICAMP.

Introduction and Hypothesis: The most common epilepsy case in adult humans is the mesial temporal lobe epilepsy (MTLE), where the hippocampus is located[1], which therefore induces the death of hippocampal pyramidal neurons[2]. There is an animal model that studies MTLE in rats, which involves electrically stimulating the perforant pathway in order to induce similar injuries seen in human MTLE. This model consists in two consecutive days of pre-conditioning and a third day of electric stimulation for 8 hours. The pre-conditioning sessions induce an inhibitory response to counterbalance the excitatory activity[3]. The hippocampus is responsible for cognitive functions of the brain such as explicit memory of spatial information[4]. The objective of this project is to analyse the impacts of the pre-conditioning sessions on spatial memory in rats using the object displacement recognition test. **Objective:** Evaluate and investigate the effects of the pre-conditioning process in the hippocampal system, through electric stimulation of the perforant pathway, over functions regarding explicit memory. **Methods:** This project makes use of Wistar rats, divided in three groups: control, sham and stimulated. Sham and Stimulated groups will undergo surgery process in order to implant the electrodes used in the electric stimulation of the perforant pathway. Control group will not undergo surgery nor electrode implantation. Sham group will have electrode implantation but will not be stimulated. All three groups will be subjected to object displacement recognition tests. **Relevance:** The results of this project might suggest possible mechanisms that could explain why the pre-conditioning process is necessary in the electric stimulation of the perforant pathway model, since it is known to induce an inhibitory neuronal response that counterweights the excitatory activity caused by the electric stimulation. It is also expected that these results give indications as to whether the pre-conditioning impacts the formation and/or access to explicit memory regarding spatial information.

References: [1] Squire, L. et al (2007). Nature Reviews. Neuroscience, 8(11), 872–883, 2007; [2] Blümcke, I. et al. Epilepsia, 54(7), 1315–1329, 2013; [3] Norwood, B. et al. excitation in awake rats, 518(16), 3381–3407, 2011; [4] Assini, F. et al. Behavioural Brain Research, 204(1), 206–211, 2009.

FUNCTIONAL CONNECTIVITY BASED DECODING PERFORMANCE ON SSVEP BRAIN-COMPUTER INTERFACES

P. G. Rodrigues[1,2], J. I. Silva Júnior[1,2], T. B. Costa[2,3], R. Attux[2,3], G. Castellano[2,4], D. C. Soriano[1,2]

[1]Center for Engineering, Modeling and Applied Social Sciences (CECS), Federal University of ABC (UFABC), [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), [3]School of Electrical and Computer Engineering (FEEC), UNICAMP; [4]Neurophysics Group, IFGW, UNICAMP.

Introduction: The study of brain connectivity by means of complex networks has been well succeeded in the diagnosis of brain diseases such as Alzheimer and Parkinson, and, more recently, in investigations concerning the functional organization of brain regions under motor imagery in brain computer interfaces (BCIs) [1,2]. Nevertheless, a deeper investigation of functional connectivity within the steady state visually evoked potential (SSVEP) BCI paradigm is still lacking, which outlines the main objective of this work. **Materials and Methods:** EEG data were collected from 15 healthy volunteers, using a g.SAHARAsys dry-electrode cap with 16 channels and g.USBamp biosignal amplifier. Subjects focused for 6 seconds on one of four visual stimuli frequencies (10Hz, 11Hz, 12Hz and 13Hz), twelve times for each frequency. The project was approved by the local ethics committee. Signals were segmented in 2 s epochs and functional connectivity was estimated by Pearson correlation. An adjacency matrix was defined using $\rho = 0.71$ as correlation threshold. Four graph-based metrics were computed (degree, clustering coefficient, betweenness and eigenvector centralities). Decoding performance was compared with feature extraction based on the fast Fourier transform (FFT) coefficients estimated on the stimuli frequencies (first scenario) and also considering coefficients up to the third harmonic (FFT-harmonic – second scenario), as usually employed in SSVEP-BCIs. In all feature extraction procedures, 24 features were used after selection by the Davies-Bouldin index and discriminated by a linear least squares classifier in a leave M out cross validation scheme. **Results:** Figure 1 shows the mean accuracy for FFT, FFT-harmonic and for the functional connectivity approach. The FFT-harmonic approach exhibited the best performance, obtaining an accuracy of 0.91 ± 0.10, significantly better than the FFT (0.77 ± 0.19) and graph measures (0.56 ± 0.12) – Kruskal-Wallis test (p-value < 0.01) with Dunn's multiple comparison test.

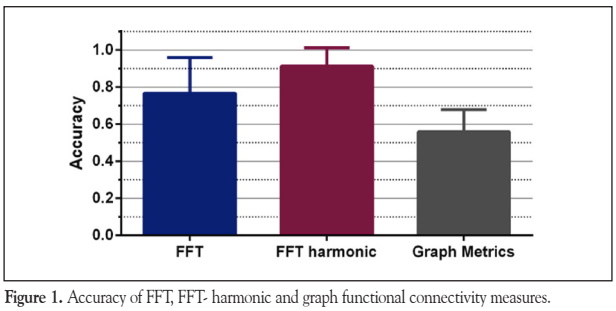


Figure 1. Accuracy of FFT, FFT- harmonic and graph functional connectivity measures.

Discussion and Conclusion: The traditional SSVEP BCI approach (FFT-harmonic) obtained the best performance, being significantly better than the graph-based metrics obtained from functional connectivity estimated by Pearson correlation. Nevertheless, there is relevant information in connectivity measures

that were able to identify differences between classes, which encourages the use of more robust measures of similarity in this context.

Support: FAPESP (2013/07559-3 and 2015/24260-7), CNPq (305616/2016-1, 305621/2015-7 and 449467/2014-7) and FINEP (01.16.0067.00).

References: [1] 10.1016/j.media.2016.03.003; [2] 10.1162/NECO_a_00838.

MULTIPLE RESONANCE PEAKS GENERATED BY ACTIVE IONIC CURRENTS IN NEURONS

R.F.O. Pena[1], V. Lima[1], C.C. Ceballos[1,2], A.C. Roque[1]

[1]Department of Physics, School of Philosophy, Sciences and Letters of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil, [2]Department of Physiology, School of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil.

Introduction: Ionic channels are responsible for the different voltage responses that neurons can exhibit when submitted to external currents. Depending on a combination of ionic channel and input frequency, voltage response can exhibit sub-threshold resonance properties which are usually measured by the impedance magnitude [1]. An example of current that provokes resonance in neurons is the hyperpolarization-activated current () [2,3]. Nevertheless, standard ionic currents that are responsible for the generation of action potentials, such as sodium () and potassium (), have their roles on the sub-threshold resonance properties neglected. This usually happens because supra-threshold effects tend to hide sub-threshold oscillations, specially during spontaneous activity. In this study we investigated how the sub-threshold resonance properties of neurons can be determined and shaped with the inclusion of different ionic channels. **Materials and Methods:** Our approach involves a neuron model based on the Hodgkin-Huxley equations containing different ionic currents. We investigate the resonance properties of the neuron by including , and .The problem is investigated with computational simulations of the neuron when submitted to the so-called "ZAP" current. Our results are concentrated at the impedance magnitude of the neuron. Although the impedance is usually defined as the ratio of the Fourier transforms between the output voltage and input current [1], here we used a simpler expression to capture the neuronal response without considering its spikes: we take as output a voltage series discretized in time whereby only local minima conveyed by the oscillatory output are considered. **Results:** Our results show that the resonance properties can be easily shaped by the inclusion of the different currents considered here. Surprisingly, a combination of different time constants of the ionic currents can shape the impedance creating: (I) a low-pass filtered response, (II) band-pass filtered response, and more importantly (iii) multiple resonance peaks. **Discussion:** The results show for the first time that a combination of ionic currents can create multiple resonance peaks. Such property emerges from the combination of the different time constants and is observed here due to the definition of the impedance magnitude. By neglecting the spiking activity and considering only the minima as responses to measure the impedance, we were able to capture the impedance that is created only by properties of the sub-threshold response of the neuron, even though action potentials were present. **Conclusion:** Different combinations and alterations in ionic channels can elicit pathologies [4]. We believe that our results have important implications in explaining response properties of neurons and can be used to predict and explain altered resonance properties.

References: [1] doi: 10.1016/S0166-2236(00)01547-2; [2] Pena RF et al., arXiv preprint arXiv:1712.00306, 2017; [3] doi: 10.1113/jphysiol.2009.185975. [4] doi: 10.1016/j.pneurobio.2008.09.007

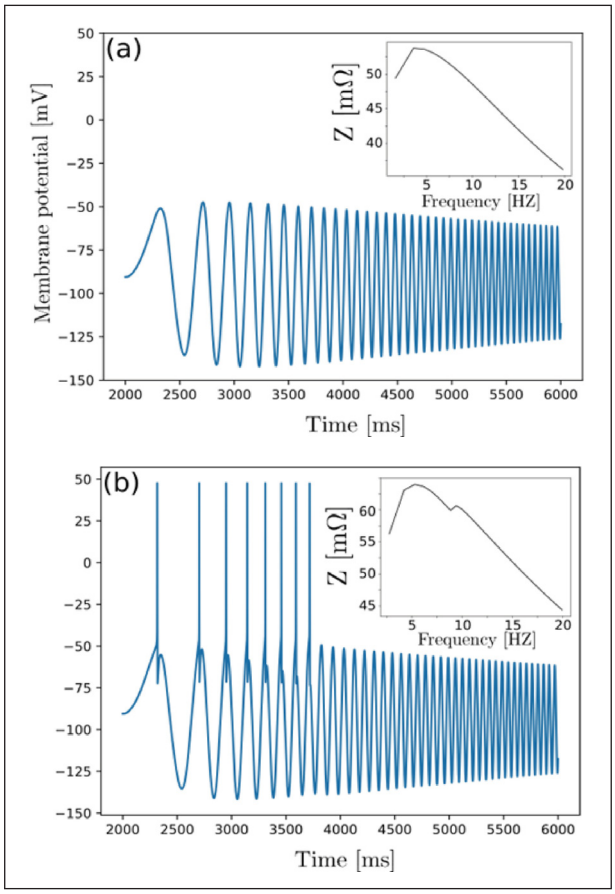


Figure 1. Neuron model submitted to the "ZAP" current. (a) Neuron model containing only I_h. (b) Neuron model containing I_Na, I_Kd and I_h. Insets in the figure are the impedance magnitude of these neurons using our procedure as described in the methods section

BIOPHYSICAL MODEL OF ACETYLCHOLINE MODULATION IN VISUAL CORTEX

Vinícius Lima[1], Parviz Ghaderi[2], Sareh Rostami[2], Rodrigo Pena[1], Renan Shimoura[1], and Antonio C. Roque[1]

[1] Laboratory of Neural Systems, Department of Physics, School of Philosophy, Sciences and Letters of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil, [2]Neuroscience Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran.

Introduction: Cholinergic inputs from the basal forebrain modulate various visual cortex functions, including visual discrimination, contrast response function, orientation tuning, signal to noise ratio (SNR), and plasticity. Acetylcholine (ACh) has been known to exert its modulatory action via two distinct Acetylcholine receptors (AChR), namely nicotinic ACh receptors (nAChRs) and muscarinic ACh receptors (mAChRs) [1]. **Materials and Methods:** To understand the mechanisms underlying cholinergic neuromodulation in the primary visual cortex (V1), we developed a biophysical model of V1 neurons incorporating both nicotinic and muscarinic neuromodulatory effects. The model allows the study of how the interaction of the different variables contribute to the observed experimental phenomenon. The model was implemented in NEURON and NetPyNe using Python [2]. The cholinergic mAChRs modulation was modeled as the inactivation of I_m and I_{KCa} channels which are mainly affected by modulatory effects, and nAChRs as an extra ohmic current [3]. The external stimulus was given by $I_{ext}(t) = \log_{10}(C + 1)\cos(\theta - \theta_0)$ [4], which enables simulation of grating bars with contrast level C and orientation

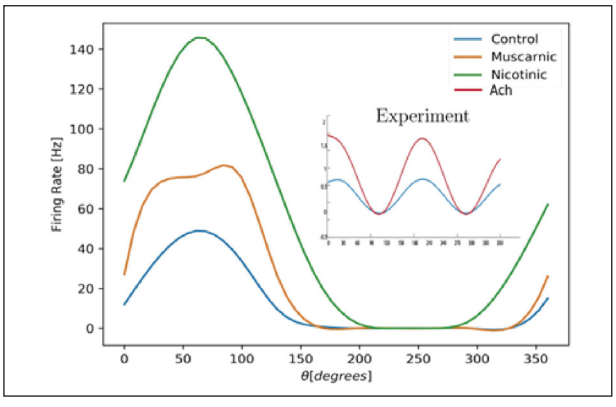


Figure 1. Tuning curves for the neuron model, in the control case (in blue), with mACh (in orange) and nACh (in green). The inset shows the tuning curve recorded in the V1 area of mice (data provided from Shahid Beheshti University of Medical Science) for the control case and with ACh (in red).

θ, where θ_0 is the neuron's preferred orientation. An extra synaptic background input was injected into the neuron to mimic *in vivo* like activity. To study how ACh modulates orientation tuning, first we estimated the orientation selectivity index (OSI) [4] both with and without ACh. The response curves and the measured OSI were compared to our own experimental data. To determine the influence of ACh on the SNR, we computed the coherence function between the membrane voltage time series and the external synaptic input. Finally, to study the influence of ACh modulation in synaptic communication and information flow we computed the Granger causality between coupled neurons. **Results:** Our results show that synaptic background is fundamental to increase the orientation selectivity in neurons with mAChRs and also nAChRs increases the information capacity of the cell. The comparisons between the response curves generated by the neuron model and experimental response curves showed good agreement.

Discussion: The analyses of our results show the crucial effect of synaptic noise in some modulatory effects. Furthermore, the model also shows significant increase in the information capacity of the cell under nAChRs modulation which suggests the role of this modulator in synaptic communication.

Conclusion: In conclusion, our results show how ACh modulation acts on the orientation selectivity, on the response curves, and on the information capacity of the cell. In addition, we show that synaptic background is fundamental in some modulatory effects of ACh.

References:[1]doi:10.1007/s00424-002-0999-2;[2]doi:10.1007/s00422-008-0263-8;[3]doi:10.3389/neuro.11.001;[4]doi:10.1523/JNEUROSCI.2831-12.2013;[5]doi:10.1523/JNEUROSCI.6284-11.2012;[6]doi:10.3389/fncir.2015.00042;[7]doi:10.1016/S0306-4522(01)00344-X;[8]doi:10.1523/JNEUROSCI.0863-14.2014.

REHABILITATION ADD-ON EFFECT USING VIRTUAL REALITY IN PATIENTS AFTER ISCHEMIC STROKE

A. F. B. Camargo[1,4], S. R. M. Almeida[1,4], A. F. Brandão[2,4], P. E. J. Campos[4], C. Ribeiro[4], L. C. Palhares[3], G. Castellano[2,4], L. M. Li[1,4]

[1]Neuroimaging Laboratory, FCM, UNICAMP; [2]Neurophysics Group, IFGW, UNICAMP; [3]Physiotherapy and Occupational Therapy Service, SFTO, HC/UNICAMP; [4]Brazilian Institute of Neuroscience and Neurotechnology, BRAINN, UNICAMP.

Introduction: The post stroke rehabilitation is a crucial factor to give back the proper functionality for daily living activities of the patients[1-2]. One of the supporting tools for this is virtual reality, in its different modalities, in order to improve and recover the functionality of patients, using several movement patterns and claiming motor and cognitive abilities – always in addition to therapies[2-4]. This study, still in progress, aims to analyze the effects of virtual rehabilitation (VR) as an add-on to conventional physiotherapy in patients post ischemic stroke (chronic phase). **Materials and Methods:** 17 individuals were submitted to clinical evaluation (made by a blind-assessor), composed by the motor variables Fugl Meyer Assessment (FMA), Berg Balance Scale (BBS) and Time Up and Go Test (TUG); and the cognitive variable Montreal Cognitive Assessment (MoCA). Of these individuals, 9 patients were selected (4 women, age 61±6.0 years). With the objective of assess the motor functional brain network, magnetic resonance images (MRI) were acquired in a 3T scanner (PHILIPS® Achieva): the resting state functional MRI (rs-fMRI) using the following parameters: 3x3x3mm^3 voxel, no gap, FOV = 240x240x117mm^3, TR/TE = 2000/30ms, flip angle = 90°, 180 volumes; and the structural 3D MRI T1-weighted following the parameters: 1mm^3 voxel, FOV = 240x240x180mm^3, TE = 3,2ms, TR = 6,9ms. The selected patients were randomized in control and experimental group (n = 5/4) and after were submitted to physiotherapy intervention protocol (2 sessions/week, during 6 weeks), which the experimental group has received the VR addition. At the end of rehabilitation protocol, all patients were reassessed and new MRI scans were acquired, following the same parameters as before. **Results:** No significant differences were found in analysis of clinical variables of separate groups. However, when the total sample (both groups, n = 9) was analyzed longitudinally, significant improvements were observed ($p < 0.05$) in FMA and BBS (Table 1). The rs-fMRI also demonstrated changes in connectivity patterns pre and post rehabilitation.

Tabela1.

	Pre (mean±SD)	Post (mean±SD)	p
Fugl-Meyer Assessment	190.2±36.6	197.3±34.5	0.007
Berg Balance Scale	40.2±13.0	44.9±13.6	0.002
Time Up and Go Test (seconds)	47.4±47.1	39.7±35.1	0.16
Montreal Cognitive Assessment	19.0±3.7	21.3±4.5	0.06

Discussion: When we analyze the obtained data, we verified that in general, physiotherapy and the adjunctive tools are able to change clinical parameters as well to change functional connectivity of patients, with or without VR – however, one limitation of the study until now refers to the size of the sample, since the target is 30 patients. **Conclusion:** Despite the limitation indicated above, clinical improvements were perceptible for both groups. The VR has a positive potential as an add-on for rehabilitation post stroke, corroborated by literature. With the progress of the research, we hope to find out more clearly the implication of VR in the recovery of these patients.

References: [1] Turolla A et al., J Neuroeng Rehabil 10(85): 1-9, 2013; [2] Cameirão MS et al., Stroke 43(10): 2720-8, 2012; [3] Fonseca EP et al., J Stroke Cerebrovasc Dis 26(1): 94-100, 2017; [4] Corbetta D et al., J Physiother 61(3): 117-24, 2015.

NEUROSCIENCES APPLIED TO INCLUSIVE EDUCATION (NEUROEDU) MEETING: WHAT IS THERE FIVE YEARS LATER

S. Adestro[1], C. Toneloto[2], L. M. Li [1,2,3,4]

[1]ASPE, [2] ADCiência, [3] Cepid BRAINN, FCM, UNICAMP, [4] Dept. of Neurology, FCM, UNICAMP.

Introduction: Neurosciences applied to Inclusive Education Meeting (NeuroEdu) is part of the Brainn Congress. It's main objective is to discuss topics of neurosciences that promote inclusion and new paradigms to improve learning at school. However, a wishfull hope is that participants engage in actions that embody the objectives above in addition to learning the contents presented during the meeting. **Materials and Methods:** The NeuroEdu is an annual meeting for multidisciplinary audiences whose primary interest is education. Over the four editions since 2014 the event has had 980 participants and 87 papers presented. In these events, one day/meeting long, the participants were encouraged to keep in touch and to form academic network relationships. This (after meeting) contact proved to be a very effective motivator. **Results:** Five participants that attended the first meeting (NeuroEdu2014) were deeply influenced and took a step further in initiatives that include: i. Academic: reviewing and upgrading Pedagogical curriculum at an Undergraduate Institution; ii. Publishing: organization and edition of a neurolearning didactic book; iii. Entrepreneurship: learning games business model; iv. Course: sleep and learning course creation; v. Advocacy: creation of MAPE (person with epilepsy support movement). **Discussion:** The results are of interest and qualitative from the perspective of five professionals, who produced professional, academic, entrepreneurial and social actions, and developed products based on their individual motivation influenced by NeuroEdu and continuous follow-up relationship. Yet, we understand the singularity of these five cases, and although causality size effect is hard to measure, all five acknowledge some degree of eureka realization after NeuroEdu. **Conclusion:** NeuroEdu has resulted in the dissemination of neuroscience knowledge applied to education and multidisciplinary areas. Since 2014, the public has been able to learn and update with speakers of national and international relevance and to disseminate the results of their initiatives in the form of posters and oral presentations. Five years later, we observed that NeuroEdu has motivated participant to take actions to disseminate and share more knowledge about neuroscience in the context of education.

References: [1] I Neurosciences to Inclusive Education Meeting - 360º, 2014. Available at: http://gigsunicamp.wixsite.com/neuroedu; [2] II Neurosciences to Inclusive Education Meeting - 360º, 2015. Available at: http://neuroeduinclusiva.blogspot.com.br/2015/03/convite-especial-do-prof-li-li-min.html; [3] III Neurosciences to Education Meeting - 360º, 2016. Available at: http://adciencia.wixsite.com/neuroedu2016; [4] IV Neurosciences in Education Meeting 2017. Available at: http://neuroeventos.wixsite.com/neuroedu2017; [5] V Neurosciences to Inclusive Education Meeting: what is there five years later, 2018. Available at: https://neuroeventos.wixsite.com/neuroedu2018

MR-BASED MACHINE LEARNING TOOL TO AID ATHEROSCLEROTIC PATIENT DIAGNOSIS

M. Bento,[1-3] M. Saluzzi,[1,3] L. Rittner,[4] R. Frayne[1-3]

[1]Departments of Radiology and Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary; [2]Seaman Family MR Centre; [3]Calgary Image Processing and Analysis Centre, Foothills Medical Centre, Calgary, Alberta; [4] School of Electrical and Computer Engineering, University of Campinas, SP, Brazil

Introduction: Machine learning (ML) techniques have been applied in medical imaging as computer-aided diagnosis (CAD) support tools. Their goal is to aid specialists in diagnosis by providing quantitative information, improving

decision making, and reducing subjectivity. Their output is often less subject to error and to inter-operator variability. [1-3] We propose a ML-based CAD tool that distinguishes carotid artery atherosclerosis patients from healthy controls. **Materials and Methods:** Experiments were performed on a multi-center dataset containing T2-weighted FLAIR images. Data (Fig. 1a) were acquired from 270 controls (Calgary Normative Study, CNS [4]) and from 61 carotid artery atherosclerosis patients (Canadian Atherosclerosis Imaging Network, CAIN [5]). CNS data were acquired at one site on a 3-T MR scanner (Discovery 750, GE Medical Systems with 3 mm slice thickness, TR = 9000 ms, TE =141.4 ms and TI = 2250 ms). CAIN data was acquired at three sites: two with the same 3-T scanner (Discovery 750) and one with a different 3-T scanner (Achieva, Philips Medical Systems) using the same acquisition sequence with similar parameters. The proposed supervised ML method was trained to distinguish controls subjects from atherosclerosis patients by only using brain images. Our method had three main steps (Fig. 1b): 1) pre-processing (image normalization); 2) feature extraction (combining texture handcrafted and convolutional features); [6] and 3) classification using support vector machine (SVM). [7]
Results: We achieved a 98.5% ± 1.9% accuracy rate when distinguishing control subjects from atherosclerosis patients (Fig. 1c). This degree of accuracy was achieved even though the dataset was heterogeneous, comprising images acquired with scanners from different MR vendors. Convolutional features were the most relevant features to accomplish the proposed classification task (Fig. 1d). **Discussion:** The usage of robust and discriminative features allowed the identification of patients based only on structural MR imaging; a task that may be challenging even for expert specialists. **Conclusion:** The present work serves as proof-of-concept that ML-based CAD tools have a role in multicenter studies. They can aid diagnosis and direct additional analysis of patients. Future work includes examining other brain pathologies and the application of combining other MR image data.

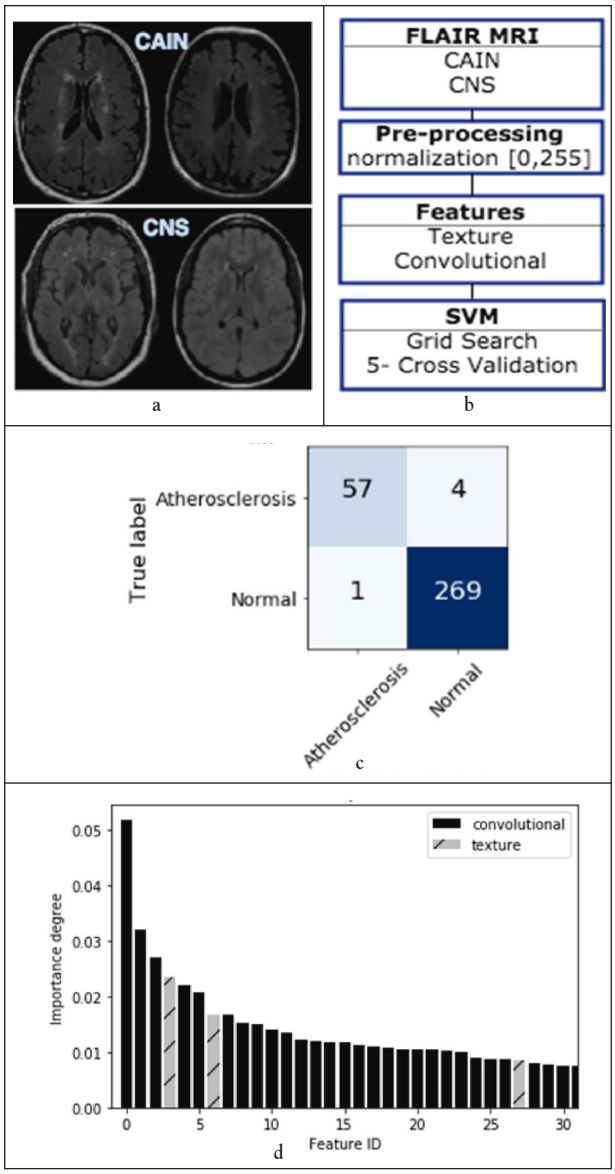


Figure 1. (a) Sample MR images from each class; (b) flow-chart of the proposed method; (c) resulting confusion matrix; and (d) visualization of the most relevant features to classification.

References: [1] doi: 10.1016/S1474-4422(13)70124-8; [2] doi: 10.1117/1.JMI.2.1.014002; [3] doi: 10.1016/j.neuroimage.2017.08.021; [4] doi:10.3389/fnagi.2017.00144; [5] doi: 10.1016/j.cjca.2012.09.017; [6] doi: 10.1117/1.JEI.21.2.023016; [7] Yichuan T., Proc of Int Conf on Machine Learning, 2013.

SEIZURE OUTCOME AND BRAIN ATROPHY IN TEMPORAL LOBE EPILEPSY PATIENTS

L.L. Montanher[1]; L.F. Ribeiro[1]; J.C.V. Moreira[1]; G. Artoni[1,2]; F. Cendes[1]; C.L. Yasuda[1]
[1]Neuroimaging Laboratory; [2] IMECC-UNICAMP.

Introduction: Although several studies have reported grey and white matter atrophy in patients with temporal lobe epilepsy[1], few have evaluated the impact of fluctuating seizure control on structural alterations. Therefore in this study we aimed to compare groups with refractory seizures and patients with alternating course of seizure control. **Materials and Methods:** We included 178 TLE patients from Unicamp's Epilepsy Service and divided in 2 groups [G1- pharmacoresistant, 99 subjects; G2 – fluctuating, 79 subjects). For group comparisons, 192-paired healthy controls were selected from an MRI bank of healthy volunteers. Images were acquired at Hospital de Clínicas (Unicamp) using a 3 Tesla Philips MRI scanner including 3D-T1 weighted images (WI) (isotropic voxels of 1 mm^3, acquired in the sagittal plane; 1 mm thick, flip angle=8°, TR= 7ms, TE 3.2ms, FOV= 240 x 240 x 180 mm^3). All images were segmented according to standard SPM12/CAT 12 protocol (http://www.neuro.uni-jena.de/cat/) (www.fil.ion.ucl.ac.uk), which included: spatial normalization [MNI-152], tissue segmentation and smoothing. Quality control of image segmentation was performed. Statistical analyses of images were performed with SPM12 (T-tests between patients and controls). **Results:** Group of patients and controls were balanced regarding gender ($p>0.05$) and age ($p>0.05$). The Figure below shows significant areas of GM and WM atrophy on both groups, more widespread on G1 group. ($p<0.05$, corrected with FWE).
Discussion: Comparison between groups of individuals with refractory and fluctuating TLE revealed significant areas of brain atrophy in relation to healthy individuals. In addition, the level of atrophy varies significantly from one group to another. Patients with refractory seizures (G1) have a more intense and

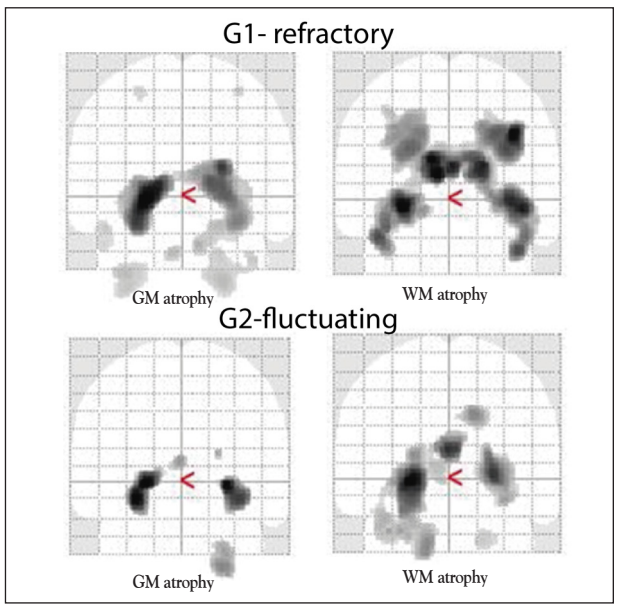


Figure 1.

broader atrophic effect when compared to those with fluctuating seizures (G2). **Conclusion:** Pharmacoresistant group presented more widespread patterns of GM and WM atrophy. These results not only corroborate the hypothesis of the deleterious impact of epilepsy on brain's white and gray matter of the affected individuals, but also the different degrees of these effects in function of disease severity.

References: [1] Yasuda CL, Betting LE, Cendes F. Expert Rev Neurother, 2010. 10(6): p. 975-84.

EEG INITIAL ANALYSES OF ATTENTION NEUROFEEDBACK TRAINING IN HEALTHY SUBJECTS REVEAL VIRTUALLY NO ALTERATIONS IN THEIR RESTING STATE FREQUENCY BANDS' POWER

C. A. Stefano Filho[1,2], L. T. Menezes[1,2], J. O. F. Pigatto[3], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), [3]São Francisco University, Campinas, Brazil.

Introduction: Neurofeedback training (NFBT) has been used as an alternative or supplementary technique to treatments involving disorders such as attention deficit, hyperactivity, anxiety, amongst others [1,2]. However, it has been subject of great debate in the literature, encompassing controversial findings and non-rigorous and non-standardized studies. Our aim was to conduct a controlled NFBT study for attention training in healthy subjects using their electroencephalography (EEG) signals. **Materials and Methods:** Data from four volunteers (3 men) were acquired with the g.USBamp (g.tec®) amplifier, at a 256 Hz sampling frequency, with 16 dry electrodes. Subjects were placed sitting comfortably in a chair facing a computer screen. They were instructed to modulate a combination of their C3 beta (13 – 18 Hz) and C2 sensory-motor rhythms (12 – 15 Hz), aiming to maintain it above a threshold that was calculated at the beginning of each session, at rest, prior to the NFBT. We used the difference (D) between the power of their EEG signal in these frequencies and this threshold to assess the success or failure of the subject's performance. Three NFBT interfaces were used: (I1) a vertical red bar that would go up and down according to the subject's signal, which they were instructed to attempt to maintain above the threshold; (I2) an interface with two competing cars, one representing the subject's signal and the other, the threshold; (I3) the subject's signal would control the screen brightness, while they were reading a text. In each session, all three interfaces were applied, in random order, for 5 minutes each. Moreover, 2 minutes resting-state (RS) recordings were performed prior and immediately after the NFBT. **Results and discussion:** Fig. 1 displays color matrix graphics of the alpha band's power difference between pre and post-training conditions for each subject. Results for the theta and beta bands were very similar, and are not displayed here. A Wilcoxon rank test revealed that only electrode 'Cz', in the alpha band, for Subject 1, showed a significant variation ($p < 0.05$) between pre and post RS conditions after all the NFBT sessions. **Conclusion:** We could not identify any significant pattern that might be related to our NFBT protocol, either indicating that our protocol may have not been effective for the desired effects, or that NFBT, indeed, could not produce changes in the studied features. Had we found any definitive pattern, the inclusion of sham and control groups would be necessary to assess how much of the change is due to the NFBT itself.

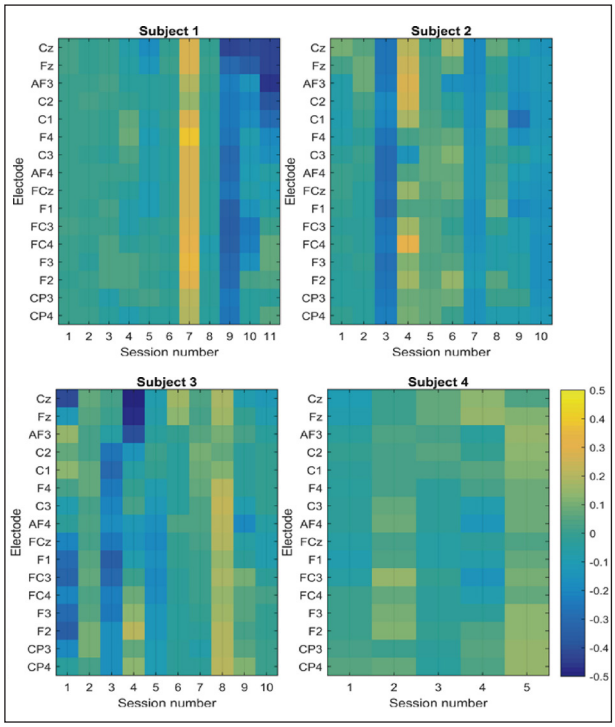


Figure 1. Difference between post and pre NFBT alpha band's power for each subject. Color scale is shown in arbitrary units.

References: [1] Fuchs T et al., Applied Psycophisiol. Biofeedback 8(1) : 1-12, 2003; [2] Ulhmann C et al., Seizure 10: 34-38, 2001.

IMMEDIATE EFFECT OF VIRTUAL REALITY FOR THE PARETIC UPPER LIMB ON ELECTROENCEPHALOGRAPHIC ACTIVITY IN INDIVIDUALS AFTER STROKE

Miqueline Pivoto Faria Dias[1], Viviane Aparecida de Oliveira[1], Daiane Marques Ferreira[1], Ruanito Calixto Júnior[1], Sarah Cristina dos Santos[2],Adriana Teresa Silva Santos[3], Andréia Maria Silva[3]

[1]Master's Degree Student, Federal University of Alfenas /UNIFAL; [2]Graduation Physiotherapy Student, Federal University of Alfenas /UNIFAL [3]Teacher at Federal University of Alfenas /UNIFAL.

Introduction: Subjects affected by stroke present a limitation on daily life activities, especially the upper limb may be the most affected.[1] One of the interventions used for this impairment is Virtual Reality (VR), a technique that provides integrated motor and cognitive stimulation for these patients.[2] This study aimed to evaluate the immediate effect of virtual reality for the paretic upper limb on the electroencephalographic activity in individuals after stroke. **Materials and Methods:** A Controlled Randomized Clinical Trial was conducted in which the immediate effect of VR on the electroencephalographic activity was evaluated in a single day. Twenty-seven hemiparetic subjects with ischemic stroke, aged 53.70 ± 12.08, participated in the study; with more than three months of injury; good mental competence assessed by the Mini-Mental; being 15 men and 12 women. Subjects with severe spasticity assessed by modified Ashworth muscle tonus scale were excluded from the study. The patients were randomized into a control group, with 13 individuals (side affected: 8 right and 5 left) and intervention group with 14 participants (affected side: 7 right and 7 left). The patients in the intervention group (G2) underwent 4 sequences of 1 minute of VR training offered by the Xbox through the game Fruit Ninja, which requires active shoulder and elbow movements. The control group (G1) performed the same active movements, however without the stimulation of the VR game. Electroencephalographic assessment of resting individuals was performed and during the execution of active movements in both groups. Statistical analysis was performed using the Shapiro-Wilk Test (normalization), Friedman Test and Anova one way (intragroup for non-parametric and parametric) and Mann-Whitney and T Test (intergroup for non-parametric and parametric) tests with the SPSS 20.0 software. The respective EEG data channels of the ipsilesional area, and the right and left hemisphere, AF3/AF4, F3/F4, F7/F8, FC5/FC6 were analyzed using Matlab R2017a and EEGLab v14.1.1. **Results:** The VR promoted immediate changes in frequency and power data in the intra and intergroup evaluation in the analysis of the right hemisphere channels (FC6 – increase the frequency p = 0,007; decrease the power p=0,015; AF4 increase de power p = 0,018 (G2); F8 decrease the power p=0,005 (G1)); in the left hemisphere (AF3; F7 and F3 for initial, during intervention and final evaluation increase de power p=0,00 (G2)) and ipsilesional area (F7 and F8 increase the frequency p=0,012 (G2)). The results suggest that the intervention group demonstrated an increase in the alpha frequency band and in the power data indicating less brain effort, compared to the control group. **Discussion:** The main finding of the study was that the virtual stimulus promotes changes in the pattern of brain activity in the frontal areas. Fernandes *et al.* 2014[3] also observed the effect of VR on central excitability in subjects post stroke. They concluded that individuals with right brain injury benefited most from training in a virtual environment, with reduction of neural effort in ipsilesional areas and increase of the training performance. **Conclusion:** The VR promoted immediate changes mainly in the left and right Pre-Frontal cortex (AF3 / AF4); in the left and right Frontal cortex (F3/F7/F8); and in the right

Primary Motor cortex (FC6) on the power and frequency data. The results suggest that the virtual environment may promote changes in the pattern of brain activity in the patient's ipsilesional hemisphere.

References: [1] Lima R C, Salmela L T, Michaelsem S M. Effects of trunk restraint in addition to home-based modified constraint-induced movement therapy after stroke: a randomized controlled trial. International Journal of Stroke, 2012, v.7, p. 258-264. [2] Fong K N K, Chow K Y K, Chan B C H, Lam K C K, Lee J C K, Li Thy, et al. Usability of a virtual reality enviroment simulating an automated teller machine for assessing and training persons with acquired brain injury. J Neuro eng Rehabil 2010;7:19. [3] Fernandes A G B S, Passos J O, Brito D P, Campos T F. Comparison of the immediate effect of the training with a virtual reality game in stroke patients according side brain injury. Neuro Rehabilitation 35, 2014: 39–45.

AUTOMATIC DETECTION OF THE LESION IN CHILDREN WITH PHARMACORESISTENT EPILEPSY SECONDARY TO FOCAL CORTICAL DYSPLASIA

S. V. Gouvêa[1], C. M. Cavalcante[2,3], B. M. Campos[2], F. Cendes[2], M. A. Montenegro[3], M. M. Guerreiro[3], A. C. Coan[2,3]

[1]Graduation program, FCM, UNICAMP, [2]Neuroimaging Laboratory, FCM, UNICAMP, [3]Child Neurology Service, FCM, UNICAMP.

Introduction: Focal cortical dysplasia (FCD) is the most common cause of pharmacoresistant epilepsy in childhood. FCD has a good prognosis of seizure control after surgery if the complete lesion is resected[1]. However, FCD have a range from easily visually detected lesions to lesions with subtle abnormalities in magnetic resonance imaging (MRI)[2]. This study aims to evaluate post-processing protocol of MRI for the improvement of the detection of abnormalities suggestive of FCD. **Materials and Methods:** Twelve 12 children with clinical diagnoses of pharmacoresistant epilepsy secondary to FCD followed in Clinical Hospital of Unicamp were selected. The images were acquired in a 3T MRI with volumetric T1-weighted sequences. Using voxel based morphometry (VBM) technique, we applied an algorithm based in the gray and white matter maps and compared each patient with a control group of 100 healthy subjects. Pre-process of T1-weighted images included gray and white matter segmentation, normalization, modulation and smoothing. The algorithm based on increased gray matter volumes and decreased white matter volumes was applied for each patient looking for areas with abnormalities suggestive of FCD. The clinical data was based in the pre-surgical investigation. **Results:** From the 12 patients, 5 had a lesion visually detected in de MRI image (MRI-pos) and 7 had the MRI image considered normal (MRI-neg). In the MRI-pos group, 3/5 (60%) cases presented VBM abnormalities concordant with the MRI visual analysis. All concordant cases in the MRI-pos group had extra-temporal lesions and the 2 discordant results were lesions in the temporal lobe. In the MRI-neg group, 3/7 (43%) cases presented VBM abnormalities concordant with the presumed epileptogenic zone defined in the pre-surgical evaluation. Among the concordant cases of the MRI-neg group, 2 were extra-temporal and 1 temporal lobe case. **Discussion:** This is a preliminary analysis with an adult control group. Subsequently these analyses will be repeated with a pediatric control group, so we hope to improve the results. Also, we have a worse result in temporal cases due to the worse resolution in MRI image in this area. **Conclusion:** This preliminary analysis showed that this automatized post-processing protocol may be a useful toll to detect FCD areas, especially in extra-temporal lobe epilepsies. However, a larger number of cases need to be evaluated to confirm the effectiveness of this method.

References: [1] Coan, AC & Guerreiro, MM., Journal of International Chid Neurology Association 16(115): 7 pages, 2017; [2] Cendes, F., Continuum (Minneap Minn) 19(3): 623-642, 2013.

BRIDGING NEUROSCIENCE AND MUSIC TO CREATE SOUND PROCESSES TO PROBE HUMAN EMOTIONS

G. S. Spagnol[1,2], J. Manzolli[1,3], L.M. Li[1,2,4]

[1]Brazilian Research Institute of Neuroscience and Neurotechnology, UNICAMP; [2]Neuroimaging Laboratory, FCM, UNICAMP, [3]Interdisciplinary Nucleus for Sound Communication, UNICAMP, [4]School of Medical Sciences, UNICAMP.

Introduction: Emotions are a psychophysiological process triggered by conscious and/or unconscious perception of an object or situation and are often associated with mood, personality, and motivation [1]. We have applied the technique called Mandalas of Emotions (ME) to study human emotions. ME defines nine steps to welcome emotions and develop abilities for reflection, as follows: to identify, receive, accept, access, revisit, understand, resignify, reflect and release emotions [2]. This technique uses five colored, walnut-sized stones that are placed around the patient or on the person's abdomen for periods of 10 to 15 minutes, creating mandalas that correspond to five colors (green, red, yellow, white, black) and five emotions with its positive and negative correspondents (anger/comprehension, euphoria/compassion, concern/gratitude, joy/sadness, fear/courage) [2]. Variations in sounds may evoke what Huron [3] described as the expectation-related emotion response system, which arouse corresponding limbic activations and contrasts, and may enhance access to emotions. This project proposes the creation of 'sound processes', a term for systematized variations of sound, as an add-on tool to provide immersive experiences and enhance reflection during ME application. **Materials and Methods:** This project establishes a bridge between composition of sound processes and emotions. This study designed a correspondence between the circumplex model of Russel (Western) [4] and the classification proposed by the Mandalas Emotions technique (Eastern), in order to create a heuristic for composition of sound processes for each mandala. The circumplex model of affection proposes that all affective states result from two fundamental neurophysiological systems, one related to valence (a continuum of pleasure-dislike) and another to arousal or alertness [4]. As described by Huron, in order to amplify the magnitude of emotional response, we created a sound composition with large contrasts between predicted and actual outcome [3]. **Results:** This is a theory-based creation of sound processes considering Russell's circumplex model [4] for each of the five Mandalas of Emotions. GSS and JM created five sequences of five minutes, varying the following sound parameters: scale material (minor, semitone, major, augmented), timbre (harsh, distorted, bright, mellow), tempo (very slow, slow, fast, very fast), sound level (low, moderate, loud), articulation (legato, non-legato, staccato) and time deviations (none, moderate) according to definitions of each mandala and its expected valence and arousal. **Discussion:** According to the circumplex model, specific emotions arise from activation patterns within two neurophysiological systems associated with valence and excitation, along with cognitive interpretations and labeling of these central physiological experiences. Music composition applies the expectation-related emotion response system as described by Huron [3], which comprises imagination, tension response, prediction response, reaction response, appraisal response, in order to create absorbing sounds, as applied in this project. **Conclusion:** Musical theories on creation of sound processes can be applied for study of emotions, through establishment of an add-on tool for therapeutic purposes based on a neuroscientific understanding of emotions. Further testing will be required to validate the tool.

References: [1] Russell JA, Psychological Review110:145–172, 2003. [2] Ling LH. Curitiba: Insight, 2013. [3] Huron, D. Sweet anticipation: music and the psychology of expectation. 2006. [4] Russell JA. Journal of Personality and Social Psychology 39:1161– 1178, 1980. [5] Wassermann et al, IEEE Computer Society 2003. 1070-986X/03.

STRUCTURAL AND FUNCTIONAL NEUROIMAGING EVALUATION OF BENIGN EPILEPSIES IN CHILDHOOD WITH TYPICAL AND ATYPICAL OUTCOMES

Cavalcante, C. M.; COAN, A. C.

Epileptology group, Child Neurology department, Hospital de Clinicas, UNICAMP.

Introduction: The term "focal genetic (idiopatic) epilepsies of childhood" represent a full spectrum of epileptic syndromes, which ranges from benign childhood epilepsy with centrotemporal spikes (BECTS) to more neurologic compromising diseases, such as atypical benign partial epilepsy (ABPE), continuous spike-waves during slow sleep (CSWS) and the Landau-Kleffner Syndrome (LKS). Better understanding of the physiopathology of these syndromes is essential to comprehend the different phenotypes and the impact of the epileptic activity to brain function, in order to determine the best therapeutic options for each of these phenotypes. This study proposes the analysis of clinical peculiarities of focal genetic epilepsies of childhood, as well as structural and functional neuroimaging alterations, comparing typical or atypical outcomes, correlating clinical and electroencephalographic phenotypes to possible changes in white or grey matter and functional brain connectivity. **Materials and Methods:** All images are being acquired in a 3 Tesla scanner (Philips Achieva) and will be reviewed by epileptologists, with knowledge about clinical and electroencephalographic data of each patient. Tractography will be done by semiautomated deterministic method. EEG-fMRI will be possible due to the paramagnetic capacity of deoxihemoglobin molecules, creating the blood oxygen level dependent (BOLD) contrast, while EEG signal will be obtained by 64 electrodes. Second level statistical analysis will be performed to compare cerebral connectivity maps of these patients to a compatible control group.

References: [1] GONSALES, Marina C. et al . Recent developments in the genetics of childhood epileptic encephalopathies: impact in clinical practice. Arq. Neuro-Psiquiatr., São Paulo , v. 73, n. 11, p. 946-958, 2015. [2] Zhang Z, Lu G, Zhong Y, et al. Altered spontaneous neuronal activity of the default-mode network in mesial temporal lobe epilepsy. Brain Res, 2010. [3] Ibrahim GM, Cassel D, Morgan BR, et al. Resilience of developing brain networks to interictal epileptiform discharges is associated with cognitive outcome. Brain 2014.

FUNCTIONAL CONNECTIVITY CHANGES AFTER TEMPORAL LOBE SURGERY

Silva, B. F., Ishikawa, A., Amaral, I., Morita, M. E., Alvim, M.K, Ghizoni, E., Tedeschi, H., Cendes, F., Yasuda, C. L

[1]Neuroimaging Laboratory, FCM, UNICAMP

Introduction: Surgical removal of mesial temporal lobe structures has been the leading treatment for refractory MTLE. This study aimed to evaluate postoperative changes of functional connectivity networks, integrating neural changes with surgical result. **Materials and Methods:** We performed a longitudinal study of 32 patients with unilateral hippocampal sclerosis, who underwent preoperative (before surgery)/postoperative (after 6 months of surgery) T1-weighted MRI and RS-fMRI acquired in a 3T scanner (Philips). Functional connectivity analysis was performed with UF²C toolbox (https://www.lniunicamp.com/uf2c), running within MATLAB/SPM12. After preprocessing, we generated individual matrices based on ROIs derived from a functional parcellation (70 ROIs from 12 functional networks). Finally, we used t-tests for comparisons between the groups of preoperative and postoperative images, to analyze possible changes between the 2 times. Analyses were reported with uncorrected alpha =0.01. **Results:** As preliminary results, we identified increased (red lines, Figure1) FC inter and intra-networks on post-operative period compared to the preoperative period. As shown in the figure, we observed reduced connectivity (blue lines) involving a few number of networks on frontal lobes.

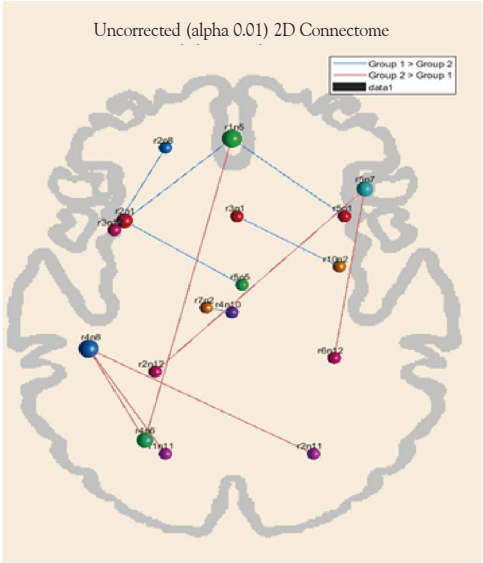


Figure 1. Altered connections between Pre (Group 1) and Postoperative (Group 2). The blue lines demonstrate diminished connectivity between pairs of ROIs; the dashed lines indicate connections with opposite correlation signal and the red line shows increased connectivity. The spheres represent different networks, and their sizes denote the degree of altered connectivity

Discussion: Our preliminary results show postoperative increase of connectivity networks that involve not only the temporal lobe, but also the frontal, parietal and occipital lobes, confirming the hypothesis that dynamic processes after surgery affect the whole brain. Previous functional analysis studies found similar results, but their neuropsychological essence remains unclear. A further extension of the follow-up period may reveal whether the alteration represents a temporary compensation or a progressive construction. **Conclusion:** We demonstrated that functional connectivity analysis can reveal a reorganization of brains networks, suggesting that dynamic processes persist after the removal of the hippocampus. Our next step is to broaden the sample of patients in order to divide them into subgroups according to crisis management, analyze how these changes behave in the long term and establish its relation with the surgical outcome.

References: [1] Liao, W., et al., Sci Rep, 2016. 6:23153.; [2] Yasuda, C.L., et al., Neuroimage, 2010. 49:71–9.; [3] Tang, Y., et al., Seizure, 2017. 46 43–49.

EFFECTS OF NUMBER OF DIFFUSION GRADIENT DIRECTIONS AND B-VALUES ON THE DTI INDEXES: A CLINICAL PROTOCOL STUDY

E. M. Souza[1,2,3,4], E. T. Costa[1,2], G. Castellano[3,4]

[1]Biomedical Engineering Department, FEEC, UNICAMP, Campinas, Brazil; [2]Biomedical Engineering Center, UNICAMP, Campinas, Brazil; [3]Neurophysics Group, IFGW, UNICAMP, Campinas, Brazil; [4]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, Brazil.

Introduction: Diffusion tensor images (DTI) have many applications in clinical routine and research. However, the measured signal is susceptible to the influence of noise and artifacts, being thus important to check if these factors do not compromise the parameters calculated from the images [1]. In this context, the main goal of this work was to evaluate how the number of diffusion gradient directions (NDGD) and b-values can change the DTI parameters for the following clinical protocols: epilepsy and brain tumors. **Materials and Methods:** An anisotropic diffusion phantom was built, and DTI acquisitions were performed in the 3T Philips Achieva MRI scanner using the clinical protocols for epilepsy and brain tumors, changing b-values and NDGD. The phantom had 6 bundles of 10 mm diameter and 190 mm length composed of Spectra, Dyneema or Polyamide fibers. For each acquisition, the DTI parameters calculated were: mean diffusivity (MD), fractional anisotropy (FA), relative anisotropy (RA) and volume ratio (VR). The Coefficients of Variation (CV) of each DTI parameter were evaluated, as well as the tracts reconstruction obtained. **Results:** The Spectra and Dyneema fiber bundles were seen in all tracts reconstructions. For both protocols tested, it was observed that Dyneema bundles had the lower CV values for all DTI parameters calculated. The FA values found for Dyneema bundles were in the range of those observed for the brain white matter (0.72 ± 0.04), which did not occur for Spectra or Polyamide fiber bundles. MD values found for all fiber bundles were out of the range found for human brain tissues, showing higher CV values for Polyamide and Spectra fiber bundles. **Discussion:** The results obtained showed that for both protocols, variations in DTI acquisition parameters can change the values of the parameters obtained from the images. The use of heat-shrinking tubes, when applied to fiber bundles, improved significantly the bundles' anisotropy values, which were near the range observed for the brain white matter. The highest FA values were found for Dyneema fiber bundles. Although Spectra is a multifilament line, it has memory, which makes it difficult building bundles with high anisotropy. Among all bundles used, the diffusion signal from Dyneema was higher than from other materials, for both protocols applied. **Conclusion:** The present study showed that the acquisition parameters' changes can modify DTI results for both clinical protocols tested. Higher anisotropy fiber bundles made of Dyneema are less susceptible to these changes when compared to lower anisotropy bundles made of Spectra or Polyamide lines.

References: [1] Fieremans E et al, J Magn Reson 190: 189-199, 2008.

BRAIN GREY MATTER EVALUATION IN STROKE-FREE PATIENTS WITH ATRIAL FIBRILLATION

D.S. Silva[1], W.M. Avelar[1], M.F.B. Roma[2], A. Fattori[2], M.J.O. Figueiredo[3], F. Cendes[4], A.C. Coan[4]

[1]Neurovascular Group, Dep. of Neurology, UNICAMP, Brazil, [2]Geriatric department, UNICAMP, Brazil. [3]Department of Cardiology, UNICAMP, Brazil, [4]Brazilian Institute of Neuroscience and Neurotechnology, BRAINN, UNICAMP, Brazil.

Introduction: Atrial Fibrillation (AF) is the most common arrhythmia in clinical scenario and has high incidence especially in the elderly. Several studies has indicated AF could produce brain damage and structural impairment even without stroke. Furthermore, AF has been associated to cognitive impairment independent of stroke. We aimed to determine whether in the absence of stroke and dementia, patients with AF has brain grey matter atrophy compared to controls without that arrhythmia. **Materials and Methods:** Structural brain images were acquired in a 3.0 T scanner for 10 stroke-free patients with AF and no dementia at University of Campinas (UNICAMP) and compared with 30 healthy controls from brain imaging bank (Neuroimaging laboratory, LNI-UNICAMP) matched for sex and age. All patients were submitted to the same clinical protocol performed by a neurologist in order to exclude dementia, history of stroke, severe head trauma and neurodegenerative disorders. Clinical evaluation included clinical examination and a short cognitive test for cognitive performance (Mini Mental State Exam). Blood exams were made in all patients to exclude hypovitaminosis B12 and thyroid, liver or renal severe dysfunction.

Subjects with carotid stenosis and cardiac severe dysfunction were excluded. Brain grey matter was evaluated, in patients and controls with Voxel Based Morphometry (VBM) using SPM 8 (Wellcome Department of Cognitive Neurology) after normalization to MNI -124, segmentation, modulation and smoothed of grey matter. The grey matter's maps were compared between patients and controls using a Two-sample T-test ($p < 0{,}001$). Only clusters with a minimum of 20 contiguous voxels were considered significant. **Results:** We found grey matter atrophy in stroke-free patients with AF. This atrophy was more evident in left cerebellum, bilateral frontal lobe (gyrus rectus, medial frontal gyrus and superior frontal gyrus), left parahippocampa gyrus and hippocampus as well as right inferior parietal lobe (angular gyrus). **Discussion:** The results found in this study are similar to those reported in the literature in stroke-free patients with AF [1, 2]. However, the exact mechanisms by which brain atrophy may occur in AF even without stroke evidence are not understood and is a matter of speculation [3]. Growing evidence has emerged in recent years to put AF as a major risk factor for dementia even in absence of clinical stroke [3, 4]. Grey matter atrophy may play a role in the development of dementia in patients with AF and no history of stroke. In our study, grey matter atrophy occurs in brain regions important for cognitive process. Future researches could provide additional evidence of brain structural abnormalities in stroke-free patients with AF and help clarify the main mechanisms beyond stroke in dementia development in AF. **Conclusion:** The present study showed that in a small sample of patients with AF, there was brain grey matter atrophy even without history of stroke or dementia.

References: [1] Piers R.J et al., Heart Rhythm 2016; 13 (10): 2020-2024; [2] Stefansdottir H et al., Stroke 2013; 44:1020–1025. [3] Alonso A, Arenas de Larriva AP, European cardiology 2016; 11(1):49-53. [4] Kalantarian S et al., Ann Intern Med 2013; 158(5 Pt 1):338–46.

1H-MRS NEURONAL-GLIAL AND INFLAMMATORY MARKERS IN PHARMACORESISTANT MESIAL TEMPORAL LOBE EPILEPSY

L. R. Pimentel-Silva[1], R. Barbosa[1], R. F. Casseb[2], M. M. Cordeiro[1], M. K. M. Alvim,[1] B. A. G. Campos, C. L. Yasuda,[1] F. Cendes[1]

[1]Neurology Dept., FCM, UNICAMP, [2]Seaman Family MR Research Centre, University of Calgary.

Introduction: Mesial temporal lobe epilepsy (MTLE) is usually associated with hippocampal sclerosis (HS). However, a minor part may present with no abnormalities in the magnetic resonance imaging (MRI) examination. Nearly 70% of MTLE with HS are resistant to anti-epileptic drugs (AED-R). Glial and inflammatory alterations are possible mechanisms of pharmacoresistance in MTLE [1]. Proton-magnetic resonance spectroscopy (1H-MRS) is a non-invasive, *in vivo* technique to quantify several metabolites, including n-acetylaspartate (NAA, a neuron marker), myo-inositol (mIns, a gliosis marker) and glutamate (Glx, the main excitatory neurotransmitter, often implicated in epileptogenesis and excitoxicity), which reflect the expected neuronal-glial abnormalities of MTLE. Thus, we aimed to investigate the influence of the pharmacoresponse, presence and side of HS on the metabolite levels, and to evaluate inflammatory peripheric process regarding pharmacoresponse. **Materials and Methods:** We acquired structural and 1H-MRS data from unilateral MTLE patients (on MRI visual analysis and EEG grounds) and controls. To confirm visual analysis, we performed hippocampal automatic volumetry using the *Freesurfer*. Metabolic data was quantified using the LCModel software (92 unilateral MTLE patients and 50 healthy controls). We evaluated peripheral inflammatory mediators using multiplex assay (70 unilateral MTLE patients and 50 controls): tumor necrosis factor alpha (TNF-α), interleukin 1β (IL1β) and IL6. All the metabolites were expressed in ratios of creatine (Cr). Statistical analyses comprised two-way ANCOVA, covarying for age, and Kruskall-Wallis with follow-up planned comparisons using Mann-Whitney U tests. We applied Bonferroni correction for multiple comparisons. An alpha level of $p < 0.05$ was set as significant. All the statistical analyses were performed using SPSS. **Results:** We included 92 patients and 50 controls. The analyses showed that pharmacoresponse and HS independently affect the NAA/Cr and mIns/Cr values. NAA/Cr was reduced bilaterally in AED-R and left-HS patients and only ipsilaterally in right-HS. mIns/Cr was increased ipsilaterally to the lesion in AED-R and left-HS patients. Glx/Cr was reduced in AED-R patients with HS. We found no differences between AED-R patients, seizure-free patients and controls regarding the cytokine levels. **Discussion:** The widespread neuronal-gial alterations in AED-R and left-HS reflects the differential impairment associated to HS side, as demonstrated in metabolic[2], neuropsychological[3] and functional connectivity studies[4]. Glx/Cr reduction reflects functional damage related to pharmacoresponse and presence of HS. This is confirmed by Glx increase in more preserved areas, where alterations of Glu excitability and Glu turnover are less expected[5]. Although these are non-invasive markers of inflammatory processes, peripheral inflammation was not related to pharmacoresponse. Thus, other factors might be involved, such as psychiatric comorbidities[6]. Our results are promising since it points different MTLE profiles which might benefit from better clinical and surgical treatment. **Conclusion:** There was an independent effect of pharmacoresponse and HS on metabolic abnormalities. Pharmacoresistance and left-sided HS were the most impaired MTLE profiles.

References: [1]Filibian M, et al., Epilepsia 2012;53:1907-1916; [2]Campos BA et al., Epilepsia 2010;51:783-788 ; [3]Alessio A et al. Hum Brain Mapp 2013;34:186-199 ; [4]de Campos BM et al. Hum Brain Mapp 2016;37:3137-3152 ; [5]Doelken MT, et al. Seizure 2008;17:490-497.[6]Vieira EL, et al. Epilepsy Behav 2015;53:131-134.

UNDER PRESSURE: A CASE SERIES OF UNUSUAL STROKE MIMICS

F. F. Graça[1], T. S. Prado[1], L. G. Matias[1], W. M. Avelar[1] , P. C. Azevedo[1]

Neurology Dept., FCM, UNICAMP.

Introduction: Stroke Mimics (SM) are nonvascular conditions with neurological symptoms that resemble stroke[1]. Since intravenous thrombolysis (IVT) was established as the standard therapy for acute ischemic stroke (AIS), an effort to reduce the door-to-needle time increasing the success in earlier administration was made. However, the short time range turns decision making into a challenging situation[2] **Materials and Methods:** We present a case-series of four patients from the University of Campinas Hospital that went under IVT and were further diagnosed as unusual causes of SM. **Results:** Case 1: Female, 73yo, 3 hours of confusion, slurred speech and tetraparesis. Whereas the hypothesis of brainstem stroke, IVT was performed. Family, not present at the admission, related that the patient had five years of non-investigated ataxia. MRI and clinical evaluation confirmed the diagnosis of MSA-C. Acute confusion was attributed to delirium due to pneumonia. Case 2: Female, 70 yo, 2 hours of acute onset of right hemiplegia. The patient was under treatment for otitis media since five days ago. IVT was initiated and needed to be interrupted due to difficult glycemic control. The patient developed fever and neck stiffness, CSF analysis confirmed the diagnosis of pneumococcal meningitis. Case 3: Male, 61 yo, 1,5 hour of acute onset of right hemiparesis and dysarthria. Noncontrast CT scan was normal. IVT was performed but interrupted once patient decreased consciousness level. Further neuroimaging evidenced an extensive SAH (figure 1). After an appropriate investigation, endocarditis diagnosis complicated with a mycotic aneurysm was done. Case 4: Male, 71 yo, 2 hours of left hemiparesis, no trauma or prior bleeding history. IVT was performed with slight improvement of symptoms. Posterior CT Angiography to cervical vessel and MRI (figure 2) demonstrated a cervical epidural hematom. **Discussion and Conclusion:** In a nutshell, commom SM found in clinical practice are conversion disorder, seizures and migraine, nevertheless many others, including acute exacerbation of chronic diseases or life threatening conditions, need to be investigated in cases with atypical evolution.

References: [1] Vilela P Eur J Radiol. 96:133-144, 2017; [2] Tsivgoulis G et al., Stroke 46(5):1281-7, 2015.

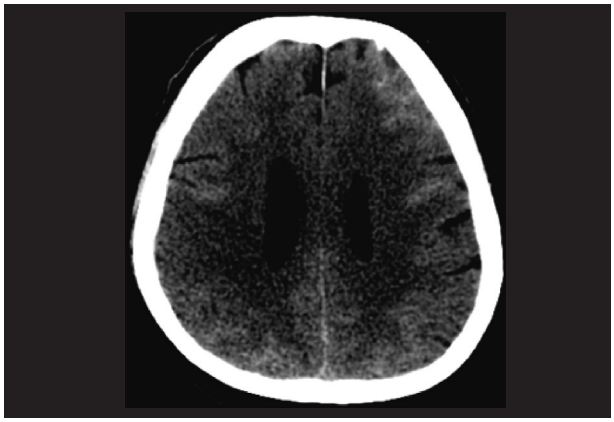


Figure 1.

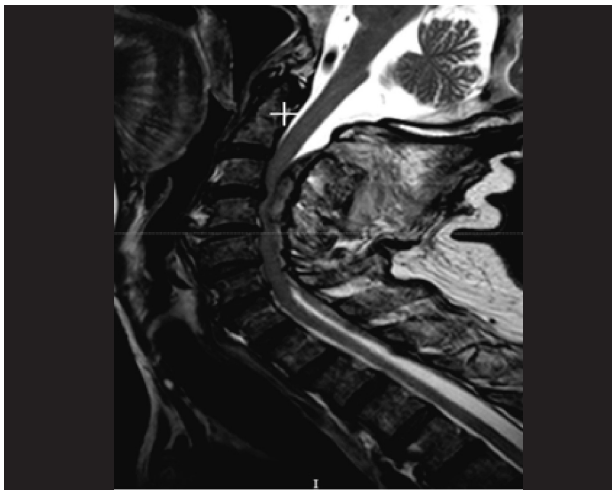


Figure 2.

DATA AUGMENTATION ON MEDICAL IMAGES TO DEEP LEARNING USAGE

I. Fantini[1], L. Rittner[1], C. Yasuda[2], R. A. Lotufo[1]

[1]Medical Image Computing Lab, FEEC, UNICAMP, [2]Neuroimaging Laboratory, FCM,UNICAMP

Introduction: Deep Learning is considered the most effective tool for image classification, but its use requires a considerable amount of annotated data [1]. Medical images annotation is costly and time-consuming, becoming scarce. On the other hand, medical image datasets are increasing due to noticeable benefits of supporting clinical analysis. The use of small datasets on Deep Convolutional Neural Networks (CNNs) is allowed by transfer learning and data augmentation techniques [2,3]. This study explored these techniques to automatically identify MRI corrupted by motion artifacts. **Materials and Methods:** The Magnetic Resonance Image (MRI) data were acquired at the University of Campinas, on a 3T Phillips Achieva scanner. A T1-weighted volumetric sequence was acquired in the sagittal plane (thickness = 1 mm, flip angle = 8 degrees, TR = 7.1 msec, TE = 3.2 msec, matrix 240x240x180, FOV 24x24 isotropic voxels of 1 mm) from 37 healthy volunteers. The dataset is divided into two classes: control images, which contains 24 acquisitions (matched by gender and age); and images corrupted by motion, which comprises 13 acquisitions (8 females, 5 males, aged from 21 to 53). An InceptionV3 [4] was used to perform the transfer learning experiment, which consists of fine-tuning the pre-trained model using the specific dataset. Since MRI is a 3D sequence while the architecture is a 2D CNN, one model for each MRI axis was trained using their 40 central slices. As the dataset contains 37 acquisitions, we performed data augmentation by rotating, translating and normalizing image intensity. The transformations were combined and applied to each slice. Two intensity normalizations were applied: maximum of 3-sigma or a range from 0.8-1.2 of original maximum. The other parameters obeyed realistic conditions: maximum rotation of 15 degrees; maximum translation of 15 pixels; and were selected randomly per acquisition. As a result, each slice has a different rotation, translation, and intensity range. We opted to extract 128x128 patches size from slices, thereby the InceptionV3 was adapted to the new input size removing the multiclass classifier and the last Inception block layer, and then attaching the new binary classifier. Since the control group was bigger than the motion corrupted group, it was required a different number of patches from each group to balance the data. Also, the positions of the patches were selected randomly, covering the four quadrants of the brain area. Combining the cited transformations, we extracted 40 different patches from each slice from motion corrupted acquisition group and the half for slices from control acquisitions group. The dataset was separated, on acquisition level, into 60% training data (14 control, 8 motion) and 40% validation data (10 control, 5 motion).

Table 1. Accuracy, Sensitivity and Specificity, in percentage, for each axis.

	Axial	Coronal	Sagittal
Accuracy	95.06	91.03	88.60
Sensitivity	99.15	94.50	86.99
Specificity	89.21	86.08	90.92

Results: The adapted InceptionV3 model detect if the patch has motion artifact or not. The results are shown in Table 1. Checking the original data, without transformations, the trained networks achieve similar performance. percentage, for each axis. **Discussion:** Although the dataset contains only 37 acquisitions the Deep CNN results reported good accuracy. This indicate that the data augmentation generated the necessary extra data to perform the deep network fine-tuning. **Conclusion:** The present work confirmed that data augmentation and transfer learning are useful techniques to train Deep CNNs using limited annotated medical images data.

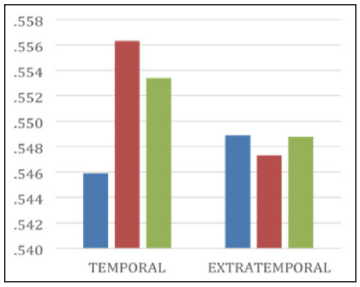
References: [1] doi:10.1038/nature14539; [2] doi:10.1146/annurev-bioeng-071516-044442; [3] doi:10.1109/TMI.2016.2535302; [4] SZEGEDY, C. et al., Computer Vision and Pattern Recognition: 2818-2826, 2016.

DYNAMIC PROCESSES AFTER EPILEPSY SURGERY SUGGEST PARTIAL RECOVERY OF WHITE MATTER INTEGRITY

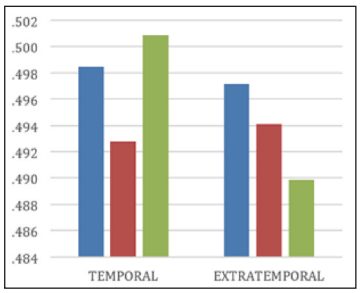
Amaral, I.,[1] Cendes, F.,[1] Yasuda, C.,[1] Silva, B. F.,[1] Ishikawa, A.,[1] Morita, M. E.,[1] Alvim, M.K,[1] Ghizoni, E.,[1] Tedeschi, H.[1]

[1]Neuroimaging Laboratory, FCM, UNICAMP.

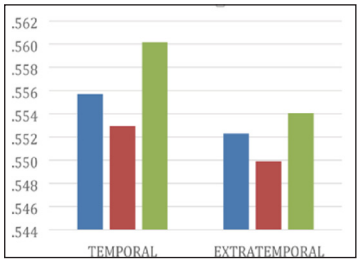
Introduction: Several studies have shown that structural and functional changes in mesial temporal lobe epilepsy extend beyond the temporal mesial region, including the contralateral hemisphere[2,3]. We investigated how the acute and chronic postoperative alterations affected Fractional anisotropy (FA) of white matter (WM) tracts in the contralateral hemisphere of both temporal and extra-temporal epilepsy. **Materials and Methods:** In this study, we performed automatic tractography in three moments (preoperative, acute postoperative (first week) and long-term (at least 6 months)) for 58 temporal temporal lobe epilepsy and



a. FA Values of the body of the corpus callosum



b. FA Values of the genu of corpus callosum



c. FA Values of the splenium of corpus callosum

Figure 1.

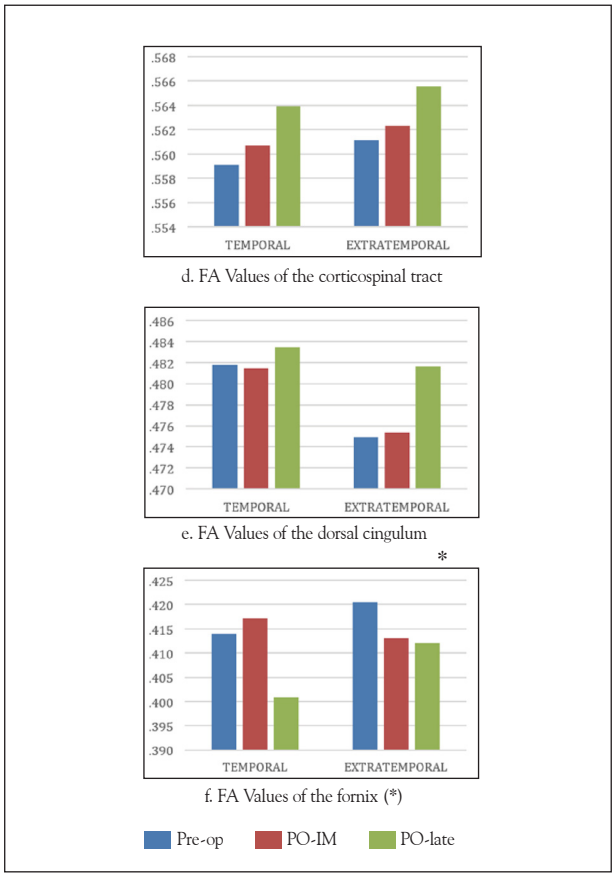


Figure 1.

46 extratemporal patients. We used ExploreDTI software (www.exploredti.com) for tractography of Diffusion Tensor Image (DTI) MRI, acquired on a PHILIPS 3T scanner. Statistical analyses with mixed models were performed with SPSS 22 software for longitudinal evaluation of FA values, including Dunn-Sidak test to adjust for multiple comparisons. **Results:** Our preliminary analyses showed a general trend of increased FA in most tracts after surgery, more pronounced in the TLE group ($p<0.05$, corrected with Dunn-Sidak). However, we identified significant FA decrease in the fornix (fig f.*) of TLE patients ($p=0.02$, corrected with Dunn-Sidak). **Discussion:** The value of FA is an important tool that allows us to make inferences about the WM integrity. Although not statistically significant, our results suggest that most of the tracts present an improvement of FA after surgery regardless the local of surgery. It is probable that the progressive FA decrease in the fornix of TLE group result from hippocampal deafferentation after hippocampal removal, which may not be related to postoperative seizure outcome. **Conclusion:** There is a tendency to axonal regeneration of the fibers after withdrawal of the epileptogenic focus, in both temporal and extratemporal patients.

References: [1] Yasuda, C.L., et al., Neurology, 2010. 74(13): p. 1062-8 (5): 1014-1018, 2010; [2] Coan, A.C., et al., Epilepsia, 2014. 55(8): p. 1187-96. [3] Yasuda, C.L., L.E. Betting, and F. Cendes, Expert Rev Neurother, 2010. 10(6): p. 975-84

REFRACTORY SEIZURES DISRUPT BRAIN CONNECTIVITY IN TEMPORAL LOBE EPILEPSY

Ribeiro, L F[1] ; Montanher, L[1]; Cendes, F[1]; Yasuda, CL[1]
[1]Neuroimaging Laboratory.

Introduction: Alterations of functional connectivity in TLE patients with unilateral hippocampal sclerosis (HS) have been repeatedly reported[1]; however, little attention has been directed to evaluate the impact of seizure control on resting state functional connectivity. Therefore in this study, we investigate the influence of seizure control on resting state networks. **Materials and Methods:** Resting-state fMRI was acquired on 3T-PHILIPS from 3 groups of patients TLE-HS [G1- refractory, 55 subjects; G2 – fluctuating, 42 subjects; G3 – sz-free 18] and 59 controls. To compare interactions of 12 RSNs (from resting-state functional-MRIs, parcellated in 70 regions of interest (ROIs)), images were processed with UF^{2}C-toolbox[1] (running on MATLAB2014/SPM12) (www.fil.ion.ucl.ac.uk), for ROI parcellation, matrix construction and statistical analysis (with intranetwork and internetwork connectivity). For each ROI, we extracted time-series which were used to generate individual matrices with Pearson's correlation tests. After converting to z–score, these matrices entered group analyses (patients x controls). Each group of patients was compared with a group of controls (two-sample T-test). Reported results have a 0.05 alpha, FDR corrected. **Results:** We identified both intranetwork and internetwork dysfunctions (reduced connectivity) in all groups, compared to controls. We observed that G1 showed reduced connectivity in a larger number of networks in comparison with G2 and G3. We did not identify increased or reversed connectivity in these TLE groups ($p<0.05$, corrected with FDR).

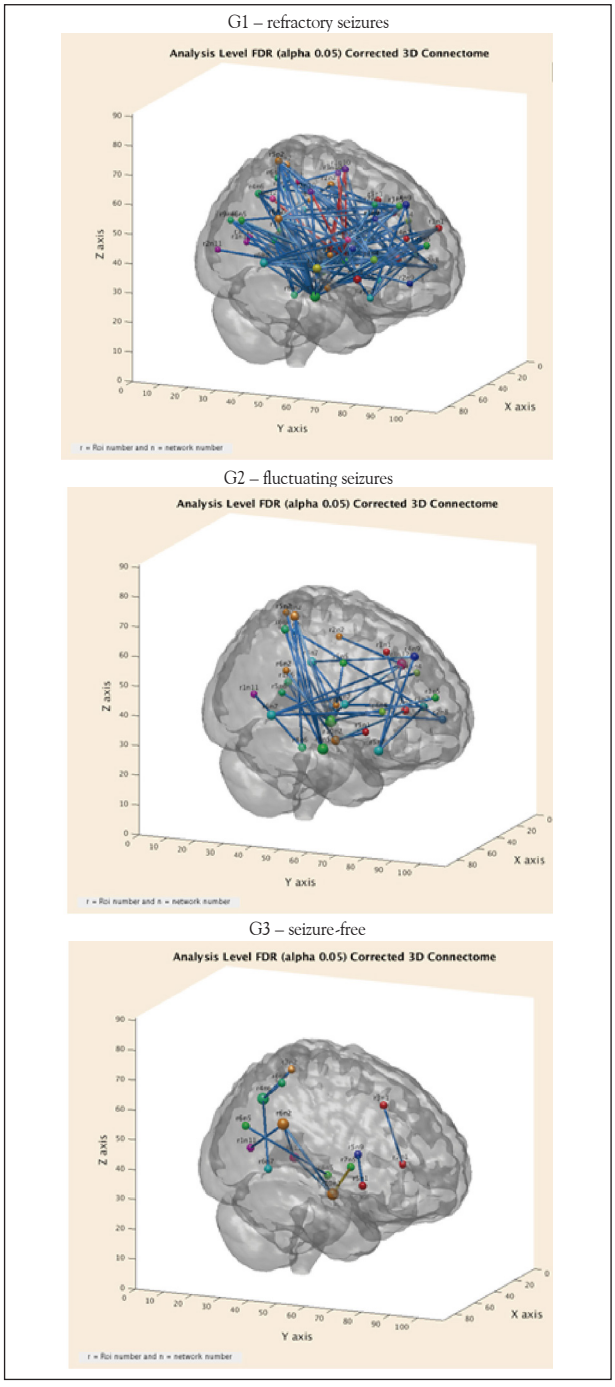


Figure 1. Mean connectivity of G1, G2 and G3 in comparison with controls.

Discussion: Our preliminary results indicate a deleterious effect of pharmacoresistant seizures on brain connectivity, as we observed severe and widespread alterations in G1 and G2. Further analyses may investigate the association between FC and both cognition and aging processes. **Conclusion:** patients with worst patterns of seizure control present reduced intranetwork and internetwork connectivity in comparison with seizure-free individuals.

Reference: [1] de Campos, B.M., et al. Hum Brain Mapp. **37**(9): p. 3137-52., 2016.

A CASE REPORT OF CEREBELLAR COGNITIVE AFFECTIVE SYNDROME DIAGNOSED BY ACCIDENT IN THE EMERGENCY DEPARTMENT

L. A. Y. Suemitsu[1], F. F. Graça[1], L.G. Piovesana[1], P. C. Azevedo[1]

[1]Dept. of Neurology, FCM, UNICAMP.

Introduction: the role of cerebellum in non-motor functions is observed in patients with cerebellar damage from different acquired and non-acquired etiologies [1,4]. The Cerebellar Cognitive Affective Syndrome (CCAS) was first described in 1998 and characterized by executive dysfunction, impaired spatial cognition, personality change and language deficits. [2]. Topography and anatomy studies discovered that different areas of cerebellum act in diverse cognitive and affective domains depending on their connection to supratentorial areas. Posterior vermis is connected to the limbic system and modulates emotion. Posterior lobes of cerebellum are related to cognitive function [3,4,5,6]. **Materials and Methods:** this article is a case report of a patient in follow-up in the Department of Neurology of University of Campinas. **Results (case report):** patient R.V. was hospitalized in April 2017 due to a traumatic brain injury (TBI) after she swerved to avoid being hit by a car and fell to the ground. In the CT scan, no hemorrhage was seen, but a chronic cerebellar atrophy was found. Patient presented a brief confusion state that resolved after one day. On neurologic exam cerebellar signs were present, patient had mild appendicular dysmetria and an incapacity of performing tandem-gait. Furthermore, patient had humor alterations: hyperthymia, with inadequate laughing and commentaries; and an accelerated speech. The patient had also language disturbance with mild agrammatism. Patient´s brother said the humor alteration was chronic. Clinical history included a TBI with 12 years old, after a fall from own height, while patient was running, cigarette smoking and dyslipidemia. Ambulatorial investigation was performed and MRI showed severe cerebellar atrophy predominantly in vermis and posterior lobes bilaterally. MOCA exam resulted in 18 points revealing dysfunction in executive tasks, abstract reasoning and language (patient had 11 years of education). CSF had no significant alterations. Only laboratorial abnormality was B12 vitamin dosage below 150 pg/ml, which was restored, with no change in clinical findings. Affective and neurological signs and symptoms plus CNS image are compatible with CCAS diagnosis.

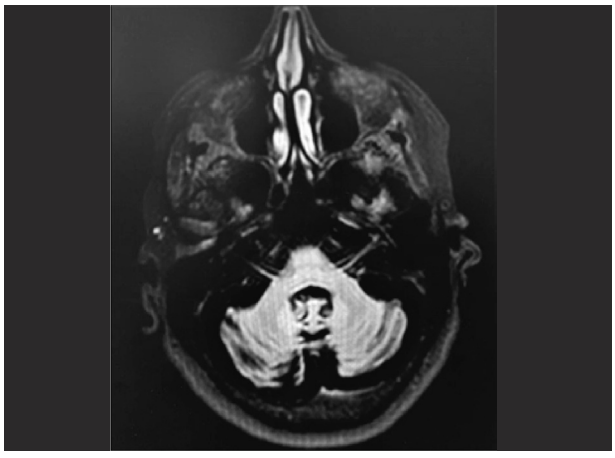


Figure 1.

Discussion and conclusion: this case report supports evidence of non-motor function of cerebellum. Vermis atrophy and posterior lobe atrophy of cerebellum are clearly visible in patient´s MRI image, and affective and cognitive symptoms may be related to these areas, respectively. The accidental diagnosis of the CCAS in this patient may rise concern about structural investigation in psychiatric patients. Besides, medical assistants should pay more attention to identifying emotion symptoms of patients with cerebellar diseases.

References: [1] Schmahmann JD, J Neuropsychiatry Clin Neurosci 16:367–378, 2004; [2] Schmahmann JD et al., Brain 121 (4):561-79, 1998; [3] doi:10.1016/j.cortex.2009.11.008; [4] doi:10.1093/brain/awm201; [5] doi:10.1093/brain/awr266; [6] Middleton FA et. al, J. Neurosci., 21(2):700–712, 2001.

CELLULAR DAMAGE AND NEUROGENESIS IN ZEBRAFISH LARVAE BRAIN AFTER PROLONGED SEIZURES

De Moura, T.C.[1], C. V. Maurer-Morelli[1]

[1]Zebrafish Laboratory, Department of Medical Genetics, School of Medical Sciences, UNICAMP, Campinas, SP- Brazil.

Introduction and Hypothesis: Recently, zebrafish (*Danio rerio*) emerged as a popular model to investigate cellular and molecular mechanisms underlying epilepsy and seizure events, providing several advantages in comparison to other animal models, such as higher fecundity rate, ease manipulation, high degree of genetic conservation with mammals, including humans, as well many advantages for drug screening [1,2]. Although studies using zebrafish model resemble behavioral and electrical brain activity of mammalian seizures [2], the characterization of cellular and histological changes in larval seizure model remains incomplete. It is known that zebrafish has been validated as a seizure model; however, it is not clear if this model is able to become chronically epileptic. Among the cellular events that occur in response to the brain initial insult, neuronal death has received significant attention and may lead to the epileptic state [3]. Zebrafish brains have higher regenerative capacity compared to mammalian brains [4], what may contribute to a recover from seizure insults. In this way, it is important to investigate the impact of prolonged seizures on zebrafish larvae brain (*status epilepticus*-like model) by analyzing pathways and genes related to cell damage and recovery after pentilenetetrazole (PTZ)-evoked seizures. We hypothesize that zebrafish has a specific mechanism that prevents epileptogenesis in this model. **Objective:** The main aim of this project is to investigate cellular damage and neurogenesis in zebrafish larvae brain in a model of *status-epilepticus*-like (SE-like) proposed by our group. **Methods:** Wild-type zebrafish larvae at 7dpf will be separated into two groups: (a) Control – animals exposed to bath medium for 3 hours; and (b) SE-like – animals exposed to PTZ 15mM for 3 hours. Analyses will be performed at four different time-points after seizure-induction: 1, 5, 15, 30 days. Markers for apoptosis (*bax, caspases 9,8,3 and 7, apaf1*), gliosis (*gfap*) and neurogenesis/cell proliferation (BrdU, PCNA) will be analyzed by using whole-mount immunofluorescence and whole-mount in situ hybridization (WISH) in order to achieve the spatial distribution and cell quantification. Acridine Orange and Fluoro-Jade C stainings will be used to detect apoptotic cells and neurodegeneration, respectively, using a stereological cell counting method. Significant differences will be considered when $p \leq 0.05$. In addition, transcriptome results from our laboratory in the zebrafish SE-like model will be used to identify other genes and pathways differentially expressed, providing new avenues of investigations. **Relevance:** By elucidating the mechanisms underlying cellular response after SE, we hope to shed some light on the epileptogenesis processes in the zebrafish brain. Through understanding the damage/regeneration impact on the zebrafish brain, we may clarify if this animal is prone or not to become chronically epileptic. This information will be valuable for further therapeutic approaches.

References: [1] doi: 10.1016/j.neuroscience.2004.11.031; [2] doi:10.1038/nn.3934; [3] doi: 10.2174/157015912804143504; [4] doi:10.1186/1749-8104-8-3.

RELATIONSHIP BETWEEN INFLAMMATORY MEDIATORS AND WHITE MATTER INTEGRITY IN ALZHEIRMER DISEASE AND MILD COGNITIVE IMPAIRMENT

Mariana de Abreu[1];Thamires N. C. Magalhães[1]; Christian L. B. Gerbelli[1]; Luciana R. P. Silva[1]; Camila V. L. Teixeira[1]; Thiago J. R. de Rezende[1]; Fernando Cendes[1]; Marcio L. F. Balthazar[1].

[1]Neuroimaging Laboratory, Department of Neurology, University of Campinas (Unicamp), Brazil.

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease whose pathophysiologic mechanisms are not completely understood. New evidences demonstrate that inflammation may play an important role in the pathogenesis of AD, by the imbalance of regular homeostasis with up and down regulation of certain cytokines. However it is not known how inflammatory cytokines may be related to white matter integrity in AD spectrum (amnestic

mild cognitive impairment –aMCI- due to AD and mild AD dementia). To evaluate the relation of serum IL-6, MCP-1 and IL-18 and cerebrospinal fluid (CSF) MCP-1 with white matter (WM) integrity in mild AD, aMCI due to AD and normal elderly. **Materials and Methods:** All subjects underwent (n=137): blood analyses to quantify cytokines levels and Magnetic Resonance Imaging in a 3T scanner. To analyze WM integrity, we used an automated segmentation method – MultiAtlas, which evaluates Diffusion Tensor Imaging (DTI) data. Partial correlations was used to explore the relationship between inflammatory mediators' levels and fractional anisotropy (FA) measures of WM from regions of interest using the SPSS software controlling the data for age and schooling. The WM regions were chosen considering previous literature in AD [1]. **Results:** There were no significant correlations in control and aMCI groups. In AD group, there were moderate to strong correlations between left Posterior Corona Radiata and IL-6 (r=-0.405/ p= 0.033); left Superior Corona Radiata and serum MCP-1 (r=0.508/ p=0.031); left Cingulum and CSF MCP-1 (r=0.667/ p=0.002); right Cingulum and CSF MCP-1 (r=0.498/p=0.036); right Posterior Corona Radiata and IL-6 (r=-0.509/ p=0.006); right Fornix and IL-6 (r=0.378/ p=0,047); right CorpusCallosum Genu and IL-6 (r=0.379/p=0.047). **Discussion:** We found both positive and negative significant correlations between inflammatory cytokines and WM integrity. Unexpected positive correlations (simultaneous increase of pro-inflammatory cytokine levels and WM integrity) might signify that, in some concentrations, even pro-inflammatory cytokines might have protective effects in AD. **Conclusion:** These findings highlight the importance of systemic inflammation in AD pathophysiological process.

Support: Grant 2017/04637-4, São Paulo Research Foundation (FAPESP).

References: [1] doi:10.1016/j.neurobiolaging.2014.05.027.

CLASSIFICATION OF ALZHEIMER'S PATIENTS AND COGNITIVE DEFICIT THROUGH MRI

M. Pereira[1], W. G. Herrera[1], R. Lotufo[1], L. Rittner[1]

[1]Medical Image Computing Laboratory (MICLab), School of Electrical and Computer Engineering (FEEC), UNICAMP.

Introduction: Alzheimer's disease (AD) is a type of dementia that affects millions of people around the world. By 2050, more than 14 million people will suffer of AD [1]. To date, there is no cure for AD and its early-diagnosis is a challenging task. Magnetic Resonance Imaging (MRI) has aided in the diagnosis *in-vivo* of various diseases, especially neurodegenerative ones, since it can provide details of tissue and its microstructures therein. The current techniques to predict the diagnosis of AD have explored the microstructural information contained in MRI. Among these techniques, convolutional neural network (CNN) is the most promising and has been used successfully applied to medical imaging problems due to its ability to extract characteristics and transfer knowledge. **Materials and Methods:** We use the ResNet[4], a well known CNN architecture, to classify the three main stages of AD: controls (NC), mild-cognitive impairment (MCI) and pathologically proven AD stage (AD). We aimed to generalize our model using two datasets. The first dataset was composed by 240 T1-weighted images from the ADNI[2] and the second dataset by 30 T1-weighted images from CADDementia[3]. While the ADNI images were balanced (80 for each class), the CADDementia images were distributed in 12 NC, 9 MCI and 9 AD. For both of two datasets, 50 slices containing the most relevant pixel-wise information were chosen among the coronal plane and cropped at the same size. The ResNet34 model was adapted, by replacing the last layer by a convolution layer, max-pooling, a dense layer, dropout, and lastly another dense layer followed by a softmax. The datasets were divided into train, validation and test sets. The train set was normalized between 0 and 1 and this normalization was applied to validation and test sets. Data-augmentation technique was applied in order to insert more value data by either random 80x80 cropping or mirroring the images. The model was trained using transfer-learning and fine-tuning. To evaluate our results and not insert a bias into our model, k-fold cross-validation was used. **Results:** The CCN was trained along 100 epochs using cross-validation for 7 folds (Fig.1). From the proposed model an accuracy of 64% was achieved in the test set for the multi-class task (Tab.1). **Discussion:** Overfitting was registered because of the reduced dataset. The network learned well the training set reducing its error, but the same does not occur in the validation set (Fig.1). **Conclusion:** Classifying the different stages of AD is not a trivial task. Our results represent a promising approach in classification of AD phases.

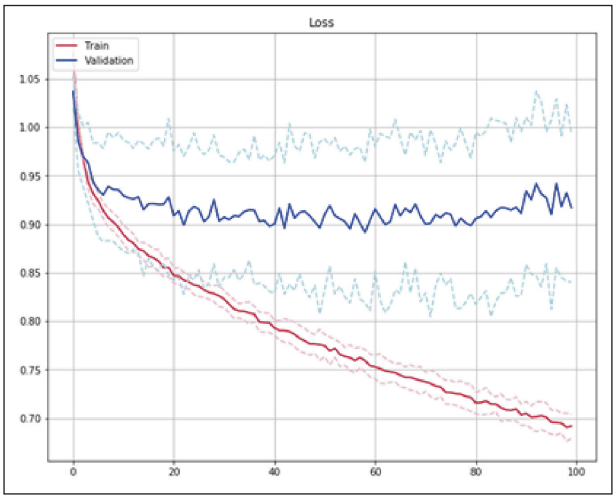


Figure 1. Loss for training and validation sets along 100 epochs. The graph depicts the mean and standard deviation along 7 folds.

References: [1] doi: 10.1152/physrev.2001.81.2.741 [2] doi: 10.1002/jmri.21049 [3] doi: 10.1016/j.neuroimage.2015.01.048 [4] doi: 10.1109/CVPR.2016.90 [5] Sørensen, L. et al., *MICCAI 2014 Workshop Proc.: 111-118*, 2014. [6] doi: 10.1109/ISBI.2017.7950647.

Table 1. Accuracy results for different tasks when compared with the literature results.

Classification task	Validation accuracy	Test accuracy	Literature results
NC vs MCI	0,69	0,7	0,58[5]
AD vs MCI	0,82	0,625	0,61[5]
AD vs NC	0,82	0,8	0,8[5]
Multi-class	0,71	0,64	0,63[6]

COMPARISON OF VOLUME OF ACTIVATION FINDINGS FOLLOWING TRAUMATIC SPINAL CORD INJURY WITH FUNCTIONAL MRI

M. C. Melo[1], D. R. Macedo[1], E. B. Carvalho[1], E. C. Muniz[1], A. B. Soares[1]

[1]Biomedical Engineering Laboratory, Electrical Engineering Department, UFU.

Introduction: According to the World Health Organization, every year, between 250,000 and 500,000 people suffer traumatic Spinal Cord Injury (tSCI) worldwide, with high economic, societal and psychologic impact [1]. Currently, the treatment of tSCI remains palliative, and several studies are focused on the development of technologies, such as Brain-Computer Interfaces (BCIs) to improve quality of life [2]. Nevertheless, BCIs present low performance for tSCIs patients, that may be affected by the cortical reorganization [3]. Studies have shown different findings related to the volume of activation in motor tasks in tSCI patients. This study aims to compare these findings, to verify their methodologies for a better understanding of brain reorganization. **Materials and Methods:** In this paper, it was included relevant studies related to brain reorganization in tSCI patients using functional Magnetic Resonance Imaging (fMRI). It was analyzed the methodology of 7 articles, in which 4 reported decreased cortical volume activation (VOA) [4-7], and 3 found increased VOA in patients with injury, in comparison to controls[8-10]. **Results:** One study from the group of reduced VOA in tSCI patients, in comparison to controls, compared motor attempt (MA) of tSCI patients with motor execution (ME) of controls, showing reduced VOA in patients [4-6] in lower limbs. Other authors compared motor imagery (MI) of lower limbs between controls and tSCIs patients, also showing reduced VOA in patients [4,7]. In the group of increased VOA in tSCI patients, one author found that during the execution of wrist flexion and extension, there was higher VOA in tSCI patients than in controls. When there is recovery from the patient, its pattern of cortical sensorimotor was similar to controls [8]. Sabre et al. (2016) also reported similarity between activation maps of chronic tSCI patients and the control group. When the authors separated the patients with complete paraplegia from the ones who were walking themselves, the activation during hand movement

was more significant among patients that did not recover, the opposite from the reported in [8]. According to [10], when SCI patients attempted to move their foot, significant regions had greater activation. Comparing the articles, they have different levels of lesion: (tetraplegic only) [5], mixed types of lesioned patients (thoracic, lumbar and cervical) [4,9-10], tetraplegics, amputees and paraplegics [6]. Some of these studies are not gender-related [4-5,8,10] and are not age-related [4]. They also have various time after lesion, except for [5,8], that made a longitudinal study. **Discussion**: There is not a methodology that evaluates the time after the injury, and if this affects the reorganization directly or indirectly; also, the effect of laterality and gender in the VOA was not evaluated. Studies show that reorganization depends on the type of injury, age, and time after injury, and current studies present heterogeneous groups, making unfeasible to find a pattern and definitive comprehension of the lesion. Besides, the authors compared ME with MA, even though the cortical command for the two techniques is different, which could influence the results. **Conclusion**: A methodology with homogeneous groups is required to have convergent patterns of reorganization. Understanding the reorganization allows decoding techniques of neural activity to be adaptive and BCIs may improve performance.

References: [1] World Health Organization, [Online]. Available at: http://www.who.int/mediacentre/factsheets/fs384/en/. [Accessed 01 09 2017]. [2] Nardone R et al., Brain Research, 1504: 58-73, 2013. [3] Moghim S et al., Assistive Technology, 25: 99-110, 2013. [4] Chen X et al., Frontiers in Human Neuroscience 10(46): 2016; [5] Jurkiewicz MT et al., Neurorehabil. Neural Repair 24: 136-140, 2010; [6] Turner JA et al. IEEE Transactions on Neural Systems and Rehabilitation Engineering 9(2): 154-160, 2001; [7] Cramer SC et al., Brain 128(12): 2941-2950, 2005. [8] Jurkiewicz MT et al., Neurorehabil Neural Repair, 21(6): 527-538, 2007; [9] Sabre L et al., Spinal Cord 54: 65-68, 2016. [10] Hotz-Boendermaker S et al., NeuroImage 39(1): 383-394, 2008.

HIPPOCAMPAL-PREFRONTAL COORDINATION DURING SLEEP IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

L. R. Zacharias[1], L.B. Peres[1], C. Lopes-Aguiar[2], J. P. Leite[1]

[1]Laboratório de Investigação em Epilepsia, FMRP, USP, [2]Núcleo de Neurociências, UFMG.

Introduction and Hypothesis: Hippocampo-cortical oscillatory coupling occurs through the coordination of sharp-wave ripples (SPW-Rs, 100-250 Hz) in CA1, and cortical delta waves (2-5 Hz) followed by spindles (9-16 Hz) in prefrontal cortex (PFC). Recent studies showed artificially-induced delta-spindle oscillations in the PFC with electrical stimulation upon online SPW-Rs detection was sufficient to improve memory consolidation [1]. In animal models of Temporal Lobe Epilepsy (TLE), such as electrical kindling, SPW-Rs are gradually substituted by Interictal epileptiform discharges (IEDs), which also presents coupling between slow cortical oscillations in PFC [2]. This oscillatory coupling, however, correlates with memory impairment. Interestingly, IEDs evoke physiological responses similar to the ones involved in memory consolidation (for instance, Delta-Spindles in PFC). The underlying mechanisms of the cognitive impact of this pathological coupling triggered by IEDs is still poorly understood. Our hypothesis is that IEDs not only presents oscillatory coupling between CA1 and PFC, but also induce changes in synaptic plasticity in these areas. **Objective:** We aimed to examine potential oscillatory and synaptic plasticity changes in PFC, CA1 and basolateral amygdala (BLA) circuits. First, we tested whether hippocampal-prefrontal oscillations are modified in urethane anesthetized animals by kindling-like electrical stimulation in BLA. Then, we performed fast-kindling (FK) [3] protocols applied in freely moving animals to access correlation between substitution of SPW-Rs by IEDs, slow oscillations in PFC, plasticity changes in BLA-PFC and BLA-CA1 pathways, sleep architecture and finally, memory impairment. **Materials and Methods:** Wistar rats (300 g, n = 6) where anesthetized with Urethane (1.25 g/kg) and single tungsten electrodes were implanted in PFC and CA1 for Local Field Potential (LFP, 4 kHz sample frequency, 1-1kHz analog filter) recordings, and bipolar electrodes in BLA for Kindling-like electrical stimulation (monophasic square pulses, 6 trains of 10 s length, 20 min inter-train interval, 50 pps, 1 ms pulse length) and to evoke Field Post-Synaptic Potentials (fPSPs, monophasic square pulses, 0.5 Hz frequency and 0.2 ms pulse length) in CA1 and PFC. In freely moving animals, single tungsten wires were implanted in PFC and CA1 for LFP recordings and bipolar electrodes in BLA for electrical stimulation. Sleep recordings were performed before, during and after a 3 days FK protocol (biphasic square pulses, 10 trains of 10 s duration per day, 20 min inter-train interval, 50 pps, 1 ms pulse length). **Relevance:** The present work provides information about plastic changes in an FK model. Amplitude of fPSPs were reduced during kindling-like stimulations in anesthetized animals ($F(2,2198) = 29,79$, $p < 0,000$ for CA1 and $F(2,2198) = 28,48$, $p < 0,000$ for mPFC), reducing synaptic efficacy both in BLA-PFC and BLA-CA1 pathways, which could relate to memory impairment previously described in the literature. To test this hypothesis, we designed a new set of experiments in freely moving animals. Our preliminary data showed that FK protocol can reproduce electrophysiological effects of classical kindling protocols, inducing SPW-Rs substitution for IEDs. Ongoing experiments will bring information about memory impairment using spatial object recognition task and sleep architecture changes in control vs. kindled animals.

References: [1] doi:10.1038/nn.4304 [2] doi:10.1038/nm.4084 [3] doi: 10.3389/fncel.2014.00200.

TRANSCRIPTOME PROFILE OF THE DG AND CA3 IN THE PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY

Matos AHB[1], Vieira AS[1], Godoi, AB[1], Canto AM[1], Rocha SC[1], Carvalho B[1], Pascoal VDB[1,2], Lopes-Cendes I[1]

[1]Department of Medical Genetics, School of Medical Sciences, University of Campinas - UNICAMP, SP, BRAZIL and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN). [2]Department of Basics Sciences, Fluminense Federal University - UFF, Nova Friburgo, RJ, BRAZIL.

Background: It is well known that gene expression profile of specific tissue provides relevant biological information about molecular mechanisms potentially involved in complex biological phenomena. Recently, it has been recognized that due to marked heterogeneity of gene expression in different subset of cells, it is important to take sub-regional specificities when studying gene expression, especially in the CNS. The aim of this study was to analyze gene expression profile using next generation sequencing technology in different sub-regions of the dentate gyrus (DG) and *Cornu Ammonis* 3 (CA3) in an animal model of temporal lobe epilepsy induced by pilocarpine. **Methods:** Male Wistar rats were injected with methyl-scopolamine (1 mg/kg) thirty minutes before of the systemic injection of pilocarpine hydrochloride (320 mg/kg) to reduce peripheral cholinergic side effects. Four hours after the administration of pilocarpine diazepam was administrated (4 mg/kg) in order to stop seizures. Control rats were injected with saline after methyl-scopolamine injection. Fifteen days after induction, rats were euthanized (n=4) and brains were processed for laser microdissection. Dorsal and ventral DG such as dorsal, intermediate and ventral CA3 were collected from each rat. RNA sequencing was performed in an Illumina Hiseq® platform. Sequences were aligned and quantified with the TopHat/DESeq2 pipeline for total RNA. Gene ontologies and gene interactions were analyzed with the MetaCore® software. **Results:** We found a total of 969, 308, 2624, 1731 and 1278 genes differentially expressed ($p<0.05$) when comparing control and pilocarpine rats for the dDG, vDG, dCA3, iCA3 and vCA3 respectively. Gene ontology analysis indicates a significant increase in expression of genes present in immune system cells, indicated by the enriched gene ontologies, such as *Classical complement pathway*, *Phagocytosis processes* and *Phagosome in antigen presentation* in pilocarpine rats. Genes involved with synaptic transmission were downregulated in both dDG and vDG. In addition, in the dDG there was a significant downregulation of gene in the calcium transport network, as well changes in expression of various genes involved in neuropeptides signaling, potassium and sodium transport. In dCA3 we observed upregulation of genes related to cytoskeleton remodeling and cell cycle. In iCA3 we identified upregulation of genes involved in oligodendrocyte differentiation in adult stem cells. In vCA3 there was downregulation of glutamatergic neurophysiological process, and upregulation of genes related to regulation of G1/S transition. **Conclusion:** The present data indicates region specific molecular mechanisms taking place in the hippocampus sub-regions of an animal model of temporal lobe epilepsy induced by pilocarpine. The transcriptome data suggest an interaction among several molecular components leading to epileptogenesis in this animal model that displays widespread hippocampal damage.

Support: FAPESP.

CHANGING MINDS AND BRAINS FOR COGNITIVE DEVELOPMENT: PRELIMINARY RESULTS

F. Bressan[1]

[1]FCA – UNICAMP / BREMAT Institute for Strategic Thinking and Leadership.

Introduction: Mental models may be understood as the usual way of neuro-

cognitive functioning of a person. There are two mental models – operational (OMM) & strategic (SMM). SMM is required for strategic thinking, but OMM is the most frequent mental model. For succeeding in Executive positions, one needs the competence for the strategic thinking. In this way, operationally minded people must face the challenge of crossing over from operational to strategic thinking. Human beings are modifiable. Modifiability is different from development. Development proceeds according to natural and biologically programmed sequences; it is linear from one point to another. By another side, modifiability may be understood as a departure from a given pattern of grows and change the course of development. Neuroscientists and Psychologists are increasingly showing that there's actually a lot that can be done for brain and cognition modification. Brain exercises like the right mental workouts can significantly improve our basic cognitive functions. Cognition may be thought essentially as a process of making neural connections in the brain. To a certain extent, our ability to excel in making the neural connections that enhance cognition may be inherited. However, because these connections are made through effort and practice, it may be said that cognition can expand and fluctuate according to mental effort. In this way, we hypothesize that a person by doing some specific exercises could produce modification in his/her cognitive structure. **Materials and Methods:** four OMM persons (Silva, 1992) are involved in this clinical project. The used exercises were selected from exercises proposed by the Art Therapy [1], Drawing with the brain left side [2], Lateral Thinking [3] and Cognitive Modifiability Theory [4] that is a theory that considers brain structures to be modifiable following clinical cognitive intervention and exercises. The project is underway and there were 15 sections with an average duration of 60 minutes. **Results:** In the interviews, they reported an increase in global perception mode, a reduction on anxiety, amplification of creativity, more significant application in the learning process, an improvement on the creativity and the individual autonomy. They also reported a marked increase of "significant intuitions", referring to them as "It comes without my thinking" which indicate an increase in the frequency of occurrence of strategic thinking. **Conclusion**: The present work indicates that the work on the proposed exercises, in controlled clinical trials, showed significantly improve on essential cognitive functions, as reported by interviewed participants. These preliminary results may be seen as an indication that cognitive functioning could be challenged and changed. These results appoint to a new avenue for research on neuron-cognition, which may have some kind of impact in many areas like executive development, learning process, leadership, mental improvement, and in the dynamic neurocognitive rehabilitation. It also may be a way for crossing over the Operational Mental Model to the Strategic Mental Model, and have implications for the decision-making process, leadership and entrepreneurship development, and for the strategic thinking competency.

References: [1] Gruce, L. Art therapy, 2012; [2] Edwards, B. Drawing with the brain left side - workbook, 2012; [3] De Bono, E. Lateral thinking, 1992; [4] Feuerstein et al. Changing minds and brains, 2015).

A COGNITIVE ARCHITECTURE FOR INSTRUMENTAL LEARNING IN SMART AGENTS

Wandemberg Gibaut[1], Ricardo R. Gudwin[1]

[1]Department of Computer Engineering and Industrial Automation (DCA), FEEC, UNICAMP.

Introduction and Hypothesis: The research field of Cognitive Architectures relates to getting inspiration from the different models of the human brain / human mind coming from neuroscience and neuropsychology and building smart artificial agents able to reproduce the cognitive capabilities found in animals. Among these capabilities, Instrumental Learning is a kind of learning where an agent learns from observing the results of its own actions on the environment. **Objective:** The objective of the present work was to propose a Cognitive Architecture, grounded on findings from neuroscience, for the smart control of an artificial creature in a computer game with a high degree of freedom on its actions. The chosen platform, Minecraft, available through the Mälmo Platform [3], is a 3D environment where, due to a huge state space, conventional control techniques are usually not suitable. In particular, we sought to analyze how models of Episodic Memory [2] may help in a cognitive agent's learning and decision making processes. To implement that, we used unsupervised learning techniques (Reinforcement Learning [1], for example) and Neural Networks. **Methods:** We took as methodology the exploration of the space state and checking the agent's learning. We used five types of controllers: Simple Look-up table Reinforcement Learning with ε-greedy policy: represents a classical method of decision-making process with guaranteed convergence. Cognitive controller purely based on Expectations: controller model whose decisions are simply based on a reinforcing structure with a neural network as approximator. Cognitive Controller with Episodic Memory: similar to the previous one, but using Memory to improve the decision-making process. Cognitive Controller with Exploration: the same as the previous one, but the agent decides to explore new situations in detriment of what it already knows. Complete Cognitive Controller: similar as previous, but this version can record sequences of actions and make plans. In each execution, the agent chooses to follow the best plan so far in 50% of cases and to explore new possibilities in the remaining ones. To validate the full controller and the Architecture, and measure its performance, we did 10 rounds of 50 consecutive executions and defined some metrics to get an overview of the agent's learning with each controller. They are: the total number of victories per round, the average victory execution time in seconds and the average number of commands per victory. **Relevance:** This artificial mind project wraps together many known techniques in the research areas of Neurotechnology and Artificial Intelligence. This allows the Architecture to be used in a wide range of applications, including those which may benefit from autonomous learning, as drones, self-driving cars and brain-computer interfaces. The proposed Architecture is also in accordance with other works present in the literature, aligning several theories in an unique framework, being potentially competitive with the existing ones.

References: [1] doi: 10.1017/S0269888999003082; [2] doi: 10.1037/h0020071; [3] JOHNSON, M. et al., Proceedings of the Twenty-Fifth IJCAI, 4246–424, 2016.

CINGULUM ABNORMALITIES AS PREDICTOR OF CONVERSION FROM AMCI TO ALZHEIMER'S DEMENTIA: A PRELIMINARY PROSPECTIVE STUDY

Thamires N. C. Magalhães[1]; Luciana R. P. Silva[1]; Camila V. L. Teixeira[1]; Thiago J. R. de Rezende[1]; Fernando Cendes[1]; Marcio L. F. Balthazar[1]

[1]Neuroimaging Laboratory, Department of Neurology, University of Campinas (Unicamp), Brazil.

Introduction: Changes in cingulum white matter (WM) pathways have not been closely investigated in mild stages of Alzheimer's disease (AD) or even in patients with amnestic mild cognitive impairment (aMCI) due to AD. Because cingulum fibers connect structures of the limbic system, we hypothesized that abnormalities in these fibers may be relevant in the progression from aMCI to AD dementia. Diffusion tensor imaging (DTI) is an advanced Magnetic Resonance Imaging (MRI) technique that can evaluate the diffusion of water molecules *in vivo* and is a powerful tool for detecting subtle microstructural alterations in WM. We aimed to evaluate if left and right cingulum tracts could predict the conversion of patients with aMCI to AD [1]. **Materials and Methods:** 38 aMCI subjects with evidence of AD pathophysiology (altered amyloid-β in the cerebrospinal fluid) were followed during 12 months. All subjects underwent MRI in a 3T scanner. Individuals who progressed to a clinical diagnosis of AD dementia were considered converters (n=11); those who remained with a diagnosis of aMCI were considered to be stable (non-converters) (n=26). To analyze WM integrity, we used an automated segmentation method – MultiAtlas, which evaluates DTI data. Logistic regression was performed using the SPSS software, considering conversion as dependent variable and cingulum fractional anisotropy (FA) measures, age and schooling as independent variables. **Results:** We found that the FA measures of the left cingulum could predict the conversion of our patients with aMCI, $\chi 2$ (2, N = 36) = 11.36, $p < .030$, indicating that the model was able to distinguish converters X non-converters. The model as a whole explained between 39% (Nagelkerke R squared) of the variance, and correctly classified 88.9% of cases. **Discussion:** The cingulum bundle carries hippocampal projections to the cingulate gyrus, areas commonly associated to AD pathology. Disconnection of these areas through WM abnormalities (e.g. lesions) may be partly responsible for clinical worsening. Accordingly to our preliminary findings, this pattern of WM alterations involving the limbic pathways might predict conversion from aMCI to AD dementia.

Conclusion: Cingulum FA may be a useful measure to predict conversion form aMCI to AD dementia. More studies with larger sample sizes are needed for safer conclusions.

References: [1]doi: 10.1093/brain/awx355.2018.

COMPARISON OF CORTICAL ATROPHY AMONG PATIENTS WITH RIGHT, LEFT, BILATERAL AND WITHOUT HIPPOCAMPAL ATROPHY TEMPORAL LOBE EPILEPSY THROUGH VOXEL-BASED MORPHOMETRY

Artoni G[1]; Moreira JCV[2]; Alvim MKM[3]; Scárdua, FL[4]; Yasuda. CL[5].
[1]IMECC, UNICAMP; [2]IC, UNICAMP; [3]Neuroimage Laboratory, HC, UNICAMP.

Introduction: Although several studies have explored patterns of grey (GM) and white matter (WM) atrophy in temporal lobe epilepsy (TLE) patients, fewer have compared side and presence of atrophy. In this perspective, this study intends to investigate and compare TLE patients with a right, left, bilateral atrophy and negative (those without apparent hippocampal atrophy) (HA). **Materials and Methods:** We selected 179 patients, divided in left, right, bilateral and negative TLE, respectively with 50, 45, 34 and 50 subjects. Two control subjects were matched for each patient (258 total controls). 3D T1 weighted images (isotropic 1mm^3 voxels) were segmented into GM and WM tissues, according to a standard SPM12/CAT 12 protocol (http://www.neuro.uni-jena.de/cat/) (www.fil.ion.ucl.ac.uk), which included: spatial normalization [MNI-152], tissue segmentation and smoothing, Quality control of image segmentation was automatically performed. Statistical analyses of images were performed with SPM12. All steps are described in detail in [1]. **Results:** Grey matter atrophy was mainly identified ipsilateral to HA in the right and left groups. While bilateral group presented more widespread and bilateral pattern of alterations, NEG group exhibited small inter-hemispheric cluster (Figure1).**Discussion:** The results we found highlight different patterns of GM/WM atrophy of patients with TLE. Our results suggest an association between GM atrophy and the presence of HA, as NEG group presented small spots of GM atrophy. On the contrary, WM atrophy was identified in four groups, regardless the presence of HA. **Conclusion:** Our results suggest that GM atrophy may be associated with the presence of HA, while WM atrophy may result from seizures, as all 4 groups presented widespread areas of WM atrophy.

Reference: [1] Friston K et al., Book Statistical Parametric Mapping.

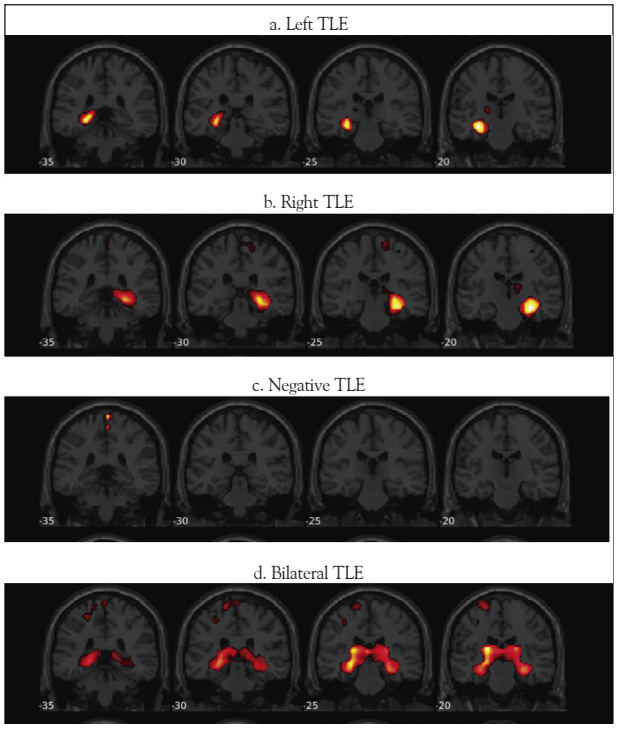


Figure 1. Grey matter atrophy regions.

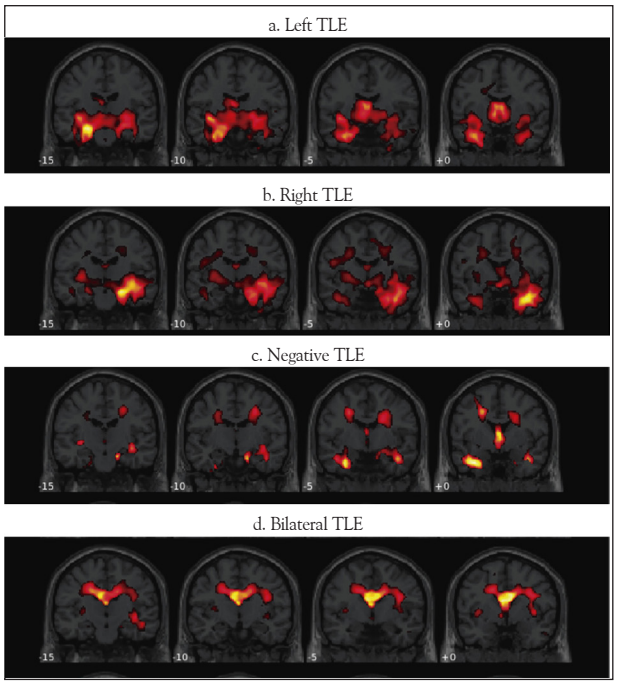


Figure 2. White matter atrophy regions.

DEVELOPMENT OF SMARTPHONE APPLICATION TO SUPPORT ADOLESCENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Queiroz G.[1], Fernandes G.[1], Appenzeller, S.[2], Rittner L.[1]
[1]School of Electrical and Computer Engineering, FEEC, UNICAMP, [2]School of Medicine, FCM, UNICAMP.

Introduction: For patients of chronic illnesses it's crucial to have a routine of medical appointments and to follow the recommended treatment. Children and teenagers with Systemic Lupus Erythematosus tend to have low treatment compliance and persistence rates. On the other hand, the physician does not always include the patient in the decision making process of which treatment to follow, since the priorities of the patient and the ones of the physician can diverge [1]. This work aims the development of a digital platform that supports, educates, and incentives patients, leading to improve the effectiveness of the treatment, as well as to generate inputs to doctors, gathering and analysing access data and search reports, and summarizing the most common concerns of the patients [2]. **Materials and Methods:** The client is being developed

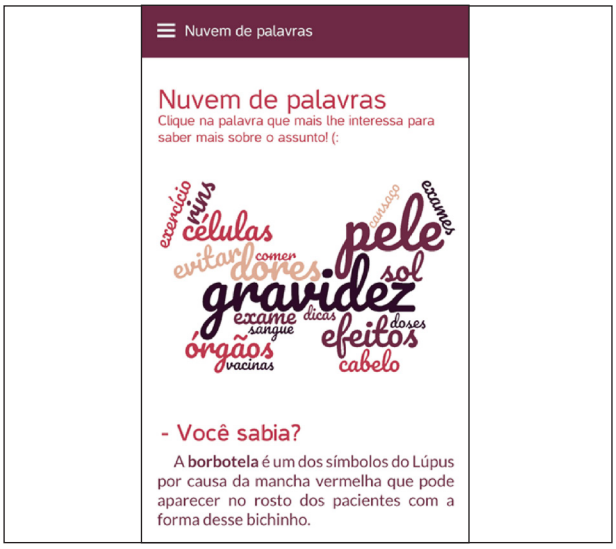


Figure 1. Home screen of the app: Word cloud with common topics of the illness.

in Android, with backend in Java and SQLite database. The user experience consists in selecting topics of interest in a word cloud (to avoid inducing the choice of topic to the user) or navigating through the main topics in a side menu (Figure 1). Each topic accessed, or word combination searched triggers an event that will be stored in the main database for future analysis of the most relevant topics in the patient's point of view. In order to respect the intimacy of the patients, the log of events triggered will not be connected to the users, only segmenting the events by type of user (patient, parent, professional, etc). **Results and Discussion:** The platform content is based on medical references and booklets published by the Brazilian Society of Rheumatology, the Lupus UK Foundation, and others. Since the material is focused in teenagers between the ages of 13 and 18, it was written, illustrated and reviewed specifically for the platform and thought to be easy to read: structured in 6 main topics explained in video and 30 subtopics that consist in short paragraphs.The development of the app is in its final stage. Textual content were organized in 6 main topics: "What is Lupus?"; "What causes Lupus?"; "How Lupus is diagnosed?"; "How Lupus affects the body?"; "What can I do to get better?"; "How it will be my day-to-day?". For each topic, 2 to 3 images were created to illustrate the topic and also to make it more user friendly. Each topic presents subtopics and also some links, which allows the user a high level of navigation freedom.
Conclusion: The developed app will help the doctors to gather information about the interests and worries of the patients. With these data, they will be able to help and improve their compliance and the treatment results. Also, the enhanced knowledge regarding the disease will improve the engagement and compliance to the treatment by the patients, thus lowering the chances of flares.

References: [1] doi:10.1016/j.pcl.2012.03.007; [2] doi: 10.5644/ama2006-124.157; [3] doi: 10.1109/LISAT.2013.6578252.

DYNAMIC CAUSAL MODELING REVEALS ALTERED EFFECTIVE CONNECTIVITY BETWEEN CONTRALATERAL HIPPOCAMPUS AND DEFAULT MODE NETWORK IN TEMPORAL LOBE EPILEPSY

Vallim, M D[1,2]; Ishikawa, A[1]; Moreira, JC V[1]; Zanão, T.[1]; Cendes, F[1]; Pinheiro, A[2]; Yasuda, C[1]

[1]Neuroimaging Laboratory; IMECC[2]- UNICAMP.

Introduction: Functional connectivity (FC) studies in temporal lobe epilepsy (TLE) have revealed several alterations in brain resting state (RS) networks, mainly in the Default Mode Network (DMN). However, FC is unable to establish causal connections [1]. Thus, we investigated effective connectivity between DMN and hippocampi in TLE (with unilateral hippocampal sclerosis), using Dynamic Causal Modeling (DCM), which reveals causal relationships between regions. **Materials and Methods:** We analyzed 3T RS-fMRI from 43 Left TLE (LTLE), 43 Right TLE (RTLE) and 62 controls (balanced for age and gender). To compare causal interactions between BOLD time-series from DMN and hippocampi, we performed DCM analyses with Bayesian approach [2] on MATLAB2014/SPM12 (www.fil.ion.ucl.ac.uk). The chosen model included bilateral intraparietal cortex, hippocampi, middle prefrontal cortex and precuneus [3]. To evaluate the robustness of the selected models, 1000 times k-fold cross-validation were performed, selecting randomly and excluding 5 subjects from the model selection. These analyses allowed us to confirm the robustness and stability of our model by removing subjects. **Results:** Compared to controls, DCM analysis showed *preserved* patterns of *ipsilateral hippocampal* connections for both LTLE and RTLE, with abnormalities on contralateral connections. While LTLE presented increased connections between DMN and right hippocampus (R-hip), RTLE patients displayed reduced connections between left hippocampus (L-hip) and DMN, ($p<0.05$). The k-fold cross-validation confirmed the results: for L-hip and R-hip on controls, the chosen models were selected 1000/1000 and 807/1000 respectively; for LTLE the models were selected 1000/1000 for both hippocampi, and for the RTLE the chosen models were selected 773/1000 (L-hip) and 900/1000 (R-hip). **Discussion/conclusion:** These results suggest that both LTLE and RTLE patients presented abnormal effective interactions between DMN and hippocampus; markedly, contralateral hippocampus displayed the core of dysfunctions. Further investigation is necessary to evaluate the impact of such dysfunction on cognition and other brain regions.

References: [1]Friston, K.J., et al., Neuroimage, 2014. 2.Razi, A., et al./ [2] Neuroimage, 2015. 106: p. 1-14. [3].Ushakov, V., et al.,. Front Hum Neurosci, 2016. 10: p. 528.

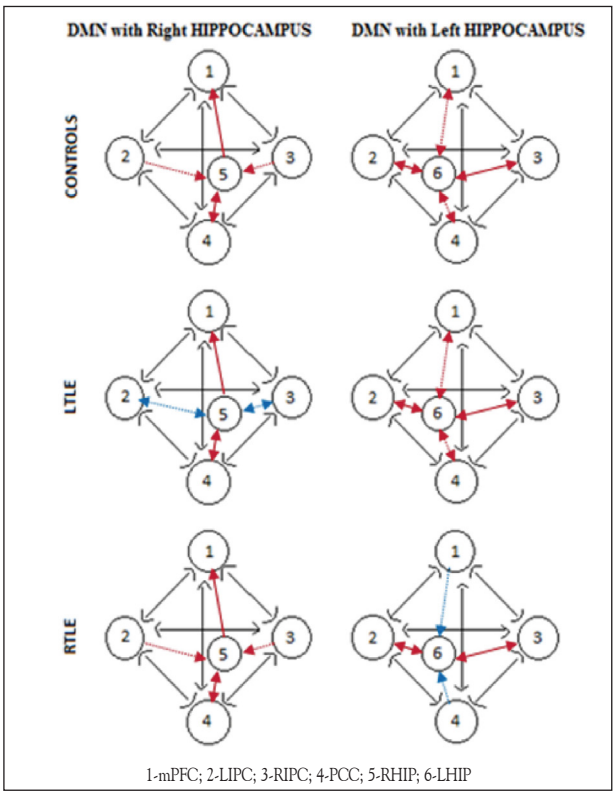


Figure 1.

CEREBELLAR ATROPHY IN NEUROMYELITIS OPTICA SPECTRUM DISEASE (NMOSD) PATIENTS

Souza, R. F. S.[1]; Von Glehn, F[2], Santos, LMB [2] ; Cendes, F[1] ; Yasuda, C L[1]

[1]Neuroimaging Laboratory, [2] Biology Institute UNICAMP.

Introduction: Neuromyelitis Optica Spectrum Disease (NMOSD) is an autoimmune neurodegenerative process which affects the optic nerve and spinal cord in inflammatory outbreaks, leading to its symptons [1]. Newly, recent studies have showed that other structures in central nervous system (CNS), like the brain cortex, thalamus and medulla oblongata are affected too [2,3]. The increased use of different techniques of magnetic resonance imaging (MRI) analysis, such the voxel-based morphometry (VBM), has improved our knowledge about the real CNS damage in NMOSD patients [4,5]. **Materials and Methods:** Thirty-nine

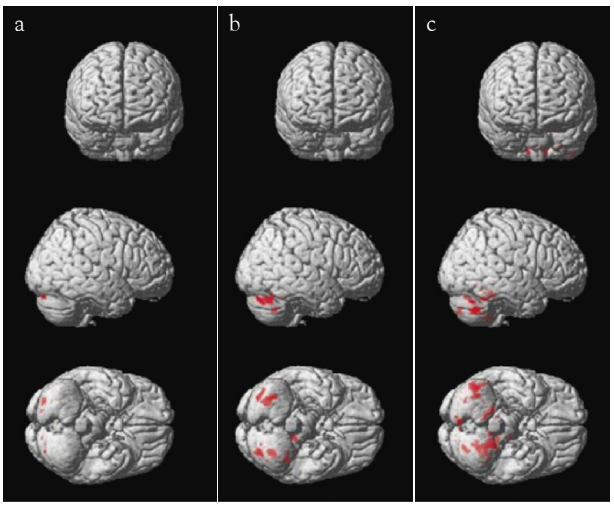


Figure 1. Distribution of cerebellar cortical atrophy in NO (a), LETM (b) and NMO (c) patients. Both cerebellar hemispheres and vermis are affected.

NMOSD AQP4-IgG positive patients from UNICAMP's Neurology Service were selected to participate in this study; fifteen of these patients presented neuromyelitis optica (NMO), nine presented longitudinally extensive transverse myelitis (LETM) and eight are diagnosed with optic neuritis only. For group comparisons, forty-two healthy controls were selected from an MRI bank of healthy volunteers. Images were acquired at Hospital de Clínicas (UNICAMP) using a 3 Tesla Achieva-Intera Philips MRI scanner including 3D-T1 weighted images (isotropic voxels of 1 mm^3, acquired in the sagittal plane; 1 mm thick, flip angle=8°, TR= 7ms, TE 3,2ms, FOV= 240 x 240 x 180 mm^3). All images were segmented according to standard SPM12/CAT12 and SUIT [6] protocols (http://www.neuro.uni-jena.de/cat/) (www.fil.ion.ucl.ac.uk) (http://www.diedrichsenlab.org/imaging/suit.htm), which included: spatial normalization, cerebellum segmentation and smoothing, Quality control of image segmentation was performed. Statistical analysis of images was performed with SPM12, while clinical information was compared with GraphPad Prism 7. **Results:** NMOSD and control were paired by gender and age. The figure below shows significant cerebellar cortical atrophy in NMOSD patients compared to healthy controls ($p<0.05$). **Discussion:** Cerebellar cortical atrophy observed in patients group confirms the recent studies results', in which other areas of CNS than the classic ones are affected by NMOSD. It is possible that these findings occurs due to direct immunomediated lesions or by a secondary degeneration mechanism in areas interconnected in the CNS [1-3]. **Conclusion:** Cerebellar atrophy can be seen in NMOSD patients, especially in the ones who present LETM or NMO spectrum of the disease. Further studies of clinical symptoms in these patients or using other MRI techniques may reveal the complete clinical meaning of these findings.

References: [1] Wingerchuk, D. M. et al. Neurology 85, 177–189 (2015); [2] Glehn, F. Von et al. Mult. Scler. J. (2014).; [3] Whittam, D. et al. J. Neurol. (2017). [4] Duan, Y., Liu, Y., Liang, P. & Jia, X. Acta radiol. 55, 589–593 (2014); [5] Chen, C. et al. Acta Acad. Med. Sin. 36, 432–438 (2014). [6] Diedrichsen, J. Neuroimage 33, 127–138 (2006).

INTERPRETABLE MODELS FOR MEDICAL DATASETS BY MEANS OF BICLUSTERING AND ASSOCIATION RULES

Rosana Veroneze[1], Fernando J. Von Zuben[1]

[1]Laboratory of Bioinformatics and Bioinspired Computing (LBiC/DCA/FEEC/Unicamp).

Introduction: Veroneze & Von Zuben [1] recently proposed an enumerative biclustering algorithm to mine all maximal biclusters in mixed-attribute datasets. A mixed-attribute dataset is composed of numerical (discrete or continuous) and categorical (ordinal or nominal) attributes, being very common in medical data. As usual examples we may mention information on weight, height, age, gender, and location of pain. Notice that strictly numerical or categorical datasets are special cases of mixed-attribute datasets [1]. Alternative biclustering proposals to handle mixed-attributes datasets either do not simultaneously exhibit four key properties (which are all present in our approach), more specifically efficiency, completeness, correctness, and non-redundancy, or, when exhibiting the four key properties, the numerical attributes should pass mandatorily through discretization before the mining process, which inevitably promote information loss. Additionally, Veroneze & Von Zuben [1] presented the biclusters in a user-friendly and intuitive form, by automatically converting them to association rules [2], more specifically quantitative class association rules (QCARs). Here, we show how this proposal is valuable to yield a parsimonious set of relevant rules, automatically providing useful and interpretable models for medical datasets. **Materials and Methods:** We used two datasets in our experiments. One of them is the Acute dataset, which contains 6 attributes of 120 patients. It has two decision variables that indicate the presence or absence of a disease of the urinary system, which are *inflammation of urinary bladder* (IUB) and *nephritis of renal pelvis origin* (NRP). The other dataset is the Heart dataset, which contains 13 attributes of 270 patients. The decision variable indicates the presence or absence of *heart disease*. Both datasets are publicly available at UCI Repository [3]. For more details about the datasets and the parameterization of the biclustering algorithm see [1]. The quality of the rules was measured by the metrics completenesses, confidence, lift and leverage [2]. **Results:** Table 1 shows some rules that we obtained for the Acute and Heart datasets. We refrained from presenting more rules due to space restriction. **Discussion:** Rule #1 shows that 83% of the patients with IUB presented urine pushing and micturition pain. Rule #2 shows that 98% of the patients without NRP did not presented fever and nausea. Rule #3 shows that 71% of the patients with NRP presented fever and lumbar pain. Rule #4 shows that 23% of the patients with a heart disease were male, presented asymptomatic chest pain, and one major vessel colored by fluoroscopy. **Conclusion:** The present work confirmed that QCARs directly extracted from biclusters are valuable and automatic means of providing useful and relevant interpretable models for medical datasets.

Table 1. Some examples of rules for the Acute and Heart datasets.

#	Dataset	Rule	Comp	Conf	Lift	Lev
1	Acute (IUB)	urinePushing{yes}, micturitionPain{yes} → IUB{Yes}	0.83	1.00	2.03	0.21
2	Acute (NRP)	temperature[35.50,37.90], nausea{no} → NRP{No}	0.98	1.00	1.71	0.21
3	Acute (NRP)	temperature[39.40,41.50], lumbarPain{yes} → NRP{Yes}	0.71	1.00	2.40	0.20
4	Heart disease	sex{M}, chestPain{asymptom.}, vesselsColor{1} → HeartDisease{Yes}	0.23	0.97	2.17	0.06

References: [1] Veroneze R & Von Zuben FJ, arXiv preprint arXiv:1710.03289, 2017; [2] Zaki MJ & Meira W, Cambridge University Press, 2014; [3] http://archive.ics.uci.edu/ml.

APPLICATION OF MACHINE LEARNING TECHNIQUES TO MRSI DATA FROM MEDIAL TEMPORAL LOBE EPILEPSY PATIENTS

A. J. Peterlevitz[1,2], L. R. Pimentel-Silva[2,3], F. Cendes[2,3], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), [3]Neurology Dept., FCM, UNICAMP.

Introduction and Hypothesis: Machine Learning (ML) is widely used in data analysis in various fields of science. It is used to make predictions and to build models from acquired data revealing important characteristics of the samples that a simple analysis could not to do. ML is particularly useful when large amounts of data are available, such as is the case, for example, of Magnetic Resonance Spectroscopy Imaging (MRSI) data from human brains. This type of data consists of MR spectra acquired from many different voxels of a grid, placed over a given volume of interest (VOI). Each MR spectrum has information about chemical compounds (metabolites) present in the corresponding voxel [1]. In particular, MRS (and MRSI) has been used to attempt to extract metabolite information from the hippocampi of medial temporal lobe epilepsy (MTLE) patients with hippocampal sclerosis (HS). Many MTLE-HS patients are pharmacoresistant, and candidate for surgery. About two thirds of patients that undergo surgery become seizure-free [2]. It would be interesting if, by applying ML algorithms to MRSI data of the hippocampi of these patients, we could predict surgical outcome. **Objective:** In this project, we want to explore the use of ML algorithms applied to MRSI data from human brains; in particular, we want to apply these algorithms to MRSI data from MTLE-HS patients that underwent surgery, in an attempt to find out if ML is able to extract information to predict success in the surgery. **Methods:** Thirty-four unilateral MTLE patients' MRSI data were acquired from both hippocampi with a 3T Philips Achieva MR scanner, using the Point Resolved Spectroscopy (PRESS) [3] pulse sequence at an echo time TE = 144 ms. The project was approved by the Ethics Committee of UNICAMP, and all subjects signed an informed consent form before data acquisition. Initially, we intend to explore these data with unsupervised ML methods: K-Means Clustering [4] to separate the data into two principal groups, or clusters; Principal Component Analysis (PCA) [5] to find a two-dimensional space formed by two axes, or principal components, where the data can be expressed as linearly uncorrelated variables; and Independent Component Analysis (ICA) [6] to find a linear representation of the data with statistically independent components. Afterwards, other ML supervised methods such as Random Forests and Support Vector Machines will be applied to the data, to see whether they can be separated into relevant groups (such as "success surgery" and "failure surgery" groups). **Relevance:** As mentioned, many MTLE-HS patients are pharmacoresistant and need surgery. In the surgery, usually the hippocampus, amygdala and parahippocampal gyrus from the side of seizure origin are removed. But the histopathology of the resected tissue has shown that the syndrome is not necessarily uniform. If relevant information from the supposedly affected brain structures could be obtained by means of ML applied to MRSI data before surgery, maybe the surgery could be better targeted.

References: [1] doi: 10.3978/j.issn.2223-4292.2015.01.03; [2] doi: 10.1002/ana.22142; [3] Klose U., European Journal of Radiology 67:194-201, 2008; [4] doi: 10.2307/2346830; [5] arXiv: 1404.1100; [6] Hyvärinen A. et al., Neural Networks 13(4-5):411-430, 2000.

CSF BIOMARKERS AND COGNITION ARE RELATED TO WHITE MATTER INTEGRITY IN AMNESTIC AMCI AND MILD AD

C. L. B. Gerbelli[1], T. N. C. Magalhães[1], M. Abreu[1], L. R. Pimentel-Silva[1], C. V. L. Teixeira[1], T. J. R. Rezende[1], F. Cendes[1], M. L. F. Balthazar[1]

[1]Neuroimaging Laboratory, Department of Neurology, University of Campinas (Unicamp), Brazil.

Introduction: AD pathophysiological process, including amyloid-beta peptide ($A\beta_{1-42}$) and phospho tau protein (p-tau), affect primarily grey matter structures and their relations with white matter (WM) is not completely known. In the same way, the role of WM in cognition in aMCI and mild AD is not fully understood. The objective of this study is to analyze the relationship between WM integrity, CSF biomarkers ($A\beta_{1-42}$, t-tau and p-tau) and neuropsychological evaluation in patients with aMCI and mild AD. **Materials and Methods:** 23 patients with mild AD and 25 with aMCI underwent: lumbar puncture to analyze $A\beta_{1-42}$, p-tau and t-tau levels; Magnetic Resonance Imaging in a 3T scanner; and a broad neuropsychological evaluation (MMSE, memory, executive functions, language and visuospatial skills). To analyze WM integrity, we used an automated segmentation method – MultiAtlas, which evaluates Diffusion Tensor Imaging (DTI) data and extract Fractional anisotropy (FA) values of all brain. We verified if there were significant correlations between FA from 30 regions of interest of WM, i.e. encephalic tracts and WM of some gyri automatically segmented by MultiAtlas, with CSF biomarkers and cognitive scores (COG). **Results:** COG and $A\beta_{1-42}$ showed a positive correlation mainly with left WM structures, while t-Tau and p-Tau correlated mainly with right regions. COG showed a strong correlation with WM regions close to GM structures classically related to clinical AD symptoms, like medial temporal and cingulum in the aMCI group. **Discussion:** The preference of $A\beta_{1-42}$ impact for the left side wasn't fully understood in this study. This result could just represent a feature of the selected subjects. In the same way the preference of p-Tau and t-Tau impact in the right side. The WM damage could mean that the AD disease impacts the gray matter and white matter even in the initial phase of the disease, not just in advanced phases like seen before. **Conclusion:** We found significant relations between WM integrity and CSF biomarkers, what could mean that AD pathophysiology affects not only GM. Also, WM is related to cognition even in the early phase of AD spectrum.

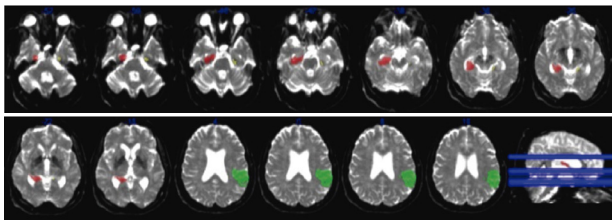


Figure 1. ROI's with significant strong correlation with CSF biomarkers in aMCI patients without HA. In red, ROI's (left hippocampus and left fornix) correleted with Aβ. In green, ROI's (WM of right supramarginal gyrus) correlated with t-Tau. In yellow, ROI's (WM of right parahippocampal gyrus) correlated with p-Tau.

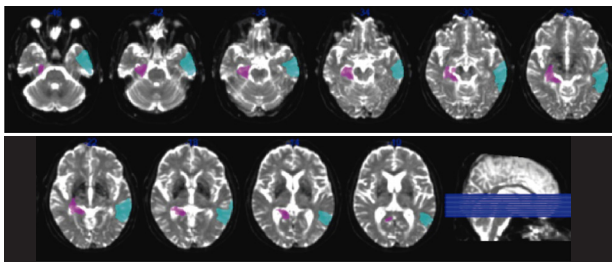


Figure 2. ROI's with significant strong correlation with CSF biomarkers in mild AD. In violet, ROI's (WM of left parahippocampal gyrus, left hippocampus, left cingulum hippocampal, left fornix stria terminalis) correleted with Aβ. In cyan, ROI's (WM of right middle temporal gyrus) correlated with t-Tau.

References: 1) doi: 10.1148/radiol.12120010. 2) Duthey, B. Background paper 6.11 Alzheimer Disease and Other Dementias. Em: A public Health Approach to Innovation, Update on 2004 Background Paper, 6.11-1 - 6.11-74, 2013. 3) http://dx.doi.org/10.1016/j.nicl.2015.06.007.

TISSUE REACTION TO THE RECORDING PROBES IMPLANTED INTO THE BRAIN

E. V. Dias[1], A. S. Vieira[1], R. Panepucci[2], R. Covolan[3], I. T. Lopes-Cendes[4], F. Cendes[5]

[1] Dept of Structural and Functional Biology, IB, UICAMP, [2]CTI Renato Archer, [3]Neurophysics Group, IFGW, UNICAMP, [4]Genetics Dept., FCM, UNICAMP, [5]Neurology Dept, FCM, UNICAMP.

Introduction: Brain probes are important tools for understanding the nervous system. They allow evaluating the electrical activity of single neurons and its relation with the subject behavior. Since the electrodes contained in the neural probes need to be positioned within tens of micrometers of the neurons of interest, the probes are necessarily invasive devices. As it happens with any foreign material that is implanted into the body, the process starts with the unspecific adsorption of proteins and the recruitment of defense cells that attempt to clean up the site and eliminate the threat of the invader. If the threat persists, a chronic inflammatory process ensues, with the attempt to shield the affected area from the surrounding tissue. The common perception is that this shielding, which in the brain consists of a capsule formed predominantly by astrocytes, gradually decreases the quality of the recorded neuronal signals. This study evaluated the tissue response to the neural probes designed and fabricated by the BRAINN research groups, comparing it with the tissue response to other recording devices implanted into the brain. Furthermore, this study also has the objective of producing new probe configurations and materials for the improvement of neural recordings in experimental animal models. **Materials and Methods:** Stereotaxic surgery for implantation of recording neural probes was performed in Fischer 344 male rats (aged 12 weeks) acquired from Cemib, State University of Campinas (Unicamp). Rats received recording neural probes developed previously in Brainn projects, or commercial silicon probes (Neuronexus), or stainless steel micro wires. Recording probes were implanted into the dentate gyrus of the hippocampus (AP -3.0; L ±2.0; V -3.5). After a period of 2 or 28 days, rats were euthanized and the nervous tissue of rats that received the probe implants were analyzed with immunofluorescence labeling for markers for foreign body reaction, such as the astrogliosis markers GFAP and microglia activation marker CD68, and for the neuronal marker NeuN. Laser microdissection of the regions proximal to probe implantation is being carried out and the removed material will be subjected to transcriptome analysis by RNA-seq. All procedures were approved by the Ethics Committee for Animal Research at the Unicamp (protocol 4438-1). **Results:** Two days after surgery, the tissue surrounding the probes is disorganized and immunostaining for CD68 around the probe sites reveals reactive microglia, which is more prominent for silicon probes. Twenty-eight days after surgery, reactive microglia is observed around the probes and an intense immunostaining for GFAP shows reactive astrocytes surrounding it. The astrocyte reaction is less intense for Brainn probes. Neuronal loss, evidenced by NeuN immunostaining, is observed in the tissue surrounding the probes and is more prominent around silicon probes. **Discussion:** Our preliminary data show a qualitative difference of tissue reaction considering both the different probes implanted into the brain and the time after implantation. Brainn probes seem to induce a less intense response in the neural tissue observed at both 2 and 28 days after implantation into the brain. Recent evidence suggests the neurotoxic effect of the signaling cytokines that are released by nervous tissue in contact with implanted probes. Once the tissue reaction is less intense, probably the neurotoxic effect is lower and, consequently, the probe performance is better. **Conclusion:** Preliminary data of the present work demonstrates the biocompatibility of the neural probes, designed and developed by Brainn team, which is crucial for the probe efficiency.

References: [1] Kozai TDY. et al; ACS Chem Neurosc. 6, 48-67, 2015.

SEIZURE PREDICTION USING ELECTROGRAPHIC DESCRIPTORS OF NEURAL SYNCHRONISM AND ARTIFICIAL NEURAL NETWORKS

L. F. F. Souza[1], M. F. S. Barroso[1], E. B. Pereira[1], V. R. Cota[1]

[1]Laboratory of Neuroengineering and Neuroscience (LINNce), Universidade Federal de São João del-Rei (UFSJ).

Introduction: Patients suffering from epilepsy are subject to high levels of anxiety and, therefore, depression and overall lower quality of life. This is due the fact that they usually cannot predict seizures, once anticipatory signs are very rare. By this token, technologies capable of predicting incoming seizures or detecting periods of high probability of seizure occurrence may be of great

value for patients and clinicians. A common approach to this issue is the computational analysis of intracranial electroencephalographic (iEEG) recordings for the extraction of features that can describe underlying neural dynamics and, thus, detect pre-ictal periods. To foster development and innovation in the field, the University of Melbourne together with the American Epilepsy Society and other institutions launched, in 2017, an open competition in which applicants should implement algorithms to predict seizures by blindly analyzing multi-channel (16 electrodes) iEEG recordings collected from epilepsy patients [2]. The challenge was to distinguish between A) ten minute long data clips covering one hour prior to a seizure (pre-ictal state) and; B) ten minute clips of one-hour long interictal activity. This work describes our participation in the contest with a biologically oriented approach: detection of synchronization patterns within neural oscillations present in the iEEG recordings. **Material and Methods:** Inspired by the fact that seizures are episodes of hypersynchronous neural activity, we devised a seizure prediction strategy by applying data classification of phase-amplitude cross-frequency couplings (CFC) between myriad distinct oscillations in different frequency bands. CFC was calculated using Modulation Index (MI) devised elsewhere [1]. The algorithm starts by filtering (finite impulse response filter of order 15) the signals in bands of interest: a low frequency one (2 Hz sized bands spanning 0 to 50 Hz) whose phase will modulate the amplitude of a higher frequency band (10 Hz sized bands spanning 0 to 400 Hz). Thus, Hilbert transform is used to calculate pairs of phase values of the low frequency oscillation versus amplitude values of the high frequency oscillation, with which a distribution is constructed. Finally, the normalized difference between this distribution and a uniform one is calculated using a variation of the Kullback-Leibler distance. All values of MI for the whole spectrum constitutes the comodulogram; a matrix of CFC values. This matrix was supplied to an artificial neural network (ANN) of a single perceptron in a single layer trained with iEEG data supplied by the contest. Results were provided by the contest system. **Results:** During the development period, in which 30% of the test data was provided so competitors could evaluate and adjust their trained algorithms, we submitted 40 trials, achieving a maximum hit ratio of 68.01%. In the final evaluation, assessing the other 70% of the data, our hit ratio was 61.83%. **Discussion:** The hit ratios obtained in our study (61.83% and 68.01%) were above chance (50%) no matter the dataset used, indicating some predictive power. Results are far from ideal and other groups have reported better performance (80.7%). On the other hand, the format of the competition imposed several limitations, such as undisclosed evaluation data, limited number of patients, limitation of the prediction period in the 60 to 10 minutes prior the seizure, and particularly important, undisclosed patient information. This is of central importance when a biologically oriented approach is used. **Conclusion:** Considering the limitation factors and the results above chance, we believe this technique to be a valid alternative to develop seizure prediction devices that may aid epilepsy patients, even though further improvements, such as using subdivisions of the ten minute windows of analysis as different inputs of the ANN and a more sophisticated ANN are in need here.

References: [1] doi: 10.1152/jn.00106.2010; [2] goo.gl/XZSvUP.

IMPACT OF THE ENRICHED ENVIRONMENT ON BEHAVIORAL RESPONSES IN ZEBRAFISH (*DANIO RERIO*)

I.C. Areias[1], V.C. Fais[1], J. A.A. Fernandez[1], C.V. Maurer-Morelli[1]
[1]Zebrafish Laboratory, Department of Medical Genetics, FCM, UNICAMP.

Introduction: *Zebrafish (Danio rerio)* is widely accepted as an alternative animal model for studies of brain functions and neurological diseases, including epilepsies. Recent studies have shown that environmental enrichment modifies behavioral and biochemical responses in many experimental models [1] [2]. In the present study, we sought to determine the impact of environmental enrichment on behavioral and molecular parameters of anxiety and stress during the development of *zebrafish* and its impact on the chemically-evoked seizure. **Materials and Methods:** This study was approved by the Ethics Committee on Animal Use (CEUA) of UNICAMP #4539-1. Zebrafish at 5 days post fertilization (dpf) were separated into two groups: Control Group (CG) and Enrichment Group (EG). Animals from CG were maintained in a bare aquarium (n=12), whereas animals from EG were placed in aquarium enriched with artificial ornaments such as shell, trunk and plants, besides cuttings and colored decorations that were alternated every week (n=15). Both groups were fed and received the same care during all the time. At 60 dpf, both groups were submitted to behavioral tests (novel-tank and light-dark box tests). Following, animals from CG and EG were exposed to pentylenetetrazol (PTZ) at 15mM until present a complete seizure with loss of posture or up to 5 minutes of PTZ-exposure. All procedures were video recorded. **Results:** Our partial data showed a decrease of the exploratory activity in the behavioral tests and an increased anxiety-like behavior in the CG compared to the EG, suggesting lower levels of anxiety in an enriched environment. Interesting, animals from the CG had a higher craniocaudal length (media ± SEM: CG 2.46±0.08 e EG: 2.23±0.05, p=0.0018). In addition, we also found a higher mortality rate in the CG during the larval stage compared to the EG. **Discussion:** Our preliminary results indicated that animals maintained in a tank containing environmental enrichment presented less anxiety-like behavior compared to those in the bare tank. Besides, it was notable that the ornaments had an impact on the zebrafish length. However; quantification of behavioral tests will be necessary to confirm these findings. **Conclusion:** Environmental enrichment can modify the length and the behavioral response in the zebrafish model.

Support: FAPESP 2014/15640-8, CEPID-BRAINN 2013/07559-3 and CNPq-PIBIC.

References: [1] Manuel R et al., Zebrafish 12(2): 152-165, 2015; [2] Varman DR et al., PloS one 10(5): e0127945, 2015.

SLEEP WAKE-CYCLE DISRUPTIONS IN AN ANIMAL MODEL OF TEMPORAL LOBE EPILEPSY

R. M. Maciel[1,5], J. C. D. Oliveira[1,5], L. C. M. Damázio[1,3,5], C. Q. Tilelli[1,4,5], V. R. Cota[1,2,5]
[1]Laboratory of Neuroengineering and Neuroscience, [2]Department of Electrical Engineering, [3] Department of Medicine, [4]Campus Centro-Oeste Dona Lindu [5]Federal University of São João del-Rei, Minas Gerais, Brazil.

Introduction: The main goal of this work was to investigate - using *in vivo* electrophysiology - the sleep-wake cycle (SWC) architecture of Wistar rats submitted to the lithium-pilocarpine animal model of temporal lobe epilepsy [1]. Recurrent and spontaneous seizures generated over time in this model are important clues to evaluate both the establishment of epileptic process and SWC quality [2]. Although electrophysiological tracings are valuable approaches to detect sleep abnormalities and to allow differential diagnosis from epilepsy patients, long-term recordings may be very difficult to understand jeopardizing interpretation. To approach this issue, in this work, we used spectral state space maps developed elsewhere [3]. **Materials and Methods:** Animals in the PILO group (submitted to lithium-pilocarpine protocol) were video monitored and recorded for 9 days consecutively and received diazepam (DZP) injection from days 4 to 6. A second animal group (CTRLPILO) underwent the very same experimental protocol of PILO animals, but receiving vehicle instead of pilocarpine. State space maps were implemented to daily track forebrain dynamics by plotting its spectral content in a two dimensional space in which each axis represents the smoothed principal components of ratios of different frequency bands [3]. The following deriving parameters were assessed: general aspect with cluster relative positions, automatic detection of clusters, stage proportion, area and position of clusters. **Results:** Animals of the PILO group showed a baseline decrease of REM stage proportion during non-DZP days, with some recovery when DZP was applied. REM cluster area was also decreased during non-DZP days with partial recovery during days of DZP application. Finally, REM cluster was displaced towards the wake cluster in non-DZP days, with partial recovery in DZP days. **Discussion:** Our results show that pilocarpine associated with lithium induces disturbances in SWC dynamics of Wistar rats, corroborating previous electrophysiological studies [4]. During the recovery process after the convulsant insult has been applied, consolidation of aberrant hyperexcitable neuronal connections takes place, which results in recurrent and spontaneous seizures [5]. Both epileptic seizures and functional/structural changes themselves may cause disruptions in the normal SWC architecture. Our results also showed REM sleep recovery during DPZ application to levels similar to those of the control group. Notwithstanding neuropharmacology of DZP in Wistar rats remain unclear, it has proven effective in stopping or attenuating epileptic seizures [6]. Moreover, due to its hypnotic effect [7], DZP has also been widely applied to improve sleep quality under pathological conditions. This suggests that functional and structural mechanisms responsible for restoring

normal forebrain dynamics are not completely suppressed in animals early on lithium-pilocarpine administration. Finally, the state space technique allowed us to identify a position shift of the REM stage within the map. This finding shows us that even though the frequency spectrum has not changed visibly, slight changes in spectral signatures may relate to a pathological sleep pattern. **Conclusion:** Our results show that the animal model of temporal lobe epilepsy displayed altered SWC and that pharmacological treatment with DZP may have some ameliorating effect.

References: [1] 10.1016/0014-4886(86)90045-2; [2] 10.1097/00004691-200103000-00003. [3] 10.1523/JNEUROSCI.3524-04.2004; [4] 10.1016/j.yebeh.2009.11.015; [5] 10.1016/j.pneurobio.2004.03.009; [6] 10.1016/S0014-2999(99)00209-5; [7] 10.1016/0006-8993(84)90229-4.

EVALUATION OF ICTAL ACTIVITY ACROSS THE SLEEP-WAKE CYCLE OF WISTAR RATS UNDER PENTYLENETETRAZOLE-INDUCED ACUTE SEIZURES

R. M. Maciel[1,5], J. C. Oliveira[1,5], L. A. Réboli[1,5], S. M. A. F. Rodrigues[1,5], L. C. M. Damázio[1,3,5], C. Q. Tilelli[1, 4, 5], V. R. Cota[1,2,5]

[1]Laboratory of Neuroengineering and Neuroscience, [2]Department of Electrical Engineering, [3] Department of Medicine, [4]Campus Centro-Oeste Dona Lindu [5]Federal University of São João del-Rei, Minas Gerais, Brazil.

Introduction: mapping electrical activity of the epileptic brain is of major importance in designing effective treatment through electrical stimulation [1]. Taking advantage of the many anatomical and physiological correlations between sleep and epilepsy [2], in this work, we used spectral state maps built out of long-term local field potential (LFP) recordings that allow for the study of the sleep-wake cycle (SWC) and its disturbances [3]. We hypothesized that acute seizures induced by pentylenetetrazole (PTZ) may induce changes in the SWC and generate states of their own. **Materials and Methods:** Animals (Wistar rats, n=11) underwent surgical implantation of electrodes for eletrophysiological recordings in: hippocampus, amygdala, thalamus, and bilateral cortical surfaces. Animals were recorded during 5 days, receiving a subthreshold PTZ dose at the 2nd day (D2) and a proconvulsant dose in the fourth day (D4). Naïve control state maps were obtained from electrophysiological data recorded from 1st day (D1). State space maps were implemented to track daily forebrain dynamics by plotting its spectral content in a two dimensional space representing their frequency bands [3]. Points in the map with high coherence were automatically clustered within a single state such as SWC normal stages (wake - WK, slow-wave sleep – SWS, and rapid eye movement – REM sleep). In order to avoid biased interpretations the original computational routine was adjusted to automatically detect the emergence of a new cluster. **Results:** Data computed from D1 showed clusters with standard parameters. Animals had only mild overt modifications in LFP tracings during D2, although they spent less time in WK stage when compared with control recordings (D1). During D4, 9 out of 11 animals developed generalized tonic-clonic seizures (GTCS). Novel clusters of epileptiform activity were automatically detected in the northwestern portion of the state map in all animals with GTCS. SWC architecture was strongly modified during D4, with ubiquitous decreased proportion of normal WK when compared to D1. **Discussion:** Slight changes on state maps were found under subthreshold PTZ injection, while high dosage of this convulsant drug provoked intense disruption of SWC. This is strong evidence that seizures impair healthy sleep, even when mild. SWC architecture of D3 and D5 (with no PTZ injection) did not display any substantial modification suggesting, on the other hand, that a few acute injections may not be able to induce permanent structural and functional changes in the brain that results in seizure susceptibility and sleep dysfunction as repeated PTZ injections may do [5]. Ictal clusters were automatically detected showing that seizures are a distinct and stable state of neural dynamics. Of particular interest, ictal clusters, in general, took place between REM sleep and SWS; a region with high occurrence of cortical spindles deeply related to memory processing [4]. By this token, we hypothesize seizures may increase spindle-like activity that induces aberrant neural plasticity or dysfunctional memory. **Conclusion:** Our results show that SWC architecture was strongly affected by PTZ injection, worsening with increments of PTZ dosage. In general, these findings suggests that studying epilepsy together with sleep, and memory, may provide novel insights on the pathophysiology of the disease that may grant efficient therapy, such as with electrical stimulation.

References: [1] doi: 10.1038/496159a; [2] doi: 10.1111/j.1528-1157.1998.tb01352.x; [3] doi: 10.1523/JNEUROSCI.3524-04.2004; [4] doi: 10.1371/journal.pcbi.1004241; [5] doi: 10.1016/j.pneurobio.2004.03.009.

SENSORY GATING EVALUATED THROUGH NEURAL ACTIVITY: ELECTROENCEPHALOGRAM PREPULSE INHIBITION TEST

San Martin, R.[1], Zimiani, M.I. [1], Noya, C.V. [2], Avila, M.A. [3], Shurama, R. [3], Del-Ben, C.M. [3], Menezes, P.R. [4], Fraga, F.J.[2], Salum, C. [1]

[1]CMCC, UFABC, [2]CECS, UFABC, [3]FMRP-USP, USP, [4]FM-USP, USP.

Introduction: The central nervous system has a sensory gating mechanism, which acts to prevent brain from information overflow [1]. This mechanism prevents upper cortical systems overload by blocking excessive sensory activation. Prepulse Inhibition (PPI) test evaluates this phenomenon assessing reduction of the reflex response to high-intensity stimuli, named Pulses (P), when these are preceded in a few milliseconds by Prepulses (PP) which are reduced intensity stimuli [2]. Although sensory gating mechanism is a neural phenomenon, it is evaluated by electromyography (EMG) through the inhibition of orbicular muscle activity [3]. Neural PPI evaluation is rarely performed because electroencephalogram (EEG) signal is inherently contaminated by artifacts as an outcome of PPI stimulation eye blinks. Herein we propose a method to reduce artifacts and enable neural PPI evaluation. In this study, we investigated the sensory gating through the PPI test in healthy subjects (HS), through the reduction of eye blink response in parallel to that of neural activity. **Materials and Methods:** Participants were 21 HS. EEG data was recorded using a 15-channel dry-electrode device (BrainProducts - Germany) following the 10-20 International System. The PPI test was done through auditory stimulation with intervals between P (115 dB) and PP (65 dB) of 30 ms (PPI30), 60 ms (PPI60) and 120 ms (PPI120). 160 trials were presented in pseudo-random order (20x P, 20x for each P-PP interval). PPI was calculated for EMG signal and also for N1-P2 Event Related Potential component for the Central Electrodes (Fz, Cz, Pz). All procedures were approved by CEP-UFABC. Removal of EEG artifacts was performed using Infomax Independent Component Analysis (ICA) decomposition [4]. Component selection was performed by visual inspection thought identification of EEG contaminants as ocular artifacts, tonic muscle artifacts, loose electrode connections, and exceptional high amplitude events and then compared to the semi-automated SASICA [5] algorithm. For SASICA, parameters were autocorrelation with threshold (r) auto and lag 20; focal components with threshold (z) 3.5; focal trial activity with threshold (z) 10; signal to noise ratio 0 to Inf, BL -Inf to 0 and threshold ratio 1; combination with EOG Inferior, Horizontal and Superior threshold (r) 0.2; ADJUST and FASTER enabled blink channels. Repeated measures ANOVA was used to evaluate EMG PPI. Normality did not hold for ERP components, then nonparametric Friedman test was applied with 5% Bonferroni corrected alpha level. **Results:** In the EMG PPI, PPI120 was reduced when compared to PPI60. The EEG signal with semi-automatically removed artifacts was validated showing no significant differences in the N1-P2 latency when compared to the visually inspected ICA artifact removal method. HS exhibited neural PPI in Fz, Cz and Pz electrodes. For Fz, PPI30 and PPI120 were reduced when compared to PPI60, for Cz, PPI120 reduced when compared to PPI60. **Discussion:** The present work confirmed that sensory gating can be evaluated through EMG and EEG. Neural PPI observed is of particular importance because artifact removal methods allowed reliable neural signal observation when compared to previous EEG studies [6]. Neural gating attenuation was observed in different stages of sensory processing, as EMG and N1-P2 PPI latency occurs around 50 and 100-200 ms, respectively. **Conclusion**: PPI paradigm proposed in this work is not novel, but rather the revamp of an existent test already consolidated in the literature. In the proposed method, additional stages of neural auditory processing with the same stimulation previously applied were be evaluated.

References: [1] 10.1016/j.biopsych.2006.08.015; [2] 10.1111/j.1469-8986.1975.tb01284.x; [3] 10.1016/j.schres.2013.12.004; [4] 10.1016/j.jneumeth.2003.10.009; [5] 10.1016/j.jneumeth.2015.02.025; [6] 10.1016/j.brainres.2007.06.026.

FIBER TRACTOGRAPHY AS PARTICLE TRACING FOR NEUROSURGERY PLANNING

[1]R.Voltoline, [2]E. Ghizoni, [1]S.T. Wu

[1]School of Electrical and Computer Engineering, [2]School of Medical Sciences University of Campinas.

Introduction: Neural tracts connect different brain cortical and subcortical regions, as well as the brain to the rest of the body. They build a large and complex brain network through which neural signals move between different regions.

When some of these connections are damaged, human behavior or cognitive functions can be drastically affected. For preserving vital brain pathways or disconnecting diseased tissues, fiber tractography is being increasingly used in pre-operative planning [1]. Diffusion-weighted magnetic resonance imaging (DW-MRI) is the most popular sequences for building tractography in-vivo and non-invasively. Using diffusion data of water molecules, the second order of diffusivity tensor is estimated at each voxel and the direction of maximum diffusion is used to reconstruct renderable brain fibers [2]. To avoid handling kissing, crossing and branching fibers, Kondratieva et al proposed in [3] to simply follow the direction of maximum diffusion of GPU-based trilinearly interpolated tensors. The goal of this ongoing work is to assess the adequacy of this interpolation approach for visual analysis of estimated neural directions during neurosurgery planning. **Materials and Methods:** We used DW-MRI sequences (voxel size=1 x 1 x 2 mm^3; 32 gradient directions; b-factor=1,000 s/mm^2; slice dimensions=256x256; number of slices=70). These sequences were acquired in a 3T MRI scanner (Philips Medical Systems, Best, The Netherlands) in the Clinics Hospital. We divide our experiments in two stages. In the first stage we assess the visual quality of the interpolated directions of maximum diffusion at each traced point, while in the second stage we use the direction of maximum diffusion of interpolated tensors. **Preliminary Results:** The GPU-based interpolation of directions of maximum diffusion computed on the CPU is implemented on top of an in-house developed software VMTK [4] for reusing available interaction functionalities. To prevent visual pollution, fibers with length less than 26mm are removed. Rendering of images of the corpus callosum (a) and uncinate fasciculus (b) is illustrated. We also show the rendering of cutting fibers after a resection in (c).

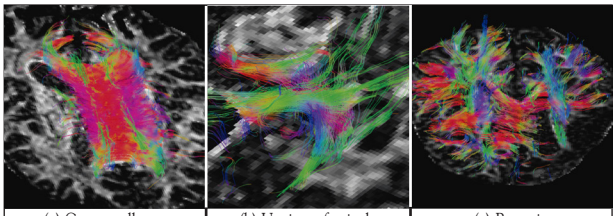


Figure 1.

Discussion: Preliminary results are encouraging. Even sparsely rendered fibers can be perceived as bundles connecting different brain regions. Further investigation of different schemes for tensor interpolation will be conducted. Overlapping with cortical and vascular relationships is planned. **Conclusion:** Despite the limitations of tractography in accurately conveying several details of connections [5], the visualized connectivity can certainly improve safety of neurosurgical planning.

References: [1] doi: 10.1016/j.nicl.2017.06.011. [2] doi: 10.1097/01.wco.0000236618.82086.01. [3] doi:10.1109/VISUAL.2005.1532780. [4] VMTK: Visual Manipulation Toolkit for NeuroImages. http://www.dca.fee.unicamp.br/projects/mtk/wu_loos_voltoline_rubianes/index.html. [5] doi: 10.1089/brain.2011.0033.

TO TELL OR NOT TO TELL? PERCEPTIONS ABOUT STIGMA OF PATIENTS WITH EPILEPSY IN DIFFERENT SITUATIONS

C. Y. Tagami[1], G. S. Spagnol[1,3], I. S. M. A. Assumpção[3], L. M. Li[1,2,3]

[1]Brazilian Research Institute of Neuroscience and Neurotechnology, UNICAMP, [2]School of Medical Sciences, UNICAMP, [3]ASPE, a non-governmental organization to assist the patient with epilepsy.

Introduction: Epilepsy imposes a major psychosocial burden. Challenges faced by the person with epilepsy include fear of revealing the condition, unpredictability of seizures and stigma. Stigma comes from an unmet expectation, a prejudice or a standard defined by society [1]. Self-esteem, self-confidence, responsibility are feelings that are associated with the individual's ability to feel free, loved and take initiatives [2]. This study explores whether patients report epilepsy depending on the context of social situation. **Materials and Methods:** We performed a qualitative and quantitative research at the Hospital of Clinics at University of Campinas, using a questionnaire adapted from Troster [3]. This questionnaire describes eight scenarios for possible disclosure: (a) a random contact with a stranger on a bus, (b) a pleasant evening with an old friend, (c) a social event to meet new members of an association (d) a family gathering to meet future in-laws, (e) a job interview with a superior, and (f) an extended visit of a close relative, (g) social media (h) school [3]. In these scenarios, patients were questioned about the likelihood of disclosing their condition to the specific interaction partner; ranking on a 6-point scale:1 is the lowest and 6 is the highest probability for disclosure. **Results:** Participants included 86 people with epilepsy (47 women), aged between 18 and 70 years; 28% had their first seizure after the age of 20 years old, 62% had no seizures in the last month, 75% used more than one type of medication for epilepsy, 25% were employed and 41% completed High School. There is a significant difference between scenarios (ANOVA, followed by pairwise comparisons Tukey, $p<0.05$), as depicted in figure.

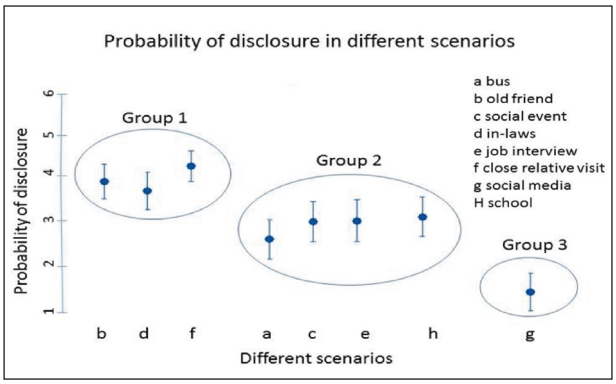


Figure 1. Situations that are not in the same group (1, 2 or 3) are significantly different.

Discussion: According to Troster [3], when patients perceive or feel stigma related to their disease in specific scenarios, they tend to predict disadvantages in disclosing their condition once they find themselves in the same situation. Different situations may corroborate with a different behavior depending of the functional classes established between stimuli and experience [4]. In scenarios within the same group (1, 2 or 3) chances of disclosure are similar, since stimuli related to this scenario also present a similarity (1- family or friends, 2- social interactions, 3- social media). In this sense, variables applied directly on stimuli may have a similar behavior on the same group [4]. Positive or negative experiences have a direct influence in probability of disclosing about the disease in similar situations. Among situations in group 2, patients reported a higher probability of disclosure to ensure that there would be a person to help in the case of having a seizure. **Conclusion:** Situations that bring greater discomfort when talking about epilepsy may also be related to a greater felt and enacted stigma. This study showed that probability of disclosure is higher in situations related to family and friends, when compared to scenarios of social interaction in other environments and in social media.

References: [1] Goffman E. Stigma: Notes on the Management of Spoiled Identity. Prentice-Hall, 1963. [2] Guilhard, H.J. Human behavior, 63-98, 2002. [3] Troster, Epilepsia, 38(11): 1227-1237, 1997. [4] De Rose, J. Psicologia teoria e pesquisa, 9(2): 283- 303, 1993.

COGNITIVE EVALUATION IN THE LEARNING PROCESS IN PARKINSON'S DISEASE.

Yanina Leon Uscapi[1], André Frazão Helene[2],Matheus Silva D'Alencar[3],Maria Elisa Pimentel Piemonte[4]

[1]Neuroscience and behavior, IP USP.[2]Institute of Biosciences -IB-USP, [3]Rehabilitation Sciences USP, [4]Departament of neurology USP.

Introduction and Hypothesis: Parkinson's disease is the second most common neurodegenerative and only the motor symptoms are used for its diagnosis[1]. However, it is known that impairment is not just motor. Pont-Sunyer et al. (2015) suggests that pathological changes in the disease may explain hyposmia, mild dysautonomia and some cognitive impairment in the pre-diagnosis phase[2]. It is generally accepted that the main non-motor symptoms of Parkinson's disease are: depression, anxiety, cognitive difficulty, sleep disorder and autonomic dysfunctions[3]. Within the cognitive alterations are alterations in memory, language, visuospatial capacity and executive functions[4]. However, non-motor signs and symptoms respond very little or nothing to dopaminergic

therapy[3]. Pavon et al.[5] studied the correlations between motor performance and implicit knowledge acquisition, using an analogous protocol. We will evaluate cognitive performance in this learning process in patients with Parkinson's using "The Goalkeeper Game", a game that measures the ability of patients to learn sequences "shots to the bow". The Goalkeeper Game is divided into three stages where the goal is to tackle as many kicks as possible in short periods of time, these kicks are developed following a probabilistic context tree (an extension of the Markov chain models),in which a random variable may be predicted in a given sequence based on the minimum necessary previous actions. We compared the learning capacity of the sequences in patients with Parkinson's, and control people, looking in this way to relate the lost cognitive skills in the different stages of Parkinson's disease. **Objective:** To evaluate the loss of cognitive skills in the process of learning probabilistic sequences. To evaluate the effectiveness of the "Goalkeeper Game" for behavioral assessment in people with Parkinson's disease**. Methods:** This game was adopted for data collection of 74 participants, the study was inserted in a protocol in progress and approved by the research ethics committee. The volunteers were divided into 16 patients with Parkinson's disease on the HY-1 scale; 21 with Parkinson's disease on the HY-2 scale; 14 with Parkinson's disease on the HY-3 scale and 23 control participants. Our approach is based in stochastic processes driven by context tree model, using structured sequences random stimuli in the game. These sequences are generated step by step by a random source. This source is defined by an algorithm which sets the probabilities of occurrence of each next unit. The context tree models generating random sequences of high probability and weak probability. We use the symbols 0, 1 and 2 to represent respectively the direction right, left or middle. $A = \{0, 1, 2\}$. **Relevance:** Experimental studies have shown that the first motor signals occur when 70% or more of the dopamine in the striatum has been lost, and this is the importance of early diagnosis in asymptomatic populations because there is no biological marker for PD yet.

References: [1] doi:10.1016/S0896-6273(03)00568-3;[2] doi:10.1002/mds.26077; [3] doi:10.1007/PL00007755; [4] doi:10.1590/S1516-18462009000600015 [5]doi:10.3389/fnint.2012.00056.

DOES THE SIDE OF ONSET AFFECT MOTOR AND NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE?

J. Silva[1], R. Guimaraes[1], A. Coan[1], A. D'Abreu[1]

[1]Laboratory of Neuroimaging, Brazilian Research Institute of Neuroscience and Neurotechnology, Department of Neurology, University of Campinas (UNICAMP), Brazil.

Introduction: PD motor symptoms are asymmetric at onset, and some level of asymmetry persists throughout the disease. There are few studies exploring the relationship between symptoms and side of onset, and even fewer considering hand dominance. Motivated by discordant results, this study seeks to deepen the knowledge about the influence of side of onset and the hand dominance in the development and aggravation of motor and non-motor symptoms. **Objective:** We aim to assess the association between motor and non-motor symptoms of Parkinson's Disease (PD) and side of onset considering hand dominance. **Methods:** This was a cross sectional study. We included 120 PD patients and classified them into two groups according to side of onset. All patients underwent a standardized questionnaire including information about: sex, PD clinical information and familiar and medical historic. Patients were also assessed by SCOPA-COG, SCOPA-PC, NMSS and UPDRS. A general linear model (GLM) was applied to assess the relation between scales scores and side of onset as the independent controlling for age, sex, time of disease and hand dominance ($p<0,05$). However, since there were only 10 left-handed subjects, we performed a second GLM including only the right-handed volunteers. **Results:** Sixty-nine percent (69,17%) of patients were men. Mean age was $61.7 \pm 10,57$ years and mean time of disease was $9,29 \pm 6.8$ years. Sixty-seven patients (55,8%) presented the first symptom on the right side, and fifty-three (44,16%) on the left. From the total sample of 120 patients, 110 (91,6%) were left-handed and only 10 (8,4%) were right-handed. Among right-handed patients (N=110), 63 (57,3%) had the first symptoms on right side, while only four (40%) of the left-handed had the first symptom on the right side. Between the right-handed (N=110) we observed that sixty-three (57,2%) has the side of onset of the symptoms on the right side and forty-seven (42,8%) on the left side. Among the left-handed (N=10), four (40%) had the side of onset of the symptoms on the right side and six (60%) on the left side. There was a larger proportion of the side of onset ipsilateral to hand dominance both left-handed and right-handed. A GLM was applied to assess the relation between scales scores from SCOPA-Cog, SCOPA-CP, UPDRS, and NMSS and side of onset as the independent controlling for age, sex, time of disease and hand dominance ($p<0,05$) only for the right-handed patients. However, since there only 10 left handed statistical analysis about them was not possible. Analysis shows that there is no relation between side of onset and the progression of symptoms in right-handed patients. The same can not be said about left-handed due to an insufficient sample size. **Discussion:** The side-of-onset did not seem to influence PD symptoms, motor, cognitive and non-motor, in right-handed subjects. This lack of association is unclear in left-handed ones. The main limitation of this study was the low number of left-handed people, preventing an analysis in regard to dominance. This difficulty was found by other researchers [1-2] in which also has been confirmed a trend showing a higher prevalence the side of onset ipsilateral to dominance side, shown by this study. Future studies, should strive to include more left-handed subjects and to perform a longitudinal evaluation considering side of onset and hand dominance to deepen the knowledge about this group as well.

References: [1] doi: 10.1016/j.neuroscience.2010.07.030 [2] doi: 10.1002/mds.24007.

NETWORK DATA INTEGRATION IN AUTISM SPECTRUM DISORDER

L. A. Castro[1], D.C. Martins Júnior[2], A.C Tahina[3]

[1]CMCC, UFABC, [2]CMCC UFABC, [3]IPQ-USP.

Introduction and Hypothesis: Autism Spectrum Disorders (ASD) are a group of complex neurodevelopmental disorders characterized by impairments in reciprocal social interactions, deficits in language and communication, and a stereotyped and repetitive behaviors and interests. ASD are multifactorial diseases, with a high genetic contribution, and concordance in twins studies ranging from 82% -92% in monozigotic twins and an estimated heritability of 90%. High-throughput technologies permitted the generation of vast amounts of DNA sequence data, RNA expression levels, methylation patterns, proteomics and metabolomics, however the investigation of each data type has been considered independently, and the genetics aetiology, and the biological networks involved in of ASD remains unexplained, which could be partly due to the focus on restrictive single-data-type study designs. Network data integration is based on the hypothesis that multiple levels of molecular variation contribute to disease risk in a nonlinear, interactive and complex way (Ritchie, Holzinger, Li, Pendergrass, & Kim, 2015), and network analysis of proteín-proteín interactions are based on network-medicine hypothesis proposed by (Barabasi, Gulbahce, & Loscalzo, 2011) as the network parsimony principle: that causal molecular pathways often coincide with the shortest molecular paths between known disease-associated components. **Objective:** The objective of this project is to improve the network medicine based method NERI method by integrating copy number variants. **Methods: Datasources:** Protein-protein interaction: IntAct, Gene expression: SNCID, Gwas: (Anney et al., 2017), Copy-number variations: SFARI. NERI (Simões, Martins, Pereira, Hashimoto, & Brentani, 2015) method entries are: protein-protein networks, gene expression and GWAS datasets. The network is composed by protein-protein interactions are integrated with gene expression datasets from controls and disease samples. Gene seeds from GWAS studies are used as starting and ending nodes for shorthest path selection (based on parsimony principle). The last step is the PPI network differentiation from disease and control network, and the output are priritized genes. **Relevance:** Network data integration can improve Autism Spectrum Disorders genetic diagnosis, by applying network-medicine hypothesis for gene prioritization.

References: [1] Barabasi, A.-L., Gulbahce, N., & Loscalzo, J. (2011). Network medicine: a network-based approach to human disease. *Nature Reviews. Genetics*, *12*(1), 56–68. https://doi.org/10.1038/nrg2918 [2] Ritchie, M. D., Holzinger, E. R., Li, R., Pendergrass, S. A., & Kim, D. (2015). Methods of integrating data to uncover genotype–phenotype interactions. *Nature Reviews Genetics*, *16*(2), 85–97. https://doi.org/10.1038/nrg3868 [3] Simões, S. N., Martins, D. C., Pereira, C. A., Hashimoto, R. F., & Brentani, H. (2015). NERI: network-medicine based integrative approach for disease gene prioritization by relative importance. *BMC Bioinformatics*, *16*(Suppl 19), S9. https://doi.org/10.1186/1471-2105-16-S19-S9.

VISUALIZATION METHOD AND A COMPARATIVE ANALYSIS FOR ADDRESSING GOOD SPECTRA IN MRSI

J. A. Fontolan[1], L. Rittner[1],

[1]Medical Image Computing Lab, Faculdade de Engenharia Elétrica e de Computação (FEEC), Unicamp, Brasil.

Introduction: Multivoxel spectroscopy (MRSI) is an MRS modality that performs in vivo acquisition of multiple spectra simultaneously, making it possible

to analyze the concentration distribution of a particular metabolite in a given region. [1] The region where the spectra were acquired defines a volume of interest (VOI). The VOI is split in m x n voxels which are associated with a spectrum. One of the greatest difficulties of this method is the interpretation of the acquired data. Furthermore, noisy spectra that do not contain useful information and can still hamper the final analysis are difficult to address. Unfortunately, there is no agreement among experts on what defines a good spectrum, but some parameter have been used to detect what potentially could configure a bad quality spectrum: Signal to Noise Ratio (SNR), linewidth and the Cramér-Rao lower bound (CRLB). [2] In this abstract, we present an analysis method for MRSI that allows selecting a subset of spectra of interest, based on a structure or determined brain tissue. We also will evaluate the threshold set by the literature to detect bad spectra using the parameters given by the Tarquin software. [3] **Materials and Methods:** Code development was performed using real data from 3 control subjects. The data were collected through a Philips Achieva 3T MR scanner, installed in the Hospital das Clinicas at Unicamp. MRSI spectra were acquired in the region of the brain above the corpus callosum. The dimensions of T1-weighted resonance magnetic image were 240 x 240 x 180 and voxel size of 1mm in the three dimensions. The proposed analysis method consists of 5 steps. In the first step, the VOI and the spectra grid are reconstructed in the patient's reference space. In the second step, the coordinates of the VOI and the grid are transformed into the reference space of the structural image. Then, in the third step, the VOI and the spectra grid are overlapped to the structural image. Also, in this third step, the correspondence between the voxels of the image that belong to a determined voxel of the VOI is made. The fourth step is to quantify the MRSI signal with the Tarquin software and overlay the metabolic map in the structural image. Finally, the last step will be to evaluate the filtered spectra with the recommended threshold values by literature for SNR, linewidth, and CRLB. These tests will be made with the quantified Tarquin results. Furthermore, a correlation study between these parameters will be performed. **Results:** The method was tested on the data specified in the Materials and Methods section. It was capable of generating the grid overlap in the image as well as the region of interest and the overlap of the metabolic map in the image. We also filtered the spectra with the SNR values > 10 and linewidth < 8 which appears to be a good indication of a good spectrum. **Discussion:** Spectra quantification was obtained by integrating Jupyter notebook with Tarquin software. The overlay of this map was made with the association of the voxels of the image with the corresponding VOI voxel and Tarquin's generated quantification file. We still need to make more studies to understand the best parameters for noisy spectra evaluation focusing more on the CRLB. **Conclusion:** The proposed visualization method will be open source, allowing MRSI analysis combined with different forms of visualization. Even though the SNR and linewidth thresholds seem to be good parameters for quality spectra, we need to improve our quality criteria including the CLRB parameter. The method will still be tested in a larger group of images.

References: [1] doi:10.4155/bio.11.320; [2] doi:10.1002/nbm.891; [3] doi: 10.1002/mrm.22579.

AUTONOMIC DYSFUNCTION IN HEREDITARY SPASTIC PARAPLEGIA *SPG4*

Carelis del V. González-Salazar[1]. Karen AG. Takazaki[1], Alberto RM. Martinez[1], Marcondes C. França Jr.[1]

[1] Department of Neurology UNICAMP.

Introduction: *SPG4* gene mutations are the most common cause of hereditary spastic paraplegia (HSP-SPG4) and characterized by progressive weakness, spasticity and hyperreflexia in lower limbs. There are few studies about non-motor manifestations in this disease and none about the autonomic system involvement. The aim of this study was to determine the frequency and pattern of autonomic complaints in patients with HSP-SPG4, as well as the clinical relevance and the possible factors associated with these manifestations. **Materials and Methods:** Clinical and electrophysiological evaluations were performed in 32 patients with HSP-SPG4 confirmed by molecular tests and 38 healthy controls. The Scales for Outcomes in Parkinson's Disease: Autonomic Questionnaire (SCOPA-AUT) was applied to quantify the severity of autonomic symptoms. Electrophysiological tests included Sympathetic skin response (SSR) recorded in hands and feet; and Quantitative Sudomotor Axonal Response Test (QSART) in the typical recording sites: the medial forearm, the proximal leg, the distal leg and the proximal foot. The groups were compared with Mann Whitney and Chi-Square test, p values < 0.05 were considered significant. **Results:** There were 20 men, with a mean age of 45.4 ± 15.3 years. The median SCOPA-AUT score was 13 ($p = 0.003$). Urinary and cardiovascular domains subscore were significant (6 vs 1 $p = 0.002$; 0 vs 2 $p = 0.028$ respectively). Absent SSR in the feet were more frequent among patients (59.4% vs 2.6%, $p < 0.01$). QSART responses were also smaller in the HSP-SPG4 group at the forearm (0.44 μL vs 1.03 $p = 0.008$), at distal leg (0.55 vs 1.15 $p = 0.028$) and the feet (0.26 vs 0.7 $p = 0.004$). **Discussion:** These results indicates that patients have sudomotor dysautonomia. The abnormalities found in QSART test indicated damage to small postganglionic cholinergic fibers. **Conclusion:** Patients with HSP-SPG4 frequently present symptoms of dysautonomia. Electrophysiological tests showed autonomic sudomotor dysfunction.

References: [1] Ben M.W., et al., Clin Auton Res. 19: 79–87, 2009. [2] Carod-Artal FJ., et al., Mov Disord 25:205-212, 2010. [3] Lo Giudice T., et al., Experimental Neurology 261: 518-539, 2014. [4] Novak P. Clin Auton Res 2017. [5] Ravits JM., et al, Muscle Nerve 20 (8): 919-937, 1997. [6] Servelhere KR., et al., European Journal of Neurology 23: 408-411, 2016. [7] Sletten D., et al., Muscle Nerve 41: 240–246, 2010.

GRAPH ANALYSIS OF NOISY EEG SIGNALS EXTRACTED DURING SLACKLINE WALK: PRELIMINARY RESULTS

L. T. Menezes[1,2], M. F. Barros[3], R. Radel[3], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, Campinas, SP, Brazil, [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN) Campinas, SP, Brazil, [3]Université Côte d'Azur, LAMHESS, France.

Introduction: This study describes a methodology that was applied to the processing of noisy electroencephalographic (EEG) signals. The signals were recorded during a walk on a slackline at two different heights: 1 m (low) and 40 m (high) from the ground. Such manipulation provided us with an opportunity to evaluate the same motor task but at different levels of subjective risk, which can have a dramatic effect on the subject's emotional and attentional state. For this reason, it was expected that the high-slackline condition would show some difference in relation to the low-slackline in spite of objectively similar motor control demands. However, EEG signals during slackline walking are contaminated with motion artifacts. The aim of the present work was to evaluate the best approach to process these signals, in order to extract relevant information from this singular protocol. Materials and Methods: EEG data from 8 trained subjects were acquired using the eegoTMsports (ANTneuro, Netherlands) 64-channel EEG device, a portable EEG system that is presumably less vulnerable to motion artifacts. There were four conditions: resting state and slackline walk for both low and high conditions. Parts of the data that were explicitly movement artifacts were manually discarded, and the remaining data were analyzed. First, a Short-Time Fourier Transform (STFT) was performed, with 1 s Hanning windows with 50% overlap. Second, using the transformed signal for every second, the spectral coherence between all pairs of electrodes was calculated using a well documented MATLAB function. The coherence values were then thresholded, to produce an adjacency matrix (relating every electrode pair) for every time point. The threshold was chosen so that the number of connections remained stable across all connectivity matrices. Next, the percentage of time in which each electrode pair was connected was computed (e.g., coherence values between electrodes Fp1 and Fp3 were above the threshold about

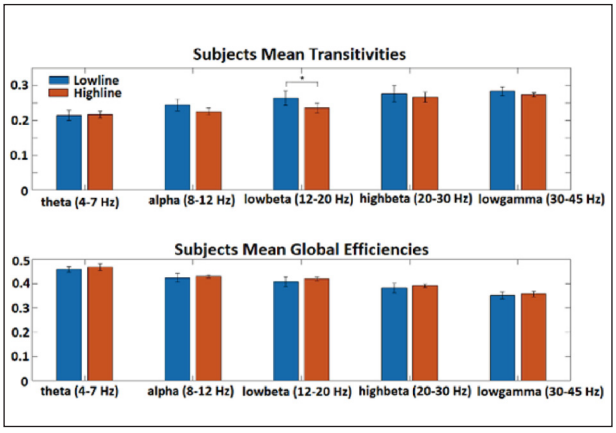


Figure 1. Subjects mean transitivities and global efficiencies.

80% of the time), producing a connectivity matrix, or undirected-weighted graph, for every subject and every condition. From these graphs, the following metrics were extracted: global efficiency and transitivity. Global efficiency is the average of inverse shortest path length, and transitivity, also called global clustering coefficient, measures the ratio of triangles to triplets in the network. **Results:** As seen in the figure, the mean transitivity (over subjects) showed a significant change (decrease) from low to high condition in the low-beta EEG frequency band ($p < 0.05$). Global efficiency showed no significant changes between conditions for none of the frequency bands. **Discussion and Conclusion:** Lower transitivity in highline condition means that there were less local connections in relation to lowline condition. Other measures should be performed in order to verify this result. In the following, a vaster search of the various graph measures should be done for a more robust analysis. Also, an investigation of artifact rejection techniques, such as ICA, may also improve the processing and probably give more accurate measures of the signal generated by the brain itself.

References: [1] Bullmore E. *Nature Reviews Neuroscience*,, 2009. doi: 10.1038/nrn2575.

ACCURATE PLACEMENT OF NIRS PROBES FOR OXYGENATION MONITORING

J.A.I. Rubianes Silva[1,4], S.T. Wu[1,4], A Quiroga[2,4], M. Katsurayama[3,4], R. C. Mesquita[2,4]

[1]School of Electrical and Computer Engineering, [2]Neurophysics Group, IFGW, [3]Department of Neurology, School of Medical Sciences, [4]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN).

Introduction: Improper cerebral perfusion and oxygenation may aggravate brain injury. Continuous oxygenation and perfusion monitoring has been increasingly recognized as a need in the neuro intensive care unit. Near-infrared spectroscopy (NIRS) has been demonstrated a prospective alternative for non-invasive monitoring of patients with traumatic brain injury (TBI). A NIRS-based oxygenation and perfusion monitoring system has been under development in the Institute of Physics [1]. Since the monitoring quality is highly dependent on the placement of NIRS probes with respect to the area to be monitored [2], we present in this work an ongoing project for improving the accuracy of the placement of NIRS probes with respect to the hidden injured area. **Materials and Methods:** Fastrak 3D digitizer is used for digitizing the points on the patient´s scalp and the CT scans that are routinely performed on the patients with TBI are rendered on the GPU. We devised a procedure that through seven correspondence digitized pairs can robustly calibrate the physical patient's space on which the digitizer moves with respect to the space of the visualized CT volume [3]. Appropriate tuning of the opacity rendering attribute allows us to visualize the relative position of the digitizer´s probe with respect to the underlying cortical structure at interactive rate. **Preliminary Results:** A prototype is implemented [4]. Figure (a) is a snapshot of a post-calibration test scene in which an operator manipulates the digitizer to assess its corresponding location on the computer screen. Figure (b) illustrates the visualization of a point captured by the digitizer in the space of the reconstructed axial CT slices rendered on the GPU. The point is highlighted by a pink 3D triad. In Figure (c) we can see how the opacity is explored to improve the perception of the cortical structure below the scalp.

(a) Post-calibration test | (b) Point digitized in the CT image space | c) Visible cortical structure

Figure 1. Subjects mean transitivities and global efficiencies.

Discussion: Preliminary validation results show that the correspondence precision between the physical patient space and the rendered volume space is very high. This may improve the reliability of the signals that NIRS probes capture, and consequently the safety of the oxygenation monitoring. However, further experiments should be conducted to assess the usage of such a system in a clinical routine and its effective gain. **Conclusion:** Facing the promising results, we plan to integrate the proposed interactive placement algorithm into the in-house developed NIRS-based oxygenation monitoring system for improving its monitoring precision.

References: [1] https://goo.gl/4z855Z. [2] doi: http://dx.doi.org/10.1117/1.JBO.18.2.027005. [3] Rubianes, J. A. I., Dissertação (mestrado), https://goo.gl/9CxBXN, (2017). [4] VMTK-EEG: Visual Manipulation Toolkit for NeuroImages, https://goo.gl/TQtwbk.

DETECTION OF REGIONS OF INTEREST FOR MR IMAGE ANALYSIS OF THE BRAIN

Samuel B. Martins[1,2], Bárbara C. Benato[1], Bruna F. Silva[3], Clarissa L. Yasuda[3], Alexandre X. Falcão[1]

[1]University of Campinas, Institute of Computing, Campinas, Brazil, [2]Federal Institute of Education, Science and Technology, Campinas, Brazil, [3]University of Campinas, School of Medical Sciences, Campinas, Brazil.

Introduction: Most methods for brain MR image (MRI) analysis rely on segmentation of the target objects to quantify variations in shape, size, and texture. However, the effectiveness of the analysis can be negatively affected by their segmentation errors, mainly in subcortical structures (e.g., the hippocampi) that can present for example low contrast and shape deformation Moreover, it might be important to analyze 3D regions of interest (ROIs) in the image, which do not include any specific object segmented by available tools. Once the ROIs are detected, deep learning techniques can be applied to the design of models for object segmentation and/or region classification. **Materials and Methods:** We propose a novel alternative: *RefObj*. For a given training image set, registered into a common template, with the specifications of the two coordinates that define each *3D* patch around each object in each image – as interactively provided by experts – and the segmentation of a reference object, *RefObj* assumes that the relative locations between each training patch and the reference object are robust to registration errors. Therefore, they are used to estimate the initial displacement and search region for ROI detection. **Results:** For validation, we use an in-house dataset with 30 MR-T1 images of 3T from control subjects with voxel size $1\times1\times1\ mm^3$ and one ROI around each individual hippocampus. We compare *RefObj* with (*SSeg*) the 3D patches of minimum sizes around the objects under analysis after their automatic segmentation by using the software *volBrain*. We consider the cerebellum as the reference object for *RefObj*. We define two measures: the percentage of missed foreground (PMF), which measures the relative number of hippocampus's voxels that are missed by the predicted patch; and percentage of extra background (PEB), which measures the percentage of background voxels outside the ground-truth patch. Resulting images and masks were mapped onto the coordinate space of the non-linear MNI152. Table 1 summarizes the results. *RefObj* takes about 3 minutes whereas *SSeg* takes about 12 minutes, due to *volBrain* segmentation.

Table 1. Comparison between the considered localization approaches for the Right (RHP) and Left Hippocampus (LHP).

Organ		PMF (%)	PEB (%)
RHP	SSeg	0.11 ± 0.27	20.95 ± 8.84
	RefObj	0.04 ± 0.08	33.61 ± 9.88
LHP	SSeg	0.09 ± 0.21	21.35 ± 8.86
	RefObj	0.07 ± 0.10	29.31 ± 9.52

Conclusion: In this paper, we propose a novel alternative for detection of regions of interest in MR brain images. Our methods presents equivalent results to the hippocampus localization based on *volBrain* segmentation, but with the advantages of being considerably faster and do not depend on the segmentation of the object of interest, which might be a problem in the absence of a segmentation tool. As future work, we intend to deeply evaluate our approach with other databases, including images of epilepsy patients before and after surgical resection.

Support: CNPq (302970/2014-2, 403726/2016-6, 308764/2015-3) and FAPESP (2013/07559-3, 2014/12236-1, 2015/10369-7).

STUDY OF CEREBRAL HEMODYNAMIC RESPONSE FUNCTION IN PATIENTS WITH FOCAL EPILEPSY USING EEG/FMRI DATA

M. M. Isikawa[1,2], C.E. G. Salmon[1,2]

[1.] Departamento de Física, FFCLRP, Universidade de São Paulo, Ribeirão Preto, Brasil; [2]Laboratório Inbrain, Universidade de São Paulo, Ribeirão Preto, Brasil.

Introduction and Hypothesis: Epilepsy is the most common neurological

disorder, around 0.5 to 1% of the world population is affected. In half of the cases, a surgical intervention is an alternative to remove the brain tissue that generates the seizures or epileptogenic zone (ZE). ZE is spatially determined using several techniques and clinical evidences during the presurgical planning. These areas can be associated to ictal activity (abnormal activities in the crisis period) or interictal (abnormal activities outside of the crisis period) [1]. The functional magnetic resonance imaging (fMRI) is an important neuroimaging technique based on the BOLD (Blood Oxygenation Level Dependency) effect [2]. It allows the observation of the so-called cerebral hemodynamic response function (HRF), measured by the cerebral blood flow variation caused by the neural activity. In epilepsy studies, the simultaneous analysis of EEG-fMRI data is a useful tool to map BOLD response associated to interictal activity [3, 4]. In conventional fMRI studies a canonical HRF is used, however significant shape variation and beginning of the HRF were demonstrated in some individuals and brain regions. J.K. Kong. et al. had demonstrated that using a specific HRF for each patient is more efficient in the ZE localization [3]. HRF shape should be dependent on specific characteristics such as: brain attack region, age of the patient, type of epilepsy, among others [4]. **Objective:** Our main aim is to obtain a specific HRF for each patient using EEG and fMRI data from patients with clear defined ZE. **Methods:** Three patients without manifestation of the epileptic crisis one year after the surgery will be selected. From EEG and fMRI data (already collected), a statistical map will be made using a canonical HRF. In a second step, time series of the BOLD signal from the ZE of the patients will be expressed in a Fourier series based on a previous method [3]. Essentially, we will convolute a series of functions impulse-spikes with a set of basic functions of sines and cosines. Afterwards, a linear regression of the fMRI signal with the points of interest versus the time series, previously obtained, will be executed. The procedure generates a coefficient set, to be used in the patient specific HRF. Once this HRF is obtained, it will be adjusted to two gamma functions, one for the positive lobe and another one for the negative lobe. **Relevance:** The deconvolution of BOLD response of an epileptogenic region with the electric response is one of the methods considered for the identification of an accurate HRF. However, this procedure can be affected by various experimental factors that harm the result accuracy, such as the signal-to-noise ratio (RSR) of BOLD signal and the firing rate [3]. The correct mapping of ZE is extreme important for the patient outcome [1].

References: [1] Luders, H., et. al. Epilepsy, 39 (9), 1006-1013; [2] Ogawa S, et. al. Proc Natl Acad Sci. 1990; 87: 9868-72. [3] J.K. Kong. et al., NeuroImage 20 (2003) 1162-1170; [4] Bénar, Chistian-G et al., NeuroImage 17 (2002) 1182-192.

PRE-OPERATIVE ANALYSIS OF FRACTIONAL ANISOTROPY IN TLE PATIENTS

Divino, N.P[1], Yasuda, C.L.[1] , Cendes, F.[1] Rezende, T.J.
[1]Laboratory of Neuroimaging, FCM.

Introduction: Temporal lobe epilepsy (TLE) is the most common etiology of refractory epilepsy in adults and surgery is the best option for most these subjects. However, around 30 to 40% of patients remain with seizures after surgery, and underlying causes of failure to achieve complete seizure control is still unclear. Here we analyzed white matter abnormalities in pre-operative diffusion images and correlated them with surgical outcome. **Materials and Methods:** We studied 42 unilateral TLE patients submitted to surgery between 2010 and 2015 and followed for, at least, two years. These patients were separated into two groups, according to the surgical outcome: group SZF (seizure free: Engel 1A, 26 subjects) and group NSZF (not seizure free: Engels 1B-4; 16 subjects). We used a control group of 42 subjects, paired for age and sex. All patients and controls performed a high-resolution MRI on a 3T Phillips Achieva Scanner, with spin echo DTI sequence. The DTI raw image was co-registered and corrected for eddy currents, motion artifacts and segmented using an automated atlas-based image method (multi-atlas label fusion –https://braingps.anatomyworks.org) that provides the fully segmented brain with 289 labels. For each subject, we selected 14 labels (based on previous studies and temporal lobe connections) to compare values of fractional anisotropy (FA) among three groups with a MANOVA test (with Tukey posthoc analysis running on SPSS22). **Results:** We performed two models of one-way MANOVAs; the first one with seven ipsilateral labels, and the second with seven contralateral labels (amygdala, hippocampus, medium cingulate gyrus, cingulum, pre-cuneus, corticospinal tract and body of the corpus callosum). In the ipsilateral analysis, there was a statistically significant difference between groups when considered the combined dependent variables (F (4,563)= 5.413; Wilks' Lambda =0.441; partial eta squared = .296 p=0.05). In the contralateral analysis there was statistically significant difference between groups when considered the combined dependent variables (F (4,563)= 3.074; Wilks' Lambda =,579; partial eta squared = .221, p=0,05). In both, the post-hoc tests showed statistical differences between patients and control group, but no significant differences between SZF and NSZF groups. While there were differences in all ipsilateral labels, in the contralateral analysis, only amygdala and body of the corpus callosum were different from controls. **Discussion:** The atlas-based image (ABA) method allowed us to compare regions of interest while avoiding voxel-wise multiple comparisons and increasing the signal-noise ratio. Compared to controls, we observed ipsilateral differences in all analyzed labels and contralateral amygdala and body of the corpus callosum. These findings suggest an extra-hippocampal damage in white matter bilaterally, that can be related to network recruitment during repeated seizures, or structural abnormalities related to underlying mechanisms of epileptogenesis. The comparative analysis of the SZF and NSZF groups did not reveal significant differences, which may be associated with the small number of subjects. **Conclusion:** The present work confirmed that are widespread bilateral microstructural abnormalities in the white matter of TLE patients (mainly ipsilaterally) when compared to a control group, suggesting a network mechanism involved in the pathogenesis of TLE. Our preliminary data did not allow us to distinguish the SZF for NSZF group.

References: [1] Li Y., et al., Image Corruption Detection in Diffusion Tensor Imaging for Post-Processing and Real-Time Monitoring PLOS ONE 2013; 8(10): e49764. [2] Westin CF, Maier SE, Mamata H, Nabavi A, Jolesz FA, Kikinis R. Processing and visualization for diffusion tensor MRI. *Med Image Anal* 2002;6:93-108.

IMPULSIVE-COMPULSIVE-ADDICTIVE DISORDERS TREATMENT ASSISTED BY NEUROMODULATORY TECHNIQUES AND VIRTUAL REALITY

W. D. Casagrande[1], A. Ferreira[1], A. Frizera-Neto[1], M. L. de Souza[1], E. M. Nakamura-Palacios[1]
[1]Brazilian Research Group on Brain and Cognitive Engineering (BRAEN) – UFES.

Introduction and Hypothesis: In recent years, some studies have shown the therapeutic benefits of low intensity transcranial Direct Current Stimulation (tDCS) modulation techniques in the treatment of drug addiction, such as alcohol and crack-cocaine addiction [1,2]. It has been progressively observed that tDCS has promising clinical effects, reducing compulsion and relapse to the use of these substances in severely dependent patients. In addition to these clinical evidences, it is also observed through electroencephalography and magnetic resonance imaging studies, that tDCS produces changes in frontal brain activation. The scientific issue that follows is that these changes in frontal activation could be important targets in the application of methods that could guarantee the maintenance of these changes induced by tDCS, such as, for example, cognitive training through neurofeedback [3]. The establishment of this method could enable the recovery of cognitive control over search behavior and compulsion for drug use and additional clinical application in other neuropsychiatric disorders, such as, for example, Attention Deficit Hyperactivity Disorder (ADHD). **Objective:** The general objective here proposed is to integrate the technique of cerebral electrical stimulation to a new strategy of cognitive modulation employing neurofeedback conducted through the recording of real-time brain activity and the continuous interaction with a computer (Brain-Computer Interface) being intermediated by complex stimuli provided by virtual reality environments [4], applied to the treatment of neuropsychiatric disorders, in the case of drug addiction, and also in impulsive-compulsive conditions. **Methods:** The method to be developed will involve modulation by synchronization of brain activity of structures related to the Default Mode Network (DMN), which is related to attentional processes and to self-monitoring, by means of wave frequencies or the current density resulting from the processing of electroencephalographic signals by the low-resolution electromagnetic tomography (LORETA) method. Performance control will be accomplished by immersing the individual in a complex environment generated by the virtual reality technique. **Relevance:** The integration of two neuromodulatory techniques and a virtual reality environment can be a promising approach to assist traditional treatment of

drug addiction and other neuropsychiatric disorders, allowing the patients to recover the cognitive control over their behavior. Additionally, this research may provide improvement and technological innovation that will have direct application to the benefit of the local society, but also in the national and international scope.

References: [1] doi: 10.1017/S1461145714000984. [2] doi: 10.1093/ijnp/pyv066. [3] doi: 10.1038/nm.2016.164. [4] doi: 10.1159/000320847.

USE OF FMRI TO ASSESS THE EFFICACY OF THE EEG-NEUROFEEDBACK TRAINING TECHNIQUE

L. T. Menezes[1,2], C. A. Stefano Filho[1,2], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN) Campinas, SP, Brazil.

Introduction and Hypothesis: Electroencephalography (EEG)-biofeedback, also called neurofeedback (NFB) [1], is a cognitive training technique that has clinical applications as alternative treatments for a variety of diseases, such as ADHD (attention deficit hyperactivity disorder). Briefly, an EEG-NFB training procedure consists of capturing the electrical potentials generated in some region of interest (ROI) of the brain, measured from the scalp; the signal is then processed in real-time by a software, and some signal's feature – e.g., the theta band (4-7 Hz) power [2] – is extracted. This feature is presented to the subject through a simple interface – e.g., a bar graph – and the subject is requested to simply increase or decrease the size of the bar graph. After performing a certain number of training sessions, the subject is expected to have altered their signal features, which should be accompanied by behavior changes, which could be evaluated through psychological tests. **Objective:** To assess NFB training efficacy through a double-blind, placebo-controlled study, where subjects will be evaluated before and after a given time period using fMRI and psychological tests. **Methods:** Healthy adult volunteers will be divided into three groups: NFB training, sham-NFB training, and control group. The experimenters will not know in which group the subject undergoing training is allocated. The two first groups will undergo at least 10 sessions of EEG-NFB training, but the sham-NFB group will receive "fake" signals (the signal displayed will not be the participant's real signal). The protocol defined for those who will underpass NFB training (and sham) is as follows: 1) Pre-assessment: fMRI procedure + 64-channel EEG (both resting-state) + Psychological tests; 2) 0th session: five 2-minute runs while doing an attention task (to assess what feature will be used particularly for each subject); 3) 5 NFB training sessions: resting-state (2 min) + first interface (5 min) + second interface (5 min) + resting-state (2 min); 4) Psychological tests + 64-channel EEG (resting-state); 5) 5 NFB training sessions: resting-state (2 min) + first interface (5 min) + second interface (5 min) + resting-state (2 min); 6) Post-assessment: fMRI procedure + 64-channel EEG (both resting-state) + Psychological tests. The training will be individualized after a first EEG signal extraction during the 0th session. In this session, an analysis to find a feature (some characteristic of the EEG signal, related to a frequency band and electrode location) that is a reliable signature of an attentive mental state for that particular subject will be performed. Then, the subject will be trained to present this feature more pronounced. Finally, differences between pre-, post- and follow-up measures will be evaluated for all groups in order to analyze the effects of the training. EEG data will be collected with the g.tec amplifier g.USBamp at 256 Hz with 16 dry electrodes. The data will be processed and analyzed using home-developed MatLab software. **Relevance:** As mentioned, NFB training is a potential drug-free alternative therapy to many different neurological and neuropsychiatric conditions. Since this training technique is being applied throughout psychological clinics, it is fundamental to assert its scientific foundation.

References: [1] Gruzelier, J. H. Neuroscience and Biobehavior Reviews 2014, 44, 124; [2] Leins, U. et al. Applied Psychophysiology Biofeedback 2007, 32, 73-88.

GLUTATHIONE DEPLETION OVERCOMES CHEMOTHERAPY RESISTANCE IN AGGRESSIVE MEDULLOBLASTOMA *STEM-LIKE* CELLS

B. D. Barbieri[1], M. Marçola[1], C. R. R. Rocha[2], O. K. Okamoto[1]

[1]Laboratory of Translational Genomics, IB, USP, [2]Laboratory of DNA Repair, ICB, USP.

Introduction: Medulloblastoma (MB) is the most common pediatric brain tumor [1]. It is a highly aggressive cancer that affects the cerebellum, being classified as a grade IV tumor by the World Health Organization (WHO) [2]. Drug resistance is a major limiting step for the successful treatment of most cancers [3]. Additionally, the overexpression of pluripotency factors in cancer cells favors the process of treatment resistance, tumor recurrence and spreading [4]. Glutathione (GSH) is a major antioxidant intracellular molecule and its levels are directly correlated with tumor resistance [5,6]. Therefore, the purpose of this study was to verify whether GSH depletion can potentiate the effect of two chemotherapeutic drugs, cisplatin (Cis) and temozolomide (TMZ), in the treatment of aggressive medulloblastoma *stem-like* cells. **Materials and Methods:** Daoy cells expressing normal (control tumor cells) or high levels of the pluripotency factor *OCT4A (stem-like* cells*)* were treated with a combination of BSO (glutathione inhibitor), cisplatin and TMZ. The effect of different drug combinations on cell viability was assessed through MTT and apoptosis assays. Additionally, we analyzed possible treatment side effects on healthy neuron cells by differentiating neural progenitor cells into neurons and proceeding with MTT assay as well. Lastly, we started analyzing treatment efficacy *in vivo* through an orthotopic and metastatic model of medulloblastoma, that consists in the intracranial surgery of tumor cells into the third ventricle of the brain. **Results:** We found that both Daoy and Daoy-*OCT4A* cells were sensitive to cisplatin but resistant to TMZ. The highest dose of TMZ used in the study reduced the viability of Daoy cells to 56%, but only to 80% in Daoy-*OCT4A* cells. When combining either BSO+Cis or BSO+TMZ, Daoy-*OCT4A* cells did not respond to the treatment with TMZ+BSO, reinforcing its chemoresistant phenotype. Next, the ideal combination of the three compounds was defined. Daoy-*OCT4A* cells required a higher dose of TMZ than control Daoy cells to attain similar death rates, however the combined treatment was effective for both: a synergistic effect was observed for Daoy-*OCT4A* cells, reducing cell viability to ~17%, in comparison with cisplatin+TMZ alone, and as for Daoy cells, an additive effect was observed, and viability was reduced to ~15%. Preliminary results in the *in vivo* model indicated that BSO or chemotherapy regimen alone is well tolerated by the organism. The combination of the three compounds *in vivo* is being performed. Lastly, analysis of the treatment effect in healthy neurons showed no significant toxicity, revealing its potential clinical application. **Discussion:** The aggressive tumor cell initially seemed to be TMZ-resistant, however, the combined treatment was able to overcome it. This synergistic effect has been observed in other brain tumors, such as glioma, and possible explanations include an increase in oxidative stress due to GSH depletion, which can lead to apoptosis, as well as the capacity of cisplatin to reduce the activity and expression of an enzyme involved in the DNA repair process of TMZ-induced damage [6]. **Conclusion:** The present results indicate that the use of a glutathione inhibitor in combination with cisplatin and TMZ may be useful in the treatment of medulloblastoma, even in the case of aggressive tumors. Similarly, this approach may also be useful in the development of therapeutic strategies for other chemoresistant tumors.

References: [1] doi:10.1038/nrclinonc.2014.181; [2] doi:10.1007/s00401-007-0243-4; [3] doi:10.1038/nrc2167; [4] doi:10.1089/scd.2015.0052; [5] doi.org/10.1016/j.semcdb.2012.03.017; [6] doi:10.1038/cddis.2014.465.

BIOMECHANICS SENSOR NODE – BSN: A WEARABLE DEVICE CONTROLLER OF VIRTUAL ENVIRONMENTS FROM GESTURAL INTERACTION FOR FUNCTIONAL NEUROREHABILITATION THERAPY IMPROVEMENT

A. Brandao[1], R. Leoni[2], L. Ruzene[2], A. Pacífico[2], T. Beltrame[3,4], D. Dias[5], G. Castellano[1]

[1]Neurophysics Group, IFGW, UNICAMP; [2]Center for R&D in Telecommunications, Devices and Sensors Dept, CPqD; [3]Institute of Computing, UNICAMP; [4]Physiotherapy Dept, CCBS, UFSCar; [5]Computer Science Dept, UFSJ.

Introduction: During a rehabilitation treatment, mainly in neurological patients, it is expected a therapy that offers the greatest possible independence for these patients, in relation to activities of daily living. Recently, virtual reality solutions, based on gestural interaction, have been explored for rehabilitation purposes. The aim of this study was to develop control devices for these solutions, namely, a biomechanics sensor node (BSN). **Materials and Methods:** The BSN device was developed from a controller board and an Inertial Measurement Unit (IMU) with 9 degrees of freedom, including the original development of the Integrated Circuit Board layout (BIOX Sensor). Initially the external packaging of the device was printed on Acrylonitrile

Butadiene Styrene (ABS), 3D printing, and the final version was packaged in flexible and antimicrobial material. **Results:** A BSN device was developed, allowing human-computer interaction through gestures. The device has the of a bracelet, allowing recognition of patient gestures (both upper and lower limbs), gestures' calibration to control the virtual reality environment, and measurement of movement kinematics (number of movements performed, axis / plane of execution, raw data of displacement in the space). A communication protocol, using Bluetooth Low Energy – BLE [1,2], was integrated into the device, ensuring low power consumption and native support with mobile operating systems, such as Android (Google). This communication protocol converts patient movement into the input for e-Street and e-House, virtual reality software tools which simulate the urban and residential environments respectively. **Discussion:** The tests performed with the BSN device allow its indication as a complement to conventional rehabilitation therapy due to personalization in relation to each patient's motor limitation and applicability to controlling virtual reality software. Unlike devices such as a Leap Motion [3], which allows manual tracking from infrared sensors, or Kinect [4], which allows body tracking from a depth camera (RGBD), the BSN recognizes the user's movement from a wearable device and allows association of a real (even partial) movement to a complete movement in the virtual environment. Thus, the patient performs a movement within his/her limitation, and in the virtual environment the same movement is identified as complete, offering a positive feedback to the patient, and indirectly eluding the brain with a visual feedback of movement completeness. **Conclusion:** The use of the BSN device in physical and neurofunctional rehabilitation therapies can increase patient motivation by inducing greater adherence to treatment and reducing avoidance during therapy. It is hoped that with this approach, greater brain reorganization will occur, such as to find the best way to perform the functions lost after a stroke. Indeed, our next steps are to evaluate brain reorganization of patients undergoing rehabilitation therapy using the developed BSN device.

References: [1] Davidson R et al., Getting Started with Bluetooth Low Energy: tools and techniques for lower-power networking, 2014; [2] Nordic Semiconductor, Getting Started with Bluetooth Low Energy wireless design, 2010; [3] Leap Motion, How controller work?, 2014; [4] Kinect Sensor, Microsoft robotics: Depth camera webcam sensor, 2015; [5] https://doi.org/10.1155/2017/6261479.