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APRIL 3th - 5th 2024 - CAMPINAS, SP, BRAZIL

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A LAGGED CONNECTIVITY APPROACH FOR INNER SPEECH EEG CLASSIFICATION

E. Abreu[1], G. Castellano[1]
[1]Neurophysics Group, IFGW, UNICAMP

Introduction: This study seeks to classify EEG data linked to imagining different words for Inner-Speech based Brain-Computer Interfaces (IS-BCI). IS-BCIs facilitate user-device interaction through mental imagery of verbal articulation. Unlike traditional methods using time-frequency domain features, which resulted in varying degrees of success [1]-[3], our approach employs functional connectivity measures for feature extraction, fed into a Support Vector Machine (SVM) classifier. **Materials and Methods:** This study uses the "Thinking out loud" dataset [4], consisting of records from ten healthy participants (34±10 years, 6 men). Participants imagined words from visual stimuli ("Up", "Down", "Left", or "Right" in Spanish) for 2.5s, 240 times. EEG data from 128 electrodes were sampled at 1024Hz using a BioSemi equipment. Preprocessing included notch filtering (50Hz), bandpass (0.5-100Hz), blink artifact removal with ICA, and downsampling to 256Hz. Analysis focused on the last 2 seconds of speech imagination to ensure task alignment. Epochs were filtered into 11 frequency bands (within 12Hz-48Hz). Node metrics (strength, PageRank) were computed from connectivity matrices obtained with the motif synchronization method [5], using 0,1,2 and 3 as lag values. A two-stage classification process followed: first, features were ranked based on their discriminatory strength (accuracy) through a SVM (RBF kernel), and then top features were combined for optimal feature selection, with 5-fold cross-validation at each step. **Results:** Table 1 displays classification accuracies, with an average of 45.8% and a standard deviation of 3.8%, significantly exceeding those from comparable studies using the same dataset (<37.0%) [2], [3]. The obtained results also surpass our previous findings [6], where the average accuracy was 38.2% with a 3.7% standard deviation. In that study, we analyzed the entire 2.5-second interval of speech imagination using a distinct set of graph metrics. **Conclusion**: Our investigation showcased the effectiveness of connectivity-based features in classifying IS brain signals, resulting in accuracies that markedly surpass those documented in prior studies using the same dataset. These findings bear notable implications for enhancing IS recognition in BCI applications and advancing assistive technology and cognitive research. Further studies are needed to assess the viability of the proposed method in real-time (online) scenarios.

Acknowledgements: FAPESP [2023/02705-3, 2013/7559-3], CNPq [304008/2021-4].

Table 1. Classification accuracies for all participants. S. = Subject, Acc. = Accuracy.

S.	01	02	03	04	05	06	07	08	09	10	Mean	Std
Acc. (%)	42.0	52.1	50.0	45.0	42.5	48.6	40.0	49.0	42.5	46.7	45.8	3.8

References: [1] Kim J et al., doi: 10.1088/1741-2560/11/3/036010. [2] Gasparini F et al. (2022) arXiv, http://arxiv.org/abs/2210.06472. [3] Van Den Berg B et al. (2021) IEEE ICHMS, pp. 1–4. [4] Nieto N et al. (2022), doi: 10.1038/s41597-022-01147-2. [5] Rosário RS et al., doi: 10.1016/j.physa.2015.07.018. [6] Abreu E et al., IV LAWCN, 2023.

ACCURACY COMPARISON IN THE CLASSIFICATION OF ALZHEIMER'S DISEASE USING BRAIN TEXTURE NETWORKS

R. V. Da Silveira[1,3], T. N. C. Magalhães[2], M. L. F. Balthazar[2,3], G. Castellano[1,3]
[1]Cosmic Rays and Chronology Dept., IFGW, UNICAMP, [2]Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), [3]Neurology Dept., FCM, UNICAMP

Introduction: Alzheimer's Disease (AD) is the most common cause of dementia. Early-stage AD shares the same symptoms as Mild Cognitive Impairment (MCI), mainly memory impairment. Several studies have attempted to distinguish between these pathologies [1]. These studies have often used brain networks [2], since this is advantageous over analyzing individual regions, in the sense that it is possible to establish relations between these regions. Machine learning (ML) can be applied to these networks to further aid in the extraction of useful information [3]. Texture brain networks are a new model that has shown good results in characterizing healthy subjects [4]. This study aims to investigate if ML methods applied to texture networks can be used to accurately classify between healthy controls (HC) and patients with AD and MCI. **Materials and Methods:** Structural T1-weighted magnetic resonance images from 55 individuals were acquired in a 3T scanner (Philips Achieva). Two acquisitions (13 ± 8 months apart) were performed on each individual. The individuals were classified by a specialist into three cohorts: HC (18, 5 males, mean age 68 ± 6), patients with MCI (24, 9 males, mean age 70 ± 5), and patients with AD (13, 4 males, mean age 73 ± 8). The images were parcellated into anatomical regions using the AAL atlas and 44 regions commonly associated with AD were selected as ROIs. A 3D gray-level cooccurrence matrix (GLCM) [4] was calculated from each ROI and 55 texture parameters were extracted. Using graph theory, texture networks were generated from these texture parameters, and the strength network measure was computed. The data were preprocessed using a z-transform and three assemblies were used: features from the first and second acquisitions, separately, and the relative difference between instances. Two supervised machine learning methods were selected – k-nearest neighbors (kNN) and logistic regression (LR) – and a grid search was performed for tuning the models. Three comparisons were made between cohorts: HC vs MCI, HC vs AD, and MCI vs AD. **Results:** Table 1 shows the accuracy values obtained from a 10-fold cross-validation, for the instances' average (± standard deviation) and for the relative difference between instances. **Discussion/Conclusion**: Our model has reached a maximum accuracy value of 64.3% between HC and MCI, 75.8% between HC and AD, and 75.7% between MCI and AD,

Table 1. Accuracy values for the instances and difference assemblies for the three cohort comparisons.

		AC (%)		
Assembly	ML	HC vs MCI	HC vs AD	MCI vs AD
Instances	kNN	54.8 ± 0.0	69.4 ± 2.3	75.7 ± 0.0
	LR	64.3 ± 3.4	75.8 ± 6.8	70.3 ± 7.6
Difference	kNN	59.5	67.7	70.3
	LR	61.9	64.5	64.9

HC: healthy controls; MCI: Mild Cognitive Impairment; AD: Alzheimer's Disease; ML: machine learning; AC: accuracy; kNN: k-nearest neighbors; LR: logistic regression.

therefore showing that texture brain networks have the potential to distinguish between these three cohorts. Further studies should aim to expand this model to include other features (e.g. other network measures) and other ML methods (e.g. random forest and support vector machine).

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4), CAPES (finance code 001).

References: [1] Li H et al., doi:10.1002/hbm.22689. [2] Ibrahim B et al., doi:10.1002/hbm.25369. [3] Du Y et al., doi:10.3389/fnins.2018.00525. [4] Da Silveira et al., doi:10.1038/s41598-023-43544-6.

ACQUISITION OF EEG SIGNALS FOR BCI-SSVEP USING A LOW-COST CYTON BIOSENSING BOARD SYSTEM

Manoel Ribeiro Caetano Junior[1], Rafael Ferrari[1]
[1]DSPCom, FEEC, UNICAMP

Introduction: A brain-computer interface (BCI) is a communication system that enables the transfer of information from an individual's brain to a computer system through the processing of brain electrical activity [1]. In this study, the aim was to test and evaluate the low-cost electroencephalography (EEG) signal acquisition system Cyton Biosensing Board in BCIs based on steady state visually evoked potentials (SSVEP) [2]. EEG signal acquisitions were conducted using this system, and the performance obtained in a BCI-SSVEP setup was evaluated. **Materials and Methods:** To generate visual stimulation, we designed a panel consisting of three arrays of LEDs, each of which presenting a flickering stimulus at 12Hz, 14Hz, and 16Hz. Three healthy volunteers (all males, aged 21-26 years) participated in the offline data acquisition. The volunteers focused their attention on each of the stimuli for 10 seconds. This process was repeated 10 times. The sampling rate used was 250 Hz. The BCI system was built employing Canonical Correlation Analysis (CCA), which allows to identify the correlation between two multidimensional variables [3,4]. In this case, the variables considered are the EEG signals and the reference signals, modeled with sine waves at frequencies equal to the stimulation signals and their harmonics. Two evaluation methods were considered, one with training and the other without (unsupervised). In both cases, the correlation was calculated using EEG data segments of 1s. Additionally, we sought to assess the impact of the number of harmonics of the reference signal on the system performance. **Results:** Table 1 shows the average accuracy for each volunteer as a function of the number of harmonics. It is possible to verify that the trained system exhibited better performance and that the number of harmonics proved to be more relevant in the untrained system. **Discussion/Conclusion**: The trained system achieved accuracy rates above 80% for two volunteers even without any preprocessing applied to the acquired signals. The low accuracy observed for volunteer 3 is explained by the high impedance of the electrodes during his acquisition section, much higher than that observed for the other two volunteers. Based on the results, we believe that the Cyton board has the potential to be further explored in more complex BCI systems, with a greater number of stimuli, and with real-time applicability.

Table 1. Accuracy for each volunteer as a function of the number of harmonics in the reference signal, (A) system without training, (B) system with training.

A

Number of harmonics	CCA Average Accuracy (%)		
	Voluntter 1	Voluntter 2	Voluntter 3
1	75	40	36
2	64	53	7
3	61	50	15
4	60	51	26

B

Number of harmonics	CCA Average Accuracy (%)		
	Voluntter 1	Voluntter 2	Voluntter 3
1	95	80	50
2	96	83	55
3	96	82	52
4	96	82	38

References: [1] Wolpaw J.R. et al., doi: 10.1016/S1388-2457(02)00057-3; [2] OpenBCI. Accessed: Feb. 20, 2024. [Online]. Available: https://openbci.com; [3] Härdle W.K. et al., Applied multivariate statistical analysis. Springer Nature, 2019; [4] Lin Z. et al., doi: 10.1109/TBME.2006.886577.

ADAPTATION IN VISUAL PROCESSING OF HIGH-LEVEL FACIAL INFORMATION: AN EYE-TRACKING STUDY

M. B. Urtado[1], R. D. Rodrigues[2], S. S. Fukusima[1]
[1]Perception and Psychophysics Laboratory, Psychology Dept., FFCLRP, USP, [2] Institute of Mathematics and Computer Science, ICMC, USP

Introduction: The adaptation in high-level visual information processing, particularly for facial stimuli, remains a gap in current neuroscience research. This study addresses this gap by mapping eye movements to investigate the occurrence of visual adaptation during perceptual responses to emotional facial expressions. Distinct levels of visual field restriction are imposed across independent experimental groups: Foveal Vision (FV), Parafoveal and Foveal Vision (PFFV), and No Visual Restriction (NVR), enabling various cognitive demand scenarios. **Materials and Methods:** The study enrolled 174 healthy volunteers, randomly assigned to FV, PFFV, or NVR. Eye tracking was used to record the visual processing of 30 distinct facial images, from The Karolinska Directed Emotional Faces database. Images were randomly presented and evenly distributed among emotional expressions. The moving window technique, controlled by the eye tracker in response to participants' gaze, computationally limited participants' visual field under conditions: FV (2º window) and PFFV (5º window). Participants were asked to indicate the perceived emotional expression under free inspection time. Recognition accuracy, inspection time, number of fixations, and fixation duration measurements (dependent variables) were examined according to experimental conditions (independent variable) to assess their distributional properties. Data analysis involved fitting various candidate models and conducting affinity tests for the power law model adequacy in describing the observed data. **Results:** A similar pattern of ocular movement was characterized throughout the experiment trials for all behavioral measures, including inspection time, number of fixations, and fixation duration. Except for cognitive performance measure (recognition accuracy), all behavioral measures across all experimental conditions demonstrated at least a good fit to power law behavior, with most exhibiting the best fit. Furthermore, it was consistently observed that the exponent of the power law distribution remained similar for each given measure across the experimental groups, while the amplitude value increased successively across the NVR, PFFV, and FV groups; see Figure 1.

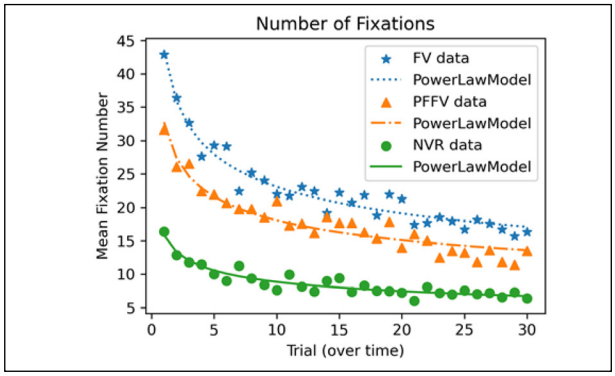


Figure 1. Power Law for Fixations.

Discussion/Conclusion: Increasing visual field restriction resulted in a rise in power law magnitude, indicating heightened cognitive effort. This relationship is supported by mean accuracy; both PFFV and NVR conditions achieved 0.91, suggesting PFFV's increased power law magnitude aimed to maintain performance. FV's mean accuracy of 0.85 suggests that despite achieving high accuracy, a maximal cognitive effort was insufficient to maintain the same performance, possibly due to foveal processing limitations. In conclusion, our findings show consistent adaptation in high-level visual processing to uphold performance amidst escalating visual field restrictions. Congruent with recent research, our observed increase in power law magnitude with heightened cognitive effort mirrors patterns observed in cortical population adaptation to sensory environments [1], suggesting a potential link between behavioral adaptation, neural response dynamics, and adaptation mechanisms across the visual system hierarchy.

Acknowledgments: This research received support from the National Council for Scientific and Technological Development (CNPq) grant number 141876/2020-4.

References: [1] Tring E et al., doi:10.1038/s41467-023-43572-w.

ALZHEIMER-TYPE PATHOLOGY AND CEREBRAL β-AMYLOID ANGIOPATHY IN AGED CAPUCHIN MONKEY

Roberta Diehl Rodriguez[1,2], Sonia Maria Dozzi Brucki[1,2], Maria da Graça Morais Martin[1], Maria Concepción Otaduy[1], Maria Clotilde Henrique Tavares[3], Leonel Tadao Takada[2], Claudia Costa Leite[1], Carlos Tomaz[4], Ricardo Nitrini[2]

[1]LIM-44, FMUSP, [2]Behavioral and Cognitive Neurology group, Neurology Dept., USP, [3]Depart. Physiology Sciences, UnB, [4]Euro-American University Center, UNIEURO

Introduction: Cerebral amyloid angiopathy (CAA) is a predominantly sporadic disease characterized by the presence of abnormal accumulation of β-amyloid (βA) protein in cerebral vessels. CAA is frequently observed in brains with Alzheimer's disease (AD). Despite its high frequency, the diagnosis is still based on neuropathological analysis. Non-human primates are important models for studies in AD and CAA. Besides their evolutionary proximity to humans and evidence that they can develop CAA spontaneously, non-human primates have relatively large brains that are favorable for imaging studies. **Materials and Methods:** After brain extraction, the whole brain of a 29-year-old capuchin monkey was fixed in 4% buffered paraformaldehyde within 12 hours of death. 7T MR images were acquired before and after brain slicing. Consecutive coronal sections from the fixed brain were embedded in paraffin, and 5μm sections from paraffin blocks were used for staining and immunohistochemistry evaluation. All brain sections were stained with hematoxylin & eosin. Immunohistochemistry with antibodies against β-amyloid (βA; 4G8), phospho tau (AT8), p62, TDP-43, α-synuclein (81A), GFAP, IBA-1, βA40 and βA42 were performed in selected areas. **Results:** 7T MRI demonstrated an old hematoma, characterized as low foci in SWI and T2 images with central cavitation, alongside multiple other smaller areas of old hemorrhage (Figure 1). On microscopical evaluation hematoxylin & eosin staining revealed cystic microcavitation with astrocytic gliosis and hemosiderin deposit in the same area of this lesion (Figure 1). Additionally, widespread parenchymal and vascular βA immunoreactivity were found. A high frequency of classic neuritic plaques was observed. Astrocyte hypertrophy and dystrophic microglia were noted surrounding plaques. Besides, CAA affected leptomeningeal and cortical arteries and arterioles with capillary involvement. βA 40 and 42 isoforms were present in most parenchymal and vascular lesions, with a predominance of βA 40. In addition, hyperphosphorylated tau aggregates resembling neurofibrillary pathology were found in the hippocampus, temporal and frontal cortex. **Discussion/Conclusion**: AD-type pathology and CAA pathology similar to those observed in human brains were observed in the 29-year-old female capuchin monkey. Furthermore, the presence of neuroinflammation markers and βA40 and 42 isoforms were also found, highlighting this non-human primate as a possible new animal model for studies in neurodegeneration.

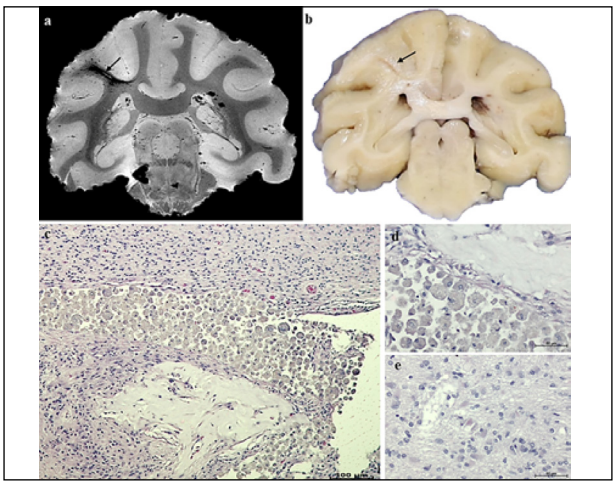


Figure 1. Lesion compatible with old hematoma in T2 weighted imaging from a 7T MRI (A) and in macroscopic slice at the same level (B). On microscopical evaluation hematoxylin & eosin staining reveled cystic microcavitation (C) with astrocytic gliosis (D) and hemosiderin deposit (E) in the region.

ANALYSIS OF THE NEURAL CORRELATES OF PROBLEM SOLVING IN PHYSICS MEASURED WITH FUNCTIONAL NEAR-INFRARED SPECTROSCOPY

L. F. Teodosio[1], L. F. Bortoletto[1,2], G. G. Martins[1,2], V. Sanchez[1], R. C. Mesquita[1,3]

[1]Institute of Physics, University of Campinas, Campinas, SP, Brazil; [2]BRAINN, Campinas, SP, Brazil; [3]University of Birmingham, Birmingham, England

Introduction: The teaching-learning process aims to delineate effective teaching strategies that foster student learning, and monitoring brain activity while students learn can bring important insights into this process. Functional near-infrared spectroscopy (fNIRS) is a brain monitoring technique that can be used in natural settings, mainly due to its portability. Therefore, this work employed fNIRS to investigate students' brain activity during problem solving, one of the most common learning strategies in Physics. **Materials and Methods:** Five undergraduate students (all male; mean (standard deviation) 22 (4) years) answered a modified version of a widely validated test used to assess the understanding of the concepts of force and motion (Force Concept Inventory, FCI). The test was presented on a computer screen, and all the answers provided by the students were recorded for posterior analysis. A commercial continuous-wave NIRS system (NIRScout, NIRx Medical Technologies) monitored their brain activity during the test. The optical probe was designed to cover the frontal, parietal, and occipital lobes. After pre-processing the data [1], we inferred brain activity using a general linear model (GLM). Regions where the hemodynamic response estimation through GLM were statistically significant than baseline () for both HbO and HbR were considered evoked by the task. **Results:** Figure 1 shows the brain areas activated during the problem-solving for one representative participant. When all questions were considered, regardless of the outcome, we observed a dominance of the frontal regions (3/5 participants). In questions answered correctly, we observed an overall activation of the frontal (4/5 participants) and occipital (2/5 participants) areas. In questions answered incorrectly, the activation was more frequent across participants, showing robust activation in the frontal (5/5 participants), parietal (2/5 participants), and occipital (3/5 participants) regions. **Discussion/Conclusion:** The consistency of brain activation in the frontal region can be associated with

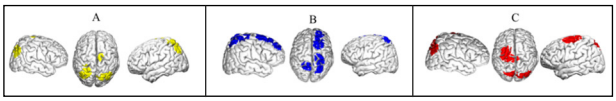


Figure 1. Activated areas in one representative participant for: A. all, correctly and incorrectly (yellow); B. questions answered correctly (blue); and C. incorrectly (red).

high-level cognitive processing required to answer these types of questions [2]. In particular, the activation of frontoparietal areas suggests that the participants attempted to integrate information during problem-solving, even when questions were answered incorrectly. Activations in the occipital lobe are also expected since they reflect visual interpretation typically inherent in problems involving motion. In the future, we plan to further understand the different steps during problem-solving and correlate the results with the behavioral outcome. Last, it is worth highlighting the value of fNIRS in shining a light on educational questions related to the teaching-learning process.

References: [1] Novi Junior SL, https://repositorio.unicamp.br/acervo/detalhe/1238827, 2022; [2] Bartley JE et al., doi: 10.1016/j.neubiorev.2018.06.009.

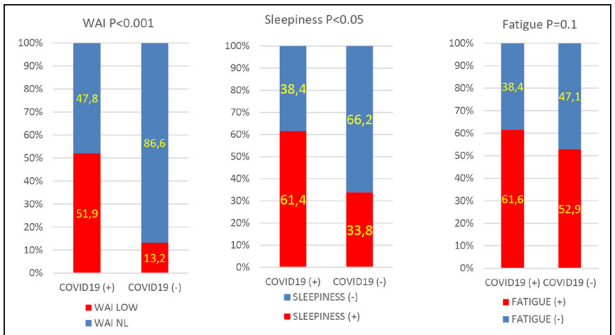
ANALYSIS SHOWS REDUCED WORK CAPACITY AND ELEVATED FATIGUE LEVELS IN THE GROUP WITH 185 COVID-19 CASES VERSUS 134 CONTROLS

Salvador, Gabriel M.[1]; Lino, Ana Paula B.L.[1]; Brancatti, Felipe S[1]., Cendes, Fernando[1], Yasuda, Clarissa Lin[1]

[1]Neuroimaging Laboratory – Department of Neurology – UNICAMP

Introduction: The literature is well-established on the impact of SARS-COV2 on the rise of neuropsychiatric symptoms of fatigue, anxiety, and depression. Unfortunately, little is known about changes in the work capacity of COVID-19 survivors. This study compares the work capacity and other neuropsychiatric symptoms between a group of post-infected individuals (confirmed COVID-19 diagnosis) and a control group using validated questionnaires. **Materials and Methods:** The study involved in-person interviews with 185 individuals testing

positive for COVID-19 (COVID-POS) and 134 COVID-19 negative (COVID-NEG). Both groups completed neuropsychiatric questionnaires: the Epworth Sleepiness Scale (ESS), The Chalder Fatigue Scale (CFQ), and the Work Ability Index (WAI). We used SPSS22 for statistical analysis with Chi-Square tests for analyses of proportions. **Results:** The COVID-POS group had an average age of 44.4 years (20 to 87), 65.9% were female, 37.8% were postgraduates, and 89.2% were in mental work. The COVID-NEG group had an average age of 42.4 years (20 to 71), 62.5% were females, and 97.1% were involved in predominantly mental occupations. Questionnaire results revealed significantly higher rates of excessive sleepiness (61.4% vs. 33.8%) and lower Work Ability Index scores (51.9% vs. 13.2%), but not fatigue, in the COVID-positive group compared to COVID-NEG. Both groups had similar proportions of individuals without a history of anxiety (20.5% vs. 21.3%) and depression (22.7% vs. 24.3%). **Discussion/Conclusion**: These findings suggest potential associations between COVID-19 infection, symptoms such as excessive sleepiness, and fatigue in reducing work capacity. Indicating the need for rehabilitation for survivors of the infection



Footnote: WAI: "Work Ability Index"; nl: normal; (+) presence of specific symptom or condition; (-): absence of specific symptom or condition.

Figure 1. Comparison of the results of the questionnaires applied in the control group and positive COVID-19.

ANATOMY OF VERTICAL HEMISPHEROTOMY: A STUDY IN CADAVERIC BRAINS

D.A. Gulhote[1], M.P. Couto[2], F.A. Cendes[1], E. Ghizoni[1]

[1]Neurology Dept., FCM, UNICAMP, [2]Microneuroanatomy Lab., FCM, UNICAMP

Introduction: Complete removal of the affected hemisphere was the preferred surgical treatment modality for patients with medically intractable epileptic encephalopathies caused by hemispheric pathology until the late 1960s. However, early and delayed surgical complications, lead the hemispherectomy to decline in use. Thus,various disconnection techniques have been developed since the report of Theodore Rasmussen in 1983, who described functional hemispherectomy (resection of the temporal lobe and suprasylvian parenchyma, with disconnection of the residual hemisphere). The two techniques, currently used, are the lateral periinsular hemispherotomy, introduced by Villemured in 1995, and the vertical parasagittal hemispherotomy, introduced by Delalande in 2007. Beyond the peculiar aspects of each technique, the main goal is the interruption of the essential white matter structures forming the projection, association, and commissural intra-hemispheric and inter-hemispheric connection systems. Complete relief from seizures can be expected, particularly in patients with completely unilateral seizure foci. However, incomplete disconnection of fibers is associated with residual seizures. The technical constraints and difficulties involved in identifying anatomic landmarks during surgery may be the reason for incomplete disconnection. To perform the procedure accurately, sufficient knowledge of the anatomy of the limbic system, and surrounding structures is necessary. We demonstrate through dissections the anatomical landmarks and anatomical aspects considered important for the vertical hemispherotomy, including the central core, the corpus callosum and the vascular relationship with ACA. **Materials and Methods:** This anatomical study with photographic documentation was performed in three adult cadaveric heads at the Laboratory of Microneuroanatomy, at State University of Campinas (UNICAMP),São Paulo. **Results:** The Surgical Technique: The step by step disconnection of the hemisphere was performed—with slight modifications—as described by Delalande. The vertical hemispherotomy is divided into 5 main parts:
1. Hyppocampus disconnection + Bulb of callosum's section (identification of the falcotentorial junction).
2. Thalamus disconnection.
3. Callosotomy.
4. Frontal base disconnection.
5. Final disconnection of the Limbic System.

Discussion/Conclusion:The aim of hemispherotomy is to isolate the pathological hemisphere by interrupting the inter-hemispheric and intra -hemispheric connections while preserving the central core. One of the most important recommendations during vertical hemispherotomy is to follow a systematic sequential order during the different phases of disconnection and to proceed to the next step only when the previous stage has been complete. For this reason, to improve the general anatomical understanding, we register a sequential of steps of the vertical hemispherotomy on cadaveric dissection. The vertical hemispherotomy surgery is a well-established treatment for intractable epilepsy secondary to diffuse, usually unilateral hemispheric disease that is intractable to medical therapy . However, even for neurosurgeons, a sound anatomic understanding of this surgery is generally difficult. Therefore a step-by-step understanding of the surgical procedure using cadaveris brains can serve as an intraoperative guide in disconnecting an entire cerebral hemisphere and can be used in most hemispherotomy procedures, especially for beginners in the field of epilepsy surgery.

ANTERIOR TEMPORAL LOBECTOMY VS AMYGDALOHIPPOCAMPECTOMY IN THE TREATMENT OF MESIAL TEMPORAL POLE EPILEPSY: A FUNCTIONAL CONNECTIVITY ANALYSIS

D.A. Gulhote[1], M.P. Couto[2], B.M. Campos[3], J.G. Tamanini1, J.C.P. Silva[1], F.A. Cendes[2], E. Ghizoni[1]

[1]Neurology Dept., FCM, UNICAMP, [2]Neuroimaging Lab., FCM, UNICAMP

Introduction: The objective of this study was to investigate from the perspective of functional connectivity any differences between the selective transsylvian amygdalohippocanpectomy (TSAH) and the non selective temporopolar amygdalohippocanpectomy (TPAH). The main hypothesis was that, from the point of view of postoperative functional connectivity, a selective amygdalohippocampectomy would behave like an anterior temporal lobectomy, which presumably has better seizure control. **Materials and Methods:** The analysis was performed from the processing of MRI images of patients surgically approached with either one of the procedures, TPAH and TSAH, and comparing differences in how the connectivity between the healthy temporal lobe and other regions of the brain were altered. **Results:** When the TSAH group was compared to the TPAH, no increase in connectivity was detected. When doing the inverse comparison, TPAH vs TSAH, the connectivity was only increased in the lingual gyrus. **Discussion/Conclusion**: This study's findings showed an almost insignificant difference in how the neuroconnectivity of the brain was altered after surgery between the two distinct approaches. Thus, despite the anatomical proposal to spare the temporal neocortex the selective approach TSAH seems to have the same functional connectivity consequences as the non selective approach TPAH.

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ASSESSMENT OF THE RELATIONSHIP BETWEEN LIFESTYLE AND DEPRESSION USING THE LE8 SCORE IN THE *NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY* (NHANES) POPULATION, 2013-2018

L. G. R. Lima[1], N. V. Ferreira[2], N. G. Gonçalves[3], J. O. Frade-Guanaes[4]

[1]Adventist University of São Paulo, UNASP, SP, Brazil, [2]Adventist College of Amazonia College, FAAMA, PA, Brazil, [3]University of São Paulo, USP, SP, Brazil, [4]Adventist University of São Paulo, UNASP, SP, Brazil.

Introduction: Depression significantly impacts an individual's quality of life, interfering with interpersonal relationships and influencing the development of

other diseases [1]. There is still controversy between the relationship between lifestyle factors and the manifestation of the disease [2, 3], and therefore, more studies are needed to help understand whether healthy habits can be protective factors in the manifestation of depression. Therefore, the aim of this study was to correlate the manifestation of depression with the Life's Essential 8 (LE8) score in individuals included in the NHANES study between 2013 and 2018. **Materials and Methods:** The sample included participants aged 19 years and above from the American National Health and Nutrition Examination Survey (NHANES) from the years from 2013 to 2018. We created the Life's Essential 8 (LE8) score based on health behaviors (physical activity, diet, nicotine exposure, and sleep) and health-related factors (body mass index, blood lipids, blood glucose, and blood pressure). Depression status was assessed using the Patient Health Questionnaire (PHQ-9). We used logistics regression to evaluate the association between LE8 and depression, adjusted for sociodemographic variables. **Results:** A total of 6,605 participants were included. The sample was predominantly female (51.5%) with a median of 48 years old. Depression was present in 9% of the sample, with a higher prevalence among women (65.5%, p <0.001). Participants with depression exhibited a lower mean LE8 score (37 ± 12.3, p <0.001). Higher LE8 score was associated with lower odds of depression (OR: 0.97, CI 95%: 0.96-0.98, p <0.001), Adherence to physical activity, longer sleep duration, lower exposure to nicotine, body mass index in the normal range, and no history of diabetes were associated with lower odds of depression. **Discussion/Conclusion**: Our results showed that higher score in the LE8 and its individual components was associated with lower odds of depression. Also, these findings underscore the importance of lifestyle and cardiovascular health on mental health, offering opportunities for the development of more comprehensive approaches to and prevention strategies. Thus, this study highlights the need for an ongoing interdisciplinary approach to promote the comprehensive well-being of the population.

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Table 1. Association between individual LE8 habits and depression (adjusted and unadjusted model).

Variable	Model 0			Model 1		
	p	OR	Confidence Interval	p	OR	Confidence Interval
Physical Activity	<0.001	0.9948	0.9925 0.9971	0.0090	0.9967	0.9943 0.9991
Nicotine	<0.001	0.9863	0.9831 0.9895	<0.001	0.9865	0.9830 0.9900
Sleep	<0.001	0.9815	0.9758 0.9872	<0.001	0.9833	0.9772 0.9894
Pressure	<0.001	1.0039	0.9963 1.0116	0.2320	1.0049	0.9968 1.0131
Cholesterol	<0.001	0.9955	0.9885 1.0024	0.6026	0.9982	0.9914 1.0051
Obesity	<0.001	0.9915	0.9885 0.9945	<0.001	0.9921	0.9892 0.9951
Diabetes	<0.001	0.9933	0.9899 0.9967	0.0046	0.9948	0.9912 0.9983
Diet	0.777	0.9985	0.9880 1.0091	0.4474	0.9955	0.9838 1.0074

OR, Odds Ratio. Logistic regression adjusted for age, sex, self-reported race, level of education and marital status.

AUTOMATED BRAIN MODEL FOR THE TEACHING OF NEUROPHYSIOLOGY IN HIGH SCHOOL

A. S. S. Santos [1], H. E. P. Cardoso[1], A. C. C. Assis[1], J. B. Marques[1], E. L. Silva[1]
[1]Institute of Physics, IF, UFMT

Introduction: The interdisciplinary approach between Physics, Biology, and Medicine, among other areas, is essential for understanding neural mechanisms and cognitive processes that occur in the brain. One of the challenges in teaching neuroscience is to demonstrate brain dynamics during a given cognitive task [1]. In this context, the present work describes the development of an experimental model aimed at integrating concepts from neuroscience, specifically neurophysiology, biology, and physics, for high school students, in order to provide an experience that stimulates interest and comprehension of these fundamental disciplines. **Materials and Methods:** The model was built using a variety of materials, including the Arduino microcontroller board, which enabled the construction of the prototype's dynamics, and electronic components, such as the piezoelectric sensor, which served as sensors for the model. The method involved installing electronic components, soldering, treating the circuit board and 3D printing the brain model itself. **Results:** The experimental model resulted in an interactive prototype, where it was possible to visualize the relation between certain stimuli and the brain regions predominantly used in processing such stimuli, allowing for a certain understanding of brain dynamics. In the model, sensors and buttons represent stimuli, such as vision, hearing, touch, among others. In Figure 1(A), we observe the final assembly of the prototype with its respective brain regions, and in Figure 1(B), what happens when the language-related stimulus (speech/auditory) is activated [2]. **Discussion/Conclusion**: In conclusion, the model proves to be an effective tool for neuroscience education in high school, integrating concepts from biology and physics in an accessible manner. Engaging educational resources make learning activities more captivating, accessible, and efficient, enabling students to actively engage and foster curiosity in educational content. This work emphasizes the importance of interdisciplinary educational interventions, contributing to the promotion of innovative teaching methods.

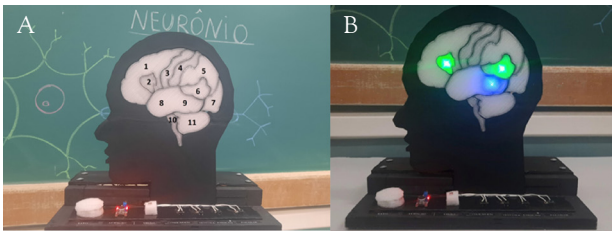

Figure 1. (A) Final assembly of the model with its brain regions 1,2, 3, 4, 5, 6, 7, 8, 9, 10, and 11, which are, respectively, the frontal lobe, Broca's area, motor cortex, sensory cortex, parietal lobe, Wernicke's area, occipital lobe, part 1 of the temporal lobe, part 2 of the temporal lobe, brainstem, and cerebellum. (B) Part 2 of the temporal lobe, Wernicke's area, and Broca's area are activated when the language (speech/auditory) stimulus is triggered.

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BEHAVIORAL AND COGNITIVE ASPECTS OF SENESCENT FEMALE RATS AFTER RESISTANCE PHYSICAL TRAINING OR HORMONAL THERAPY WITH ESTROGEN

Thainá Daguane Esperança[1,4], Beatriz Procópio Stringhetta-Villar[1,4], Débora Prazias Cavalcante[1,4], Luana Galante Douradinho[1,4], Rafael Pereira[2], Fernanda Barbosa Lima[3], Rita Cássia Menegati Dornelles[1,4,5]

[1] Multicentric Graduate Program in Physiological Sciences– SBFis/UNESP, São Paulo State University, Araçatuba, São Paulo, Brazil, [2] Integrative Physiology Research Center, Department of Biological Sciences, Universidade Estadual do Sudoeste da Bahia (UESB), Jequie 45210-506, Bahia, Brazil, [3] Federal University of Santa Catarina (UFSC), Florianópolis, Santa Catarina, Brazil, [4]Aging Biology Research Group, [5] Department of Basic Sciences, São Paulo State University (UNESP), School of Dentistry, Araçatuba, SP, Brazil.

Introduction: Aging results from the gradual cellular functional decline, where in women, the first system to age is the reproductive system. The transition from a regular to an irregular reproductive cycle, presenting fluctuations and decreases in the synthesis and secretion of progesterone and estrogen, characterizes perimenopause, and this period is essential for promoting health. Studies suggest that these hormonal changes can contribute to behavioral and neuroprotective changes, and estradiol and physical exercise can modulate such impairments. Above all, is perimenopause a critical window where exogenous factors can positively affect female physiology? Given this, this study aimed to evaluate anxiolytic responses, memory, and neurodegeneration after estrogen hormone therapy (EHT) or resistance physical training (RPT) in reproductive senescence. **Materials and Methods:** Rats in periestropause adherent to physical exercise were randomly distributed and submitted to the untrained (NT; n = 20), RPT (n = 10) and EHT (n = 10) groups (CEUA process nº 0585-2021) for 4 months. Initially (17 months) and at the end of the experimental period (21 months) the animals performed: open field test (OF) and object recognition (RO). At the end of the experimental period, animals were perfused and the brains were sent for histological analysis (Nissl staining). Data were expressed as mean ± SEM and the null hypothesis rejection level was set at 5% ($p < 0.05$). **Results:** Both 21Mo/RPT and 21Mo/E_2 groups demonstrated an anxiolytic profile in the OF test when compared to the 17Mo group. RO demonstrated

improved recognition in the 21Mo/RPT and 21Mo/E_2 groups over the 21Mo/Veh and 21Mo/NT groups, respectively. Short-term memory for the 21Mo/RPT group was significantly greater for the 21Mo/NT and 17Mo groups, while EHT showed no statistical difference. Long-term memory was superior in both groups 21Mo/RPT and 21Mo/E_2 when compared to control groups of the same age, in addition to the 17Mo group. The rats that received the interventions had a greater number of neural cells with Nissl corpuscle labeling compared to their control groups. **Discussion/Conclusion**: The results show that chronically performing resistance physical training or estrogen hormone therapy was an effective strategy to modulate the anxiolytic and non-anxiogenic profile, improving exploratory and mnemonic capabilities. Additionally, these approaches help preserve hippocampal neuronal cells. These findings highlight the benefits of RPT and EHT during the reproductive cycle transition, suggesting a reestablishment of previously performed functions. Moreover, these results point to EHT and RPT as possible preventive resources for neurodegenerative neuropsychological disorders.

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BILATERAL THALAMIC ATROPHY AND REDUCED IPSILATERAL PARAHIPPOCAMPAL CORTICAL SURFACE AREA APPEARS TO DISTINGUISH THE PATTERNS OF CLINICAL RESPONSE IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

Pamela Regina Henning[1], Aline de Fátima Dias[1], William Souza Martins Ferreira[1], Brunno Machado de Campos[1], Marina Koutsodontis Machado Alvim[1], Clarissa Lin Yasuda[1], Fernando Cendes[1]

[1]Laboratory of Neuroimaging, Department of Neurology, UNICAMP

Introduction: Epilepsy is a disabling and chronic neurologic condition. Among adult focal epilepsies mesial temporal lobe epilepsy (mTLE) associated with hippocampal sclerosis (HS) is the most common. Some damage and brain atrophy, duration-related, may occur in pharmacoresistant mTLE. Structural Magnetic Resonance Imaging (MRI) is overall suggestive of progressive atrophy in these patients; however, it is not clear a direct association with recurrent seizures. Our objective is to analyze the thickness, cortical surface area and subcortical volume in patients with long term HS-mTLE [1,2,3]. **Objective**: To correlate response to antiseizure medication (ASM) with cortical surface area (CSA) and subcortical volumes (SV) in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS). **Materials and Methods:** 111 patients with mTLE-HS who did not undergo surgery because they refused it, had contraindications, or had good seizure control with ASM (mean follow-up of 21.8 years) were categorized in three groups: pharmacoresponsive (seizure-free in the last two years or more), fluctuating-response (seizure-freedom periods of one year or longer) and pharmacoresistant (never had a seizure-free period of more than one year). T1-weighted MRIs (1x1x1mm) were processed with *Freesurfer*-6.0. We analyzed the following regions of interest for CSA: inferior, middle and superior temporal gyrus, parahippocampal gyrus and insula. Volumes of thalamus, hippocampus and amygdala, along with the CSA from each ASM response-groups were compared with 112 controls. **Results:** Groups were balanced for age, sex, and side of HS. Each ASM response-group had 37 patients. Compared with controls, ipsilateral hippocampal volumes were reduced in all groups ($p<0.0001$) without difference among groups. There was no difference in the contralateral hippocampal volumes among groups. Volumes of ipsilateral and contralateral thalami were reduced in the pharmacoresistant group ($p<0.003$), and the contralateral thalamus was reduced in pharmacoresponsive and fluctuating-response groups ($p<0.006$). Amygdala was reduced in the pharmacoresponsive group ($p=0.03$). Ipsilateral parahippocampal CSA was reduced in the pharmacoresistant group ($p=0.013$). Other CSA did not differ among groups. **Discussion/Conclusion**: Bilateral thalamic atrophy and reduced ipsilateral parahippocampal CSA appears to distinguish pharmacoresistant mTLE-HS from those with better response to ASM.

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BRAIN CORTICAL THICKNESS IN MILD COGNITIVE IMPAIRMENT AFTER 24 WEEKS OF RESISTANCE TRAINING PROTOCOL

I. C. Ribeiro[1], C. V. L. Teixeira[2], G. B. Silva[3], T. J. R. Rezende[4], M. C. Uchida[3], I. K. Aventurato[1], M. C. R. Silva[1], B. C. Gonçalves[1], P. T. Fernandes[5], T. N. C. Magalhães[6], B. M. Campos[7], F. Cendes[4,7], M. L. F. Balthazar[1]

[1] Laboratory of Imaging and Biomarkers in Cognitive Disorders, School of Medical Sciences, UNICAMP, [2] Rockefeller Neuroscience Institute, West Virginia University, [3] Applied Kinesiology Laboratory, School of Physical Education, UNICAMP, [4]Department of Neurology, School of Medical Sciences, UNICAMP,[5] Sport's Psychology and Neurosciences Study Group, School of Physical Education, UNICAMP, [6] Department of Psychological and Brain Sciences, Institute for Neuroscience, Texas A&M University, [7] Neuroimaging Laboratory, School of Medical Sciences, UNICAMP.

Introduction: Mild cognitive impairment (MCI) is a diagnostic term applied to individuals who are between preserved cognition and dementia. These individuals have their cognitive function reduced beyond what is considered normal in aging, but they maintain their functional independence[1]. The practice of physical exercise is beneficial for the cognition and physical function of elderly people with MCI and has previously been related to changes in cerebral cortical thickness[2]. However, the relationship between cortical thickness and resistance training has not yet been fully clarified. This investigation aimed to verify whether there are changes in cortical thickness in some of the Alzheimer's signature brain areas[3] in elderly people with MCI who practiced resistance training over 24 weeks. **Materials and Methods:** 38 elderly people with MCI were included in this analysis. 19 were part of the control group and 19 were part of the intervention group with resistance exercises. The exercise group performed two weekly sessions of 8 resistance exercises (3 sets of 10 repetitions at 80% of 1-RM) for 24 weeks. All participants were evaluated on an MRI (3T Achieva - Intera PHILIPS) before and after the intervention. Images were processed in FreeSurfer using a longitudinal analysis protocol. The brain areas investigated were the middle frontal gyrus, superior frontal gyrus, angular gyrus, supramarginal gyrus, inferior temporal gyrus, and medial temporal gyrus. For statistical analysis, an average of the right and left volumes of each area was considered. A mixed and repeated measures ANOVA corrected for Bonferroni and using age as a covariate was used. Significance was considered in $P<0.05$ and we used the IBM SPSS Statistics 22 software. **Results:** Comparison between groups at baseline showed that both groups presented similar thickness in the areas analyzed before the intervention period ($p > 0.05$). The analysis between times showed no significant differences for both groups in all brain areas evaluated ($p > 0.05$; Table 1). **Conclusion:** 24 weeks of resistance training was not sufficient to influence brain thickness of the AD signature areas in patients with MCI.

Table 1. Brain thickness of the AD signature areas.

		Baseline Mean (SD)	Follow-up Mean (SD)	p-value
Middle frontal gyrus	Control Group	1.64 ± 2.16	1.64 ± 2.10	0.79
	Exercise Group	1.65 ± 2.09	1.65 ± 2.09	0.63
Superior frontal gyrus	Control Group	1.78 ± 2.43	1.76 ± 2.50	0.14
	Exercise Group	1.81 ± 2.31	1.80 ± 2.29	0.39
Angular gyrus	Control Group	1.65 ± 2.04	1.63 ± 2.06	0.27
	Exercise Group	1.71 ± 1.87	1.70 ± 1.86	0.41
Supramarginal gyrus	Control Group	1.70 ± 2.05	1.69 ± 2.04	0.75
	Exercise Group	1.74 ± 2.00	1.73 ± 2.01	0.26
Inferior temporal gyrus	Control Group	1.91 ± 2.59	1.90 ± 2.49	0.17
	Exercise Group	1.85 ± 2.17	1.85 ± 2.15	0.88
Medial temporal gyrus	Control Group	1.89 ± 2.51	1.88 ± 2.48	0.15
	Exercise Group	1.89 ± 2.18	1.88 ± 2.18	0.62

Mean: E-06 values. SD (Standard Deviation): E-07 values. P-value considering age covariate: 67,93 years old.

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CANNABIDIOL EFFECTS ON GLUCOSE METABOLISM AND AUTOPHAGY IN MK-801-TREATED HUMAN ASTROCYTES: INSIGHTS FOR SCHIZOPHRENIA

D. Silva-Amaral[1], T. A. M. Vrechi[1], D. Martins-de-Souza[1,2,3,4]

[1]Department of Biochemistry and Tissue Biology, UNICAMP. [2]D'Or Institute for Research and Education (IDOR). [3]Instituto Nacional de Biomarcadores Em Neuropsiquiatria (INBION), Conselho Nacional de Desenvolvimento Científico E Tecnológico (CNPq). [4]Experimental Medicine Research Cluster (EMRC), UNICAMP.

Introduction: Schizophrenia is an incurable psychiatric disorder that affects approximately 23,6 million people worldwide [1]. Although antipsychotic drugs are the first-line treatment for symptoms control, they are not completely effective for several aspects of the disorder's symptomatology, besides leading to various side effects [2]. Dysregulated cellular processes, including glucose metabolism and dysfunctions in autophagic flux with the activation of the mTOR, are implicated in schizophrenia and can be reproduced by NMDA receptor antagonists such as MK-801 [3-5]. Clinical and neurobiological findings suggest that cannabidiol (CBD), the main non-psychomimetic compound of *Cannabis sativa*, may be employed as an alternative treatment for schizophrenia, but its mechanism is not well defined [4,6]. This project aims to investigate the interplay of CBD with mTOR-mediated autophagy and its potential neuroprotective mechanisms *in vitro* using astrocytes treated with MK-801. **Materials and Methods:** Neural stem cells-derived human astrocytes will be treated separately and concomitantly with MK-801 and CBD. To elucidate the potential mechanisms by which CBD exerts a neuroprotective role in astrocytes, they will be also treated with AM251 (cannabinoid receptor type 1 antagonist), AM630 (cannabinoid receptor type 2 antagonist), WAY100635 (selective serotonin receptor 1A antagonist), and capsazepine (TRPV1 receptor antagonist) if previous experiments reveal a neuroprotective effect of CBD. Treated astrocytes will be evaluated using techniques such as fluorescence microscopy, western blot, proteomics, and high-resolution respirometry (Seahorse), examining the mutual interactions of changes in the autophagic process and glucose metabolism modulated by CBD. **Results:** Immunofluorescence results indicate the presence of CB1, CB2, and NMDA receptors in astrocytes. In addition, we evaluated cell viability after treatment with different concentrations of CBD and MK-801 using the MTT assay. We observed that concentrations up to 10μM of CBD and 50μM of MK-801 did not affect cell viability negatively after 24 hours of treatment. Autophagic flux was investigated in response to CBD (2 hours) and MK-801 (4 hours) in the presence or absence of the autophagic inhibitor ammonium chloride (10 mM) added in the last hour of treatment. We observed a trend toward an increase in autophagic flux with CBD (10μM) and a decrease with MK-801 (50μM), although quantitative analysis requires more experiments to draw a definitive conclusion. **Discussion/Conclusion**: The results highlight the presence of the main pharmacological targets in astrocytes, validating the choice of cellular model. Moreover, the safe doses of CBD and MK-801 defined through cell viability assays provide a basis for subsequent experiments such as Western blot assays. Our preliminary data suggest that MK-801 and CBD can modulate autophagic flux, opening new research perspectives. However, more studies are needed for a complete statistical analysis and a deeper understanding of these mechanisms.

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CEREBRAL ABNORMALITIES IN CHILDREN WITH PHARMACORESISTANT EPILEPSY AND MTORPATHIES

S.V. Gouvêa[1], B. M. Campos[2], F. Cendes[2]; A. C. Coan[1]
[1]Neurology Dept., FCM, UNICAMP, [2]Neuroimage Lab., UNICAMP

Introduction: mTORpathies are related to pharmacoresistant epilepsy and other neuropsychiatric comorbidities, as autism spectrum disorder (ASD) and intellectual disability[1,2,3]. Thys work evaluated cerebral abnormalities in the white matter (WM) and gray matter (GM) and correlate to the clinical phenotype of children with pharmacoresistant epilepsies associated with mTORpathies. **Materials and Methods:** We included eight children between one and 18 years of age, with pharmacoresistant epilepsies associated with mTORpathies: three with focal cortical dysplasia (FCD), three with tuberous sclerosis complex (TSC) and two with pathogenic genetic variants of *NPRL2* or *NPRL3* genes. We looked for atrophy patterns of WM and GM using MRI post-processing T1-weighted images with voxel-based morphometry (VBM). Each patient was individually compared with a group of age-matched controls (+ or – two years). **Results:** All patients presented WM atrophy, seven with a justacortical pattern and three with a deep white matter pattern. Also, all patients presented GM atrophy, half with localized atrophies and the other half with a diffuse pattern. In three cases, we compared the longitudinal evolution with a minimum of two years between the MRIs. We observed progression of GM atrophy in all of them and progression of WM atrophy in two patients. There was no relation between the pattern of WM atrophy (justacortical or deep WM) or GM atrophy (localized or diffuse) and the age of seizures onset, epilepsy duration or cognitive comorbidities. **Discussion/Conclusion**: Children with pharmacoresistent epilepsies associated with mTORpathies presented diffuse cerebral abnormalities, particularly in WM. Our patients presented two patterns of WM and in GM abnormalities, as well as progression of atrophy in WM and GM.

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CHALLENGING EXERCISES IMPROVE COGNITIVE FUNCTION IN PEOPLE WITH PARKINSON'S DISEASE

Dimateo, E. M.[1,3], Vergari-Filho, M.[1,2], Almeida, F.[1,3], Nucci, M. P.[3], Batista, A.[3], Barbosa, E. R.[4], Horak, F. B.[5], Ugrinowitsch, C.[6], Silva-Batista, C.[1,5]
[1]Exercise Neuroscience Research Group, University of São Paulo, SP, Brazil; [2]School of Arts, Sciences and Humanities, University of São Paulo, SP, Brazil; [3]Department of Radiology, University of São Paulo, SP, Brazil; [4]Movement Disorders Clinic, Department of Neurology, School of Medicine of the University of São Paulo, SP, Brazil; [5]Department of Neurology, Oregon Health and Science University, Portland, Oregon, USA; [6]Laboratory of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport, University of São Paulo, SP, Brazil.

Introduction: Cognitive decline may be a risk factor for freezing of gait (FOG) in Parkinson's disease (PD). Challenging exercises have been suggested as potential rehabilitation strategies to decrease FOG severity and improve cognition; however, it is unknown whether improvement in cognition would explain decreased FOG severity following exercise. We evaluated the effects of the adapted resistance training with instability (ARTI-challenging exercises) compared with traditional motor rehabilitation (TMR-without challenging exercises) on cognitive function in people with FOG of PD. We also verified whether cognitive improvement predicts the FOG improvement. **Materials and Methods:** Participants were randomized either to the experimental group (ARTI, n=17) or to the active control group (TMR, n=15). Both training groups performed exercises 3 times a week for 12 weeks (80-90 min each session). FOG severity was assessed with a FOG ratio from inertial sensors during a 360-degree turning in place task. Frontal executive function (Frontal Assessment Battery-FAB), global cognition (Montreal Cognitive Assessment-MoCA), attention, and psychomotor speed (Digit Symbol Substitution Test-DSST) were evaluated before and after interventions. The study was registered in the Brazilian Clinical Trials Registry (RBR-83VB6B). **Results:** There were no differences between ARTI and TMR for any of the outcomes at posttraining ($P>0.05$). Only the ARTI group improved FOG ratio, FAB, MoCA, and DSST scores from pre- to post-training ($P<0.05$). The changes in FAB scores explained the changes in FOG ratio following ARTI ($R^2=0.47$, $P=0.002$). **Discussion/Conclusion**: This pilot study suggests that ARTI, a challenging and complex motor training, improves cognitive function in people with FOG of PD. Improvements in FAB scores help explain decreased FOG severity after challenging and complex motor training.

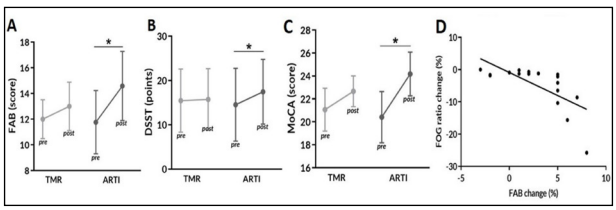

Figure 1. Mean ± standard deviation for the FAB (panel A), DSST (panel B), MoCA (panel C) outcomes at pre- and posttraining for the TMR and the ARTI groups. *Difference between pre and posttraining values ($P\leq0.05$). Panel D shows the correlation of changes in FOG ratio with changes in FAB following ARTI.

CHANGES IN AFFERENT INPUT AND THE ASSESSMENT OF SOMATOSENSORY EVOKED POTENTIALS – A PILOT STUDY

C. D. Lima[1,2], C. V. Ruas[1,2,3], B. M. Carlos[1,2], A. J. Blazevich[3], G. Castellano[1,2]
[1]Neurophysics Group, IFGW, UNICAMP, [2]BRAINN-FAPESP, [3]School of Medical and Health Sciences, Edith Cowan University, Australia.

Introduction: Maximum ankle joint range of motion (ROM_{max}) is important for functional independence and is associated with the level of motor recovery measured after an intervention following an illness or injury. Stroke survivors

can develop spasticity (muscle stiffness) immediately after the event, which can persist for years, thus significantly impairing ROM_{max}. The purpose of the present pilot study was to determine whether somatosensory evoked potentials (SSEPs) could be evoked in a person without stroke and without detectible spasticity, with the aim of using SSEP measurements to monitor outcomes of future interventions in people with stroke-induced spasticity. **Materials and Methods:** One healthy male (35 y, 1.69 cm, 81 kg) free from musculoskeletal injury participated in one testing session lasting approximately 2.5 h. Ankle joint ROM_{max} was tested using a motion tracker (KinesiOS, São Paulo, Brazil) to subsequently determine 80% of his ROM_{max}, which occurred at –26° in plantarflexion and 25° in dorsiflexion. Subsequently, the full H-reflex–M-wave recruitment curve was established at -26°, 0° (neutral) and 25° joint angles to find the stimulus intensities at H_{max} and M_{max}. The recruitment curve was tested while recording the stimulus responses at the tibial nerve (using electromyography - EMG) and at the sensory cortex Cz-Fz site (using electroencephalography - EEG; averaged over 500 data points) to quantify changes in proprioceptive input with the changes in muscle length. SSEP amplitude was measured at p37 (37 ms after the stimulus artifact), which is a reference for lower limb SSEPs. **Results:** H_{max} and M_{max} at 0° were 22% higher and 9% lower than in plantarflexion and 84% and 11% higher than in dorsiflexion. They were also 79% and 18% higher in plantarflexion than dorsiflexion (plantarflexion as reference). Thus, H:M ratios were 28% and 84% higher at 0° than plantarflexion and dorsiflexion, and 78% higher in plantarflexion than dorsiflexion. SSEPs amplitudes showed more inhibition in plantarflexion than dorsiflexion (16%) and less inhibition at 0° than in plantarflexion (59%). Finally, less inhibition was observed at 0° than in dorsiflexion (52%). **Discussion/Conclusion**: There was more inhibition of SSEPs amplitudes (values are more negative in p37) in dorsiflexion and plantarflexion, indicating that Ia afferent responses triggered by muscle lengthening may be an important driver of proprioceptive responses to the sensory cortex. Further, the H:M ratio was lower in dorsiflexion and plantarflexion than 0°, largely due to H-reflex depression. Therefore, plantarflexor stretch (i.e. dorsiflexion) may have increased presynaptic inhibition, leading to inhibition at the sensory cortex potentially through reciprocal inhibition. From this one participant there is clearly detectable inhibition at both spinal (H-reflex) and cortical (SSEP) levels as the muscles are stretched. It will be interesting to determine whether this is observed in people with stroke-induced spasticity, and whether the condition is improved by physical interventions.

Table 1. Soleus EMG and Cz-Fz EEG at plantarflexion, 0° (neutral) and dorsiflexion positions.

	Plantarflexion	0°	Dorsiflexion
$H_{max\ (mV)}$	1.51	1.94	0.31
$M_{max\ (mV)}$	8.59	7.88	7.04
H:M ratio	0.18	0.25	0.04
SSEP p37 (μV)	−76	−31	−64

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CHARACTERIZATION OF BRAIN CHANGES IN PATIENTS WITH DIFFERENT TYPES OF DEMENTIA USING FUNCTIONAL CONNECTIVITY APPLIED TO EEG DATA

G. L. D. Estadulho[1], P. F. G. Vazquez[1,2], G. Castellano[1,2]
[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN-FAPESP

Introduction: Dementia encompasses a spectrum of symptoms resulting from the dysfunction of specific brain cells, affecting cognition, behavior, and motor function. Among the various forms, Alzheimer's Disease (AD) and Frontotemporal Dementia (FTD) are prominent. While AD primarily affects memory and communication between brain cells due to the accumulation of beta-amyloid plaques and neurofibrillary tangles, FTD results in focal degeneration in the frontal and temporal lobes, impacting personality and behavior. Despite their distinct etiologies, AD and FTD share clinical similarities, often leading to misdiagnosis [1]. Accurate differentiation is crucial for appropriate treatment and support strategies, considering the progressive and irreversible nature of both conditions. Therefore, innovative approaches are warranted to enhance diagnostic precision. Electroencephalography (EEG) stands out as a non-invasive, cost-effective technique for measuring brain dynamics. Recent advancements in EEG signal processing and classification algorithms have shown promise in diagnosing various forms of dementia. This study aims to employ functional connectivity (FC) and graph metrics to EEG data from patients diagnosed with AD, FTD, and healthy controls (HC), for disease characterization and differentiation. **Materials and Methods:** For this study, we used EEG data (19 electrodes, 500 Hz rate) from the OpenNeuro platform, collected for the study [2]. This database consists of 88 participants diagnosed with AD, FTD, and HC, but we used only 10 subjects per group for the present study (AD: age 72±8, 7 men; FTD: age 68±7, 3 men; HC: age 71±8, 7 men). Preprocessing was carried out using EEGLAB [3], involving data integrity evaluation, artifact removal and bandpass filtering (1-45 Hz). The Brainstorm software [4] was used for filtering the signals into delta, theta, alpha, beta and gamma bands, segmenting them into 1 s epochs (with 50% overlap), and FC computation for each epoch/band. The FC method used was the Imaginary Coherence and the strength graph metric was obtained. Kruskal-Wallis one-way ANOVA was applied to the strength data for each electrode/band to differentiate among the three groups. **Results:** We found no significant differences among the group's strength distributions. **Discussion/Conclusion:** Our negative results may be due to the small sample size. Also, the FC method employed may not be the best to detect differences among these groups, and other methods such as phase lag index and motif synchronization could be applied [5]. The same can be said to the evaluated graph metric (strength); other graph metrics such as betweenness centrality, eigenvector centrality and assortativity could be investigated. Finally, in the future we intend to apply machine learning methods to attempt to differentiate among these groups.

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4), CAPES (finance code 001).

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COGNITIVE PERFORMANCE AND GM IN SCD AND MCI IN AT(N)

B. C. Gonçalves[1], M. L. F. Balthazar[1], M. C.R. Silva[1], Í. K. Aventurato[1], I. C. Ribeiro[1], L. Rizzi[1]
[1]Neurocience Group, FCM, UNICAMP.

Introduction: Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI) are the potentially earliest symptomatic phase of Alzheimer's disease. The AT(N) is an important system in the early diagnosis of SCD and MCI. To evaluate the neuropsychological and structural GM in patients with SCD and MCI, subdivided according to the AT(N) classification. Thus, the objective of the present study is to evaluate the neuropsychological and structural neuroimaging profile in patients with SCD and MCI, subdivided according to the AT(N) classification: NB, continuum AD, and SNAP. **Materials and Methods:** 72 individuals (16 SCD and 56 MCI) were selected and categorized into 3 subgroups: normal biomarkers (NB) for AD [A-T-(N)-]; AD continuum (A+); and SNAP [A-T+(N), A-T-(N)+ and A-T+(N)+]. MANOVA was performed to evaluate the difference in neuropsychological compounds (memory, attention/executive functions, and verbal fluency) between groups. ANCOVA were performed for each of the compounds. A linear regression was performed to verify differences in GM between groups. The correlation between neuropsychological compounds and GM of the groups was verified, followed by correction for multiple comparisons. **Results:** In the composite of attention/executive functions, there was a significant difference in the SNAP group ($p < 0.05$). There was no significant difference between

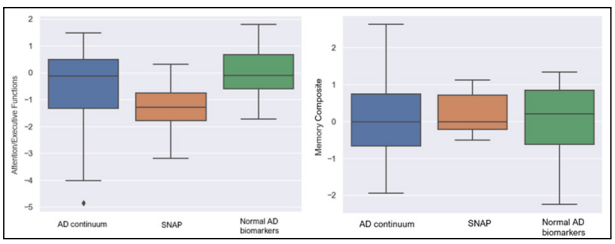

Figure 1. Results of the AT(N) subgroups in the Attention/Executive Functions Composite and Memory Composite. A - Attention/Executive Functions Composite. B - Memory Composite.

groups in the memory (p=0.91) and verbal fluency (p=0.07). There was a difference in the GM of the left ACC: SNAP > AD continuum (p=0.008, uncorrected) and, the left cuneus: SNAP > AD continuum and NB (p=0.01, uncorrected). But results did not survive after correction for multiple comparisons (FDR 10%). We found a correlation between the left fusiform gyrus and the memory composite in the AD continuum group (p-value < 0.001, uncorrected), but there was no significance after adjustment for multiple comparisons. **Discussion/Conclusion**: in conclusion, the SNAP subgroup performed worse on the attention/executive functions composite when compared to the NB and AD continuum subgroups.

COMPUTATIONAL INSIGHTS INTO POLYMORPHISMS OF THE *C9ORF72* GENE AND THEIR PATHOGENIC ROLE IN NEUROGENETIC DISORDERS

João Pedro Perin[1], Bruno Cateb Resende de Oliveira[1], Tereza Raquel Xavier Viana[2], Larissa Teodoro Rabi[2,3,4], Natássia Elena Bufalo[1,3,5]

[1] Department of Medicine, São Leopoldo Mandic and Research Center, Campinas/SP, Brazil; [2] Department of Biomedicine, Nossa Senhora do Patrocínio University Center (CEUNSP), Itu/SP, Brazil; [3] Laboratory of Cancer Molecular Genetics, Faculty of Medical Sciences, State University of Campinas (UNICAMP), Campinas/SP, Brazil; [4] Institute of Health Sciences, Paulista University (UNIP), Campinas/SP, Brazil; [5] Department of Medicine, Max Planck University Center, Campinas/SP, Brazil.

Introduction: Chromosome 9 open reading frame 72 (C9ORF72) is involved in a GTPase-interacting complex that influences the regulation of autophagy and inflammation. Moreover, C9ORF72 serves as a link between neurodegeneration, inflammation, and immune responses, with genetic evidence connecting autophagy/lysosomal pathway genes with neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and other neurodegenerative conditions. This study aimed to identify molecular biomarkers and potential pharmacological interventions to prevent or improve the neurological health challenges faced by individuals affected by these disorders.[1,2] **Materials and Methods:** This study employed computational analysis to assess the effects of missense polymorphisms on protein structure, function, flexibility, and stability using 13 bioinformatic tools. These tools include PredictSNP1 (PredictSNP, SIFT, PolyPhen-1, PolyPhen-2, MAPP, PhD-SNP, SNAP, PANTHER, and nsSNPAnalyzer), iStable (iStable, MuPRO, and I- Mutant), and DynaMut. **Results:** A range of *in silico* tools have provided new insights into the role of numerous DNA polymorphisms in predisposing and contributing to the development of neurological diseases. Within the *C9ORF72* gene, 404 missense polymorphisms were documented in the dbSNP databank, 85 of which were evaluated in this study because of their potential to induce amino acid changes in protein structure. Of these, eleven amino acid alterations (S2L-rs149095486, P24L-rs373581954, R107H- rs145645318, C215R-rs113939233, V292M-rs201261393, R296Q-rs370472336, W340R- rs371377376, S429P-rs200703028, L433V--rs368371587, K434E-rs376385318, G465R- rs369166616) were classified as deleterious by at least 5 of the bioinformatics tools within the PredictSNP1.0 consensus. The rs369166616 variant induces a cytosine-to-guanine alteration in DNA, leading to the substitution of glycine (G) with arginine (R) at position 465 of the guanine nucleotide exchange factor protein chain. This variant, classified as deleterious by seven tools within the PredictSNP1.0 consensus, also exhibits a decrease in protein stability according to analyses conducted by iStable (Conf. Score: 0.66) and MuPRO (Conf. Score: -0.38), and I-Mutant2.0 (DDG: -0.26). Moreover, upon assessing the ability to interact with adjacent amino acids in the protein structure (using Dynamut), the appearance of four hydrophobic contacts was observed, along with a prominent hydrophobic interaction. Additionally, three water-mediated hydrogen bonds and two hydrogen bonds were observed, indicating a reduction in molecular flexibility. **Discussion/Conclusion**: Preliminary *in silico* analysis revealed that the rs369166616 polymorphism within the *C9ORF72* gene plays a role in altering protein structure, resulting in reduced stability. This polymorphism facilitates novel interactions with adjacent amino acids, leading to structural changes and decreased protein flexibility, thereby complicating the interactions with other molecules. Further investigation of patients with neurological disorders is imperative, as this polymorphism could potentially serve as a crucial clinical marker for assessing risk, diagnosing conditions, predicting outcomes, or as a focal point for precision therapy.

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CONTENT SHAPES ASSOCIATION BETWEEN CONNECTOME SIMILARITIES AND METASTABILITY IN FMRI

T.D. Pereira[1], A.M. Cravo[2], C. E. Biazoli Jr[2]

[1]Graduate Program in Neuroscience and Cognition – UFABC, [2]Center of Mathematics, Computing and Cognition. ABC Federal University, São Bernardo do Campo, São Paulo, Brazil.

Introduction: A promising approach to model the brain is considering it as a metastable system that alternates between integration and segregation of regions. [1] Furthermore, recent work with MEG associates brain FC identification (i.e. connectome brain fingerprinting) with non-linear features of the signal. [2,3] In addition, movie stimuli have been presenting technical, methodological, cognitive and affective advantages. [4,5] However, each film has a specific narrative and different range of low and high features that must be considered. This work intends to investigate the correlation between metastability, identifiability at the global and large-scale functional network levels with naturalistic fMRI. Moreover, we sought to investigate how this relation is modulated by movie content. **Materials and Methods:** All images were acquired using a 1.5T Siemens MAGNETOM Avanto scanner (TR = 1 s). Eighty-six subjects were assigned to 10 different movies and watched each film in its entirety. Volumes were analyzed using the Gordon Parcellation (333 ROIs), and global meta-stability, within 8 RSNs, Similarity Between-Subjects, and Stability Within-Subjects were calculated with sliding window technique. These measures were computed over the entire duration of 91 minutes (the shortest film) by combining data from all 10 movies. Additionally, separate calculations were performed for two specific movies: a romantic-comedy (500 Days of Summer, 91 minutes, 5470 timepoints) and a documentary (Citizenfour, 113 minutes, 6780 timepoints). **Results:** We found a correlation between Similarity Between-Subjects and metastability ($r=0.634$, $p<0.001$) using an 11-minute sliding window. Attentional networks showed an even stronger correlation, with FPN ($r=0.866$, $p<0.001$), DAN ($r=0.710$, $p<0.001$), and CON ($r=0.658$, $p<0.001$). On the other hand, Stability Within-Subjects only exhibited correlation in primary networks, such as Motor ($r=0.534$, $p<0.001$) and Auditory ($r=0.428$, $p<0.001$). In the case of the two separate movies, the romantic comedy ($r=0.837$, $p<0.001$) showed a stronger correlation than the documentary ($r=0.566$, $p<0.001$). All eight networks demonstrated correlation in the first movie, while the documentary correlated in only two networks. **Discussion/Conclusion**: In this study, a notable connection was observed between levels of metastability and Similarity Between-Subjects while participants watched movies, encompassing both whole-brain and network levels, particularly within attentional networks. Additionally, a correlation was identified between metastability and Stability Within-Subjects, specifically within primary sensory-motor cortical networks. These findings not only extend our understanding of the relationship between identifiability and non-linear dynamics seen in MEG but also align with developmental processes. Networks stabilizing earlier in brain development, such as sensory-motor networks, exhibited greater Stability Within-Subjects, while attentional networks were more influenced by environmental stimuli. Furthermore, the association between identifiability and metastability varied based on the stimuli content, suggesting that distinct features of movies are linked to fMRI nonlinear dynamics.

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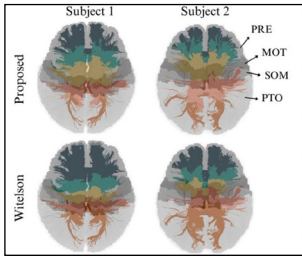
CORPUS CALLOSUM PARCELLATION ANALYSIS THROUGH TRACTOGRAPHY AND CORTICAL CONNECTION CONSISTENCY

C. P. Santana[1], J. Rodrigues[1], T. Abreu[1], P. Julio[2], S. Appenzeller[2], L. Rittner[1]

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

Introduction: Many methods were proposed to subdivide (parcellate) the Corpus Callosum (CC) into smaller regions, from geometrical to medical imaging driven approaches. They generate distinct CC subdivisions, but the absence of a gold standard makes it difficult to define the best one. In this study, we compared our proposed (diffusion MRI driven) [1] and Witelson (geometrical) [2] parcellations using tractography to assess the coherence of their connection to cortical regions. **Materials and Methods:** The CC was segmented using a CNN-based method [3] on five preprocessed dMRI volumes from HCP [4], inclusion and exclusion regions were defined through FreeSurfer [5], and

tractography was performed on MRtrix [6]. Tractograms were subdivided according to the CC parcellations and the relationship between them and four cortical regions – prefrontal (PRE), motor (MOT), somatosensory (SOM), parietal/temporal/occipital (PTO) – was assessed visually and quantitatively (percentage of streamlines ending in each cortical region). **Results:** We found Parcels II, III, and V of the proposed CC parcellation to be more consistently connected to specific cortical regions (PRE, PRE/MOT, and PTO, respectively), both visually (Fig1.A) and by percentage of streamlines (Fig1.B). On Parcel IV, Witelson approach generally presents lower standard deviations, with more connections to MOT, while the proposed method presents connections distributed between the cortical regions. For Parcel I, both methods presented almost 100% of connection to PRE, with Witelson parcellation connected to a larger extent of PRE. **Discussion/Conclusion**: The proposed parcellation seems to exhibit more consistent connections between most CC parcels and cortical regions analyzed. This may be due to its data-driven nature, adapting to specific subject's characteristics. The exception of Parcel IV might be related to its smaller size on Witelson's method. Further studies should include more subjects and other cortical regions.



	CC Parcel				
CR	Parc	II	III	IV	V
PRE	P	99±1	75±19	7±10	0±0
	W	97±5	58±22	3±4	0±0
MOT	P	1±1	25±19	36±33	2±4
	W	3±5	42±23	80±19	7±13
SOM	P	0±0	0±0	17±15	1±2
	W	0±0	0±0	12±15	11±8
PTO	P	0±0	0±0	40±32	97±5
	W	0±0	0±0	5±7	81±12

Figure 1. Parc stands for parcellation, P for proposed, and W for Witelson. A – Tractography results for 2 subjects. Parcels I-V colored (top to bottom) and cortical regions in gray. B – Percentage of streamlines (mean ± std) from CC Parcel to Cortical Region (CR).

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CORTICAL CORRELATIONS OF CSF NEUROGRANIN, VILIP-1, ALPHA-SYNUCLEIN, AND NFL IN SCD AND MCI ACCORDING TO AMYLOID STATUS

Emanuel Rodrigues Guimarães[1,2], Brunno Machado de Campos[2], Isadora Cristina Ribeiro[1,2], Ítalo Karmann Aventurato[1,2,3], Marjorie Cristina Rocha da Silva[1,2], Liara Rizzi[1,2,3,4] & Marcio Luiz Figueredo Balthazar[1,2,3]

[1]Laboratório de Imagem e Biomarcadores em Cognição (LIMBIC), Universidade Estadual de Campinas (UNICAMP), Campinas, Brazil. [2]Instituto Brasileiro de Neurociências e Neurotecnologia (BRAINN), Universidade Estadual de Campinas (UNICAMP), Campinas, Brazil. [3]Departamento de Neurologia, Hospital de Clínicas, Universidade Estadual de Campinas, Campinas, Brazil. [4]Memory and Aging Center, Department of Neurology, Sandler Neurosciences Center, University of California San Francisco, San Francisco, CA, USA.

Introduction: Alzheimer's disease (AD) pathophysiology is complex and not completely known. Emerging new biomarkers that evaluate synaptic function (VILIP-1, neurogranin), co-pathology (alpha-synuclein), and neurodegeneration (NFL) are potential candidates to be incorporated into the early AD diagnosis. To better understand the relevance of these biomarkers, we evaluated the correlations between their CSF concentrations with whole-brain grey matter volumes in SCD and MCI, according to their amyloid status (A- or A+). **Materials and Methods:** 75 participants diagnosed with SCD or MCI were included, 30 A- and 45 A+. They all underwent comprehensive neuropsychological assessment, CSF analyses (Roche Elecsys), and volumetric 3T MRI (Philips Achieva). Voxel-based morphometry was used to quantify brain volumes through CAT12 running on MATLAB 2019b. Partial correlation analysis between CSF biomarkers and cortical volumes was performed with SPSS 22, adjusting for age and sex. **Results:** Significant correlations were found in the A- but not in the A+ group. NFL and hippocampus (r=0.40, p =0.028); VILIP-1 and superior temporal gyrus (r= -0.38, p=0.035), and superior frontal gyrus (r=-0.40, p=0.025); alpha-synuclein and hippocampus (r= -0.39, p=0.036), middle frontal gyrus (r=-0.375, p=0.049), and superior temporal gyrus (r=-0.478, p=0.01). **Discussion/Conclusion**: We found different patterns of correlations between brain anatomy and emerging biomarkers, according to amyloid status, in the very early stage of the neurodegenerative process. Interestingly, these correlations were found only in the amyloid-negative group, which might suggest that different pathological processes involving synaptic function, neurodegeneration, and co-pathology occur in suspected non-Alzheimer pathophysiology cases.

DENTAL PULP STEM CELLS TRANSPLANTATION UNVEILS NEUROPROTECTIVE POTENTIAL IN PARKINSON'S DISEASE ANIMAL MODEL

E. M. Azevedo [1], L. Fracaro [2], A. H. D. Hochuli [2], L.S. Rodrigues[1], J. Ilkiw [1], E. L. Bail[1], P. R. S. Brofman[2], A. C. Senegaglia[2], M. M. S. Lima[1]

[1]Neurophysiology Lab -Universidade Federal do Paraná (UFPR), Curitiba, Brazil. [2]Core for Cell Technology, Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba, Brazil.

Introduction: Parkinson's disease (PD) is characterized by the death of dopaminergic neurons in the substantia nigra pars compacta. PD stands as the world's second most prevalent neurodegenerative disorder, affecting around 2-3% of the population aged over 65, with predictions indicating a rise in the coming decades [1]. Current treatments for PD predominantly focus on relieving motor symptoms, emphasizing the crucial need to explore novel therapeutic approaches targeting neuroprotection and/or neuroregeneration [2]. In this context, dental pulp stem cells (DPSCs) emerge prominently due their intrinsic neurogenic potential, coupled with their easy obtainability [3]. Nevertheless, large gaps regarding the mechanisms by which these cells act, as well as their safety in in vivo applications remains. Given that, this study aimed to evaluate the effects of intranigral infusion of DPSC (pre and post neuronal differentiation) on cell survival and locomotor behavior in an animal model of PD. **Materials and Methods:** This project was approved by the Local Research Ethics Committee (CAAE 28861419.2.3001.0102)/ CEUA 1372). DPSCs were obtained from third molars following enzymatic digestion, with a subset undergoing neuronal lineage induction. After characterization, both pre and post-neuronal induction DPSC were transplanted into the substantia nigra of rats with PD previously induced by 6-hydroxydopamine. Seven days post-transplantation, bioluminescence analysis was conducted to assess DPSC viability, immunohistochemistry was employed to evaluate the survival of dopaminergic neurons (N= 6 per group), and locomotor behavior was assessed through an open field test (N=13-20 per group). **Results:** DPSCs remained viable and metabolically active during the experiment duration. Both pre and post-neuronal induction DPSC were able to partially revert the neuronal damage induced by the neurotoxin (30% and 27% respectively, P<0.001). Furthermore, regardless of their differentiation state, these cells restored the animals' locomotor behavior, elevating the locomotor index in the open field test to levels comparable to the sham group (P>0.99). Additionally, these parameters presented a moderate statistical correlation (r=0.62; p = 0.006). **Discussion/Conclusion**: Taken together, our results suggest that DPSCs, whether induced or not to neuronal differentiation, possess a promising neuroprotective potential, making them a viable therapeutic strategy for PD. Importantly, the differentiation status did not significantly affect their efficacy, showcasing the versatility of these cells. However, limitations, including the short-term assessment period, warrant further investigations for a comprehensive understanding of DPSCs' long-term effects and underlying mechanisms. In conclusion, our study provides compelling evidence for DPSCs' neuroprotective potential in PD, paving the way for future research to refine and advance DPSC-based interventions.

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DETECTING CRANIAL CT SCANS WITH METAL ARTIFACTS: A DEEP LEARNING APPROACH

J. V. S. de Alcantara[1,2], G. M. Ferracioli[2], B. G. G. Pinto[2], P. V. A. Silva[2], T. M. M. Olegario[2], A. J. M. Paulo[2], K. Schumacher[2], H. M. H. Lin[2], R. M. Loureiro[2], J. P. Q. de Paiva[2], L. Rittner[1]

[1]Medical Image Computing Lab, FEEC, UNICAMP; [2] Departamento de Imagem, Hospital Israelita Albert Einstein (HIAE)

Introduction: Computed Tomography (CT) is crucial in modern medicine, enabling detailed imaging of the human body for diagnosis and monitoring of medical conditions. However, the presence of metal artifacts such as metallic prostheses, surgical objects or implants in CT images can compromise the

quality and accuracy of diagnoses (Fig.1, right) [1] . This study investigates using deep learning (DL) models to improve artifact detection in head CT images, aiming to enhance the reliability of AI-based diagnostic support systems for more effective diagnoses and treatments. **Materials and Methods:** This project used cranial CT scans from two public datasets, the CQ500 [2] and the Kaggle Metallic Artifact Reduction dataset [3] and one in-house dataset containing 4714 anonymized exams acquired at the Hospital Israelita Albert Einstein (HIAE). All datasets are composed of images from patients previously evaluated and diagnosed by medical professionals. To ensure the representativeness of the sample, patients with different characteristics found in the metadata and clinical conditions were included. The ethics committee approved the use of data from HIAE for the current project. Various DL architectures for artifact detection were explored, including EfficientNet, ResNet, and DenseNet. The dataset was preprocessed, labeled as *with artifact* and *without artifact*, and divided into training, validation and test sets (80/10/10 split). Model training was conducted using the Cross-Entropy Loss function, with progress monitored to prevent overfitting. Performance metrics such as accuracy, precision, recall, and F1-score were calculated to evaluate the model's generalization capability. **Results:** The EfficientNet model demonstrated superior performance, achieving a precision of 0.89, recall of 0.9, and an F1-Score of 0.93 (Fig.1, left). However, false positives and false negatives were observed during result analysis, indicating areas for improvement. A more qualitative analysis of these errors is needed to better understand model limitations. **Discussion/Conclusion**: This study demonstrated the effectiveness of AI in identifying metallic artifacts in cranial CT scans using various neural network architectures. The next stage includes conducting a new phase of testing with HIAE data to evaluate cases in which the model does not perform well. This analysis, carried out together with the team of experts, will be important for future retraining of the model. Preliminary results show promise in enhancing diagnostic accuracy, with plans to implement 3D Vision Transformers for improved spatial information capture. This offers potential for enhanced metallic artifact detection in CT images, with room for further model refinement.

Model	Precision	Recall	F1 Score	Size
EfficientNet	0.89	0.90	0.93	23mb
ResNET	0.84	0.87	0.89	170mb
3D CNN	0.87	0.80	0.90	54mb

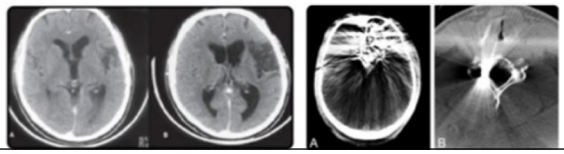

Figure 1. Comparing classification performance of different architectures (left). Examples of CT images with distortions caused by different metallic artifacts (right).

References: [1] Barrett JF, Keat N. doi: 10.1148/rg.246045065; [2] Chilamkurthy S, et al. doi: 10.1016/S0140-6736(18)31645-3; [3] Ghani MU, Karl WC. doi: 10.1109/TCI.2019.2937221.

DETERMINISTIC TRACTOGRAPHY IN ADULTS WITH DEVELOPMENTAL DYSLEXIA

B. Martins[1], E.F. Cardoso[1], E. Amaro[1], K. Lukasova[2], M.P. Nucci[1]

[1] LIM 44, Hospital das Clínicas da Faculdade Medicina da Universidade de São Paulo, São Paulo, SP, Brazil. [2] Universidade Federal do ABC, Centro de Matemática, Computação e Cognição (CMCC), Santo André, Brazil.

Introduction: Developmental dyslexia is a neurodevelopmental disorder that has received special attention as individuals exhibit difficulties in processes related to reading and writing without impairment in other cognitive domains [1]. Magnetic resonance imaging has been one of the main instruments for investigating structural differences in the brains of people with dyslexia and has aided in understanding the neuroanatomical bases of this disorder [2]. This study aimed to identify differences in brain structural connectivity between adults with developmental dyslexia and healthy adults, focusing on linguistic processing pathways. **Materials and Methods:** The sample for this study consisted of 30 adults with dyslexia who had achieved higher education (26.4 ± 6.02 years) and 48 healthy adults with similar education levels (25.5 ± 5.82 years), with a similar gender distribution. Magnetic resonance imaging was performed using a Philips Achieva 3T scanner for structural brain evaluation through diffusion-weighted imaging (DTI) collected with the following parameters: TR = 8448 ms, TE = 65 ms, b-values = 0 and 1000, slices = 70, directions = 32. Images were corrected for eddy currents and motion artifacts, and fractional anisotropy (FA) was subsequently estimated. FA measurement was analyzed using the TBSS package [3] of FSL software version 6.0 [4]. **Results:** Deterministic analysis revealed increased FA in the dyslexic group compared to controls in the superior corona radiata, bilateral superior and inferior longitudinal fasciculi, corticospinal tract, posterior and anterior thalamic radiation, corpus callosum, and inferior fronto-occipital fasciculus, predominantly on the right side in the uncorrected statistical analysis for multiple comparisons ($p < 0.05$). **Discussion:** Research on DTI in developmental dyslexia in adults is scarce and recent, with few studies reporting decreased FA in the left arcuate fasciculus [5] and in the lateral geniculate nucleus in dyslexics [6], or even finding no differences between groups [7-8]. An expansion in the number of publications is necessary for a better understanding of the topic, and this study aimed to contribute to this expansion. **Conclusion:** This study highlights bilateral structural differences, with predominance in the right hemisphere, in adults with developmental dyslexia, contributing to the understanding of neural adaptations associated with this disorder.

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DIFFERENCES IN THE TRACTOGRAPHIC ANALYSIS OF THE WHITE MATTER OF YOUNG WOMEN WITH BIPOLAR DISORDER BY ULTRA-HIGH FIELD MAGNETIC RESONANCE IMAGING (7T)

da Silva, R B[1], da Souza, M G S[2], Fernandes, F[2], Martins, B[1], Nucci, M P[1], Pastorello, B F[1], Leite, C D C[1], Otaduy, M C G[1]

[1]LIM 44 Laboratório de Ressonância Magnética em Neurorradiologia, InRad, HCFMUSP, [2]Programa de Transtornos do Humor, IPq, HCFMUSP.

Introduction: Changes in the microstructure of the white matter suggest significant demyelination and/or significant dysmyelination without axonal loss in bipolar disorder (BD), and have been proposed as structural biomarkers of this disorder. The aim of this project was to study by magnetic resonance imaging (MRI) using the fractional anisotropy calculated from diffusion tensor images (DTI) the integrity of the white matter in young women with bipolar disorder (BD) during the depressive mood state. **Materials and Methods:** In this study, women aged 18 to 45, literate, without neurological lesions or drug abuse and without contraindications for the MRI scan were selected for the experimental group (BD) when the diagnosis of BD was confirmed (assessed by the Diagnostic and Statistical Manual of Mental Disorders-V) in the depressive phase of the illness, free of medication to treat mood (time ≥ 2 weeks). Results were compared to a control group (CG) of females without personal/family history of psychiatric disorders.The participants' DTI images were acquired on 7T MRI equipment, pre-processed in the FSL software using the tools topup and EDDY to correct distortion and BET (formation of the brain extraction mask) and processed in DTIFIT to generate the fractional anisotropy (FA) maps for each subject. Group analysis was performed using tract-based spatial statistics (TBSS) to align to the mean FA template and apply statistical analysis of randomization between the groups (10. 000 permutations) run for cluster tcfe thresholded at a $p<0.05$. **Results:** A total of 25 subjects (9 controls and 16 BD patients) were included in the study. Both groups contained only young women, but there was a statistical difference in age ($p=0.003$), the CG had a mean age of 25.4+2.4 years and the BD 31.8+6.9 years. TBSS analysis revealed significant lower FA values in the BD group for the vast majority of tracts. **Discussion/Conclusion**: In conclusion, 7T MR imaging was sensitive for evaluating FA reduction in women with BD, suggesting structural disintegration of the white matter fibers that make up this tissue. There were reductions in FA in BD compared to CG, mainly in the following tracts: middle cerebellar peduncle, corona radiata L and R, anterior and posterior limb of internal capsule L and R, cingulum, body and genu of corpus callosum, posterior thalamic radiation L and R. These results are

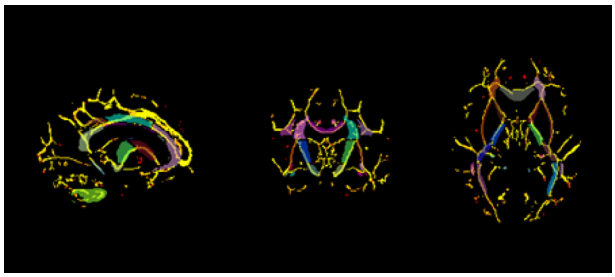

Figure 1. In yellow, regions where the Anisotropy Fraction (AF) of the Control Group was higher than that of the Experimental Group (composed of young women with bipolar disorder in the depressive phase). Mapping used with the JHU ICBM-DTI-81 White-Matter Labels atlas. Number of permutations in 10,000.

in line with studies that suggest a significant reduction in FA in drastic phases (mania and depression) of the disease [1]. It also opens up the possibility of variations in these results in patients undergoing treatment or in remission, as already suggested in the literature [2].

Reference: [1] Benedetti, F et al., DOI: 10.1016/j.biopsych.2010.07.028; [2] Wessa, M et al., DOI: 10.1111/j.1399-5618.2009.00718.x

EFFECTS OF MANUAL PERFORMANCE MODULATION

Cristiani Junqueira[1], Lidiane Aparecida Fernandes[2],Tércio Apolinário-Souza[3], Guilherme Menezes Lage[1]

[1]UFMG/EEFFTO, NneuroM Group, [2]UFJF/GV, CoMneuro Group, [3]UFRGS, GAIM Group

Introduction: The hands exhibit distinct characteristics in motor skill performance. Differences in hand performance have been attributed to the contralateral hemisphere's specialization in the organization and control of voluntary movement. Hemispheric modulation may affect the electrical conductivity of the corpus callosum fibers between hemispheres, resulting in increased or decreased inter-hemispheric communication and, consequently, a reduction or enhancement in manual performance. Thus, this study aimed to investigate the effect of the transcranial direct current stimulation in the hand performance right e left. **Materials and Methods:** Sixty volunteers of both sexes performed a touch task for groups (task adapted from Lee, Fisher, 2018) whith right e left hand. The volunteers participated in two sessions under different conditions: Dominant Hemisphere Inhibition (RH_TDCS) for estimulation left hand and Placebo (RH_PL) or non-Dominant Hemisphere inhibition (LH_TDCS) for estimulation right hand and Placebo (LH_PL). Each session consisted of a pretest, followed by the specific condition of stimulation of the primary motor (M1) and post-test for each hand. The sessions were separated by intervalo f 48 hours. **Results:** The results showed that in the pre-test, the hands are equal. There was na improvement in performance from pre to post-test. TDCS showed na effect for both hands, but RH showed better performance. Although RH shows better performance, we can assume that LH benefits more from the effects of TDCS, because the delta is greater. **Discussion/Conclusion**: In conclusion, hemispherical modulation was able to modify the performance manual of both hands in relation to the temporal aspect of the task. More studies are necessary to establish stronger links between biological handedness and manual performance.

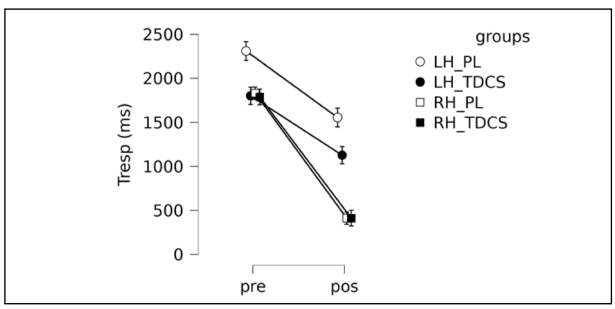

Figure 1. Response time in the sequential touch task for groups in the pre and pos test. LH_TDCS grup for estimulation left hand and Placebo LH_PL. RH_TDCS grup for estimulation right hand and Placebo RH_PL.

EMOTIVE GESTURAL EXPRESSIONS FOR ASSISTIVE HOME HUMANOID ROBOTS: SIMULATION TEST

B. M. Portela[1], C. B. da Silva[1], F. A. O. Mota[1], E. A. B. Huayhua[1], E. Rohmer[1]

[1]Dept. Computer Engineering and Industrial Automation, FEEC, UNICAMP

Introduction: A home assistive system, utilizing the Internet of Robotic Things, requires an interactive robot capable of autonomously understanding and engaging with the residential environment. This robot should express emotions through voice, movements, and expressions to pass a sensation that it is more than a mere machine and create an interaction more related between a human and a living assistant [1], and enhance the human-machine interaction experience, making it more friendly, enjoyable, and engaging [2], being even more useful and careful with elderly and people with disabilities. The article outlines a method for implementing these gestures to express a humanoid image authentically. **Materials and Methods:** A Pepper robot by Aldebaran was simulated on CoppeliaSim and linked to the software Choregraphe through a Python script, being able to send gestural expressions to the simulated robot using the Choregraphe software. The structuring of the program's communication can be seen in Figure 1. **Results:** Pepper can act with a library of gestural moods, dances, and poses. The library contains positive, negative, and neutral gestural communication, making the interaction human-machine more friendly and authentic. Figure 2 shows an example of a thinking gesture. **Discussion/Conclusion**: These gestural commands can be linked to a Large Language Model and make every response linked to a gestural expression, making robot answers more emotional. This system can be also used on other humanoid robot models, and other gestural libraries can be found in open-source repositories, making the expressions even more complex.

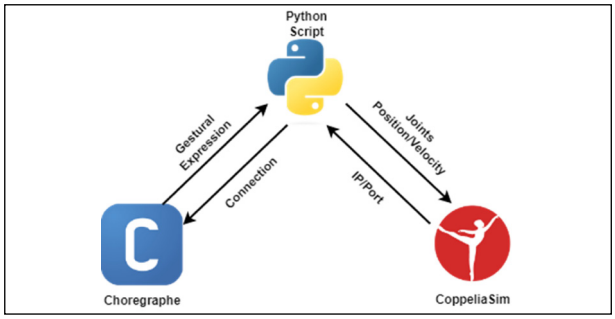

Figure 1. Program's communication.

Figure 2. Pepper thinking gestural.

References: [1] Kwon D.S. et al., doi:10.1109/ROMAN.2007.4415108 [2] Kim A. et al., doi:10.1109/HRI.2013.6483550.

ENHANCING ASSISTIVE HOME ENVIRONMENTS THROUGH IORT MULTI-AGENT INTERACTION: MODEL SELECTION AND ROBOTIC OPERATIONS

E.A.B. Huayhua[1], E. Rohmer[1], C. B. da Silva[1], F.A.O. Mota[1], B. M. Portela[1]

[1]Dept. Computer Engineering and Industrial Automation, FEEC, UNICAMP

Introduction: The ongoing improvement in the research and development of LLM (Large Language Models) aligns fascinatingly with Mobile Robotics, presenting a promising trend in artificial intelligence. This convergence holds

the potential to revolutionize assistance, especially in the care of adults or individuals with disabilities. Human-machine interaction emerges as a solution, aiming to facilitate daily activities for this group. These models, akin to chatbots and virtual assistants, offer informative assistance. Additionally, there is the possibility of simultaneous assistance from multiple robots for a user or patient, requiring exploration in "Multiple Agent Assistance." This project focuses on a chatbot with a dual purpose: providing voice assistance based on user needs and maintaining an updated database about the environment. These tasks are fundamental to creating an intelligent environment, relying on the project's architecture, which aims to establish a robust connection between robotic devices through a REST server for shared and updated context among agents. **Materials and Methods:** To carry out the robot simulations, a personally manufactured humanoid robot developed by B. M. Portela was employed. This robot is utilized for interaction in a specific environment, using specific joints that are controlled from a Python code to Naoqui. Additionally, the simulations included the interaction of the P3DX robot, representing the locomotion part of the robot in the same environment. We also took into account the presence of other IoT agents, represented by AXIS PTZ 214 cameras and Google Assistant, coexisting in the intelligent environment to provide enhanced assistance to the patient. The objects captured by the cameras serve the purpose of contextualizing communication with the Large Language Model (LLMs). In this regard, the LLMs establishes communication with a REST server, responsible for storing all relevant information generated during the simulations. **Results:** In the analysis using OpenAI's LLM, ChatGPT version 4.0 demonstrated its ability to generate desired responses during interaction, surpassing other models. Although the variability in prompt usage among models with equal parameter sizes is acknowledged. ChatGPT 4.0 stands out in providing information on multiple tasks within a conversation. The evaluation was divided into three fields: direct interaction with a user, interaction with the ROS control system, and, finally, supplying context to the REST server. This approach allowed assessing its performance in different contexts, highlighting its versatility in addressing various tasks in the robotic assistant application. The ability to provide real-time contextual information through ROS and maintain coherence in user interaction underscores the effectiveness of ChatGPT 4.0 in this specific environment. **Discussion/Conclusion**: In this project, the initial step involved interacting with multiple models to partially identify the most suitable Large Language Model (LLM) for real robot interaction. The successful selection of OpenAI's model was achieved in part. Additionally, diverse information was gathered to address the Multiagent field, diversifying communication with a server. This allows other agents to interpret actions and multitasking functions. In the next phase, the aim is to enhance the model's activity by enabling it to choose actions within the Robot Operating System (ROS) environment. The model is expected to maintain a sequence of activities for each agent and pose follow-up questions to facilitate processing within the ROS architecture and cameras. This approach seeks to empower the model's decision-making capability and enable more active participation in system operations.

EPILEPSY IN ADULTS: THE RELATIONSHIP BETWEEN THE POST-ICTAL PHASE OF THE EPILEPTIC SEIZURE AND THE CLINICAL-EEG VARIABLES AND THE PRESENCE OF PSYCHIATRIC COMORBIDITIES

Agostinho, C.F.[1], Tedrus, G. M.A.S[2]

[1]Scientific Initiation FAPESP Scholarship Holder, Medical School (PUCCAMP), [2]Neurology Department, PUCCAMP.

Introduction: In epilepsy, clinical manifestations during the post-ictal phase are often neglected in clinical practice. There are still gaps in the relationship between post-ictal phase, EEG data and psychiatric comorbidities. **Materials and Methods:** The characteristics during the ictal and post-ictal phases of epileptic seizures will be related to the clinical variables of epilepsy, to the EEG data and to the scores on the *Hospital anxiety and depression scale* (HADS) and the *Mini-Mental State Examination* (MMSE), with statistical tests and with a significance level of $p<0,05$. **Results:** 52 patients were evaluated, with a mean age of 48,6 years, and a mean age at the time of the first crisis of 21 ± 17 years, 27 (51,9%) of them were male. The mean MMSE score was 23,6, the mean HADS-A score was 7,0 and the mean HADS-D score was 6,0. There were 36 cases (69,2%) of structural epileptic syndrome (19 with TLE-HS, and other epilepsies in 16 cases). Post-ictal manifestations occurred in 44 (84,6%) patients. The symptoms were drowsiness, headache, mental confusion, motor changes, psychic changes, autonomic symptoms, and others. In 30 cases there was an association of more than one symptom. There was no difference in the occurrence of post-ictal phase according to age, to age at the first crisis, to gender, to type of crisis, to anti-seizure medication, to type of syndrome and of etiology and to the presence of depressive and anxious symptoms. **Discussion/Conclusion**: In conclusion, the occurrence of post-ictal symptoms was frequent and with various neurological/psychiatric symptoms. There was no association between post-ictal phase aspects and epilepsy aspects. The data suggest that this is a relevant aspect in the clinical epilepsy area, which justifies that new studies with a larger sample are required [1][2].

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ESTIMATING BRAIN AGE THROUGH MACHINE LEARNING AND RS-FMRI

C. L. S. Prazeres[1], L. K. F. Souza[1], M. C. G. Otaduy[1]

[1]LIM44, FMUSP, USP.

Introduction: Human brain aging is a complex process involving morphological and functional changes, including alterations in brain connectivity. It is worth noting that not only chronological age development but also cognitive, emotional, and psychological factors may be associated with these transformations. Therefore, understanding the development of gradual brain decline is of utmost importance for human health. Some methodologies, such as resting-state functional magnetic resonance imaging (rs-fMRI), offer assessments of brain connectivity, allowing the identification of changes in brain function. Thus, determining brain age based on functional magnetic resonance imaging (fMRI) images and machine learning (ML) could be an important strategy for personalized and precision medicine, interpreting the results as a potential health biomarker. **Materials and Methods:** Using a pre-processed open dataset "MRI data of 3-12 year old children and adults during viewing of a short animated film" and the 1mm BN246 atlas, a research methodology was developed to create ML regression models using a dataset ($n=155$ subjects), divided into 80% training/validation and 20% testing. The models included linear regression, support vector regression with linear kernel and radial basis function, Ridge, and a model combining these approaches. **Results:** The stacked regressor, on average, showed the best performance in terms of coefficient of determination, both in 10x10 cross-validation (0.74 ± 0.019) and in the test set (0.81 ± 0.043). However, there was no significant difference between this regressor and the linear regression algorithms (cross-validation: $p=0.506$, test: $p=0.943$) and ridge (cross-validation: $p=0.506$, test: $p=0.943$). **Discussion/Conclusion**: The application of rs-fMRI-based functional connectivity to estimate brain age under the highlighted experimental conditions shows promise, considering its potential as a health biomarker.

EVALUATION AND DIFFERENTIATION OF EDEMA AND TUMOR INFILTRATION IN PATIENTS WITH HIGH-GRADE GLIOMA - INITIAL EXPERIENCE USING T2 RELAXOMETRY TESTS

M.S., Leticia[1], L. P.F., Sérgio[2] , M.C., Brunno[1], C. Fernando[1], M.S., Thiago[2], F., Cleiton[2], V.G., Marcus[2], G. Enrico[1]

[1]UNICAMP, CEPID BRAINN, [2] FCM, UNICAMP

Introduction: The differentiation between edema and tumor infiltration in high-grade gliomas is fundamental for surgical planning. However, this distinction is challenging using conventional magnetic resonance imaging (MRI). New advanced magnetic resonance imaging (MRI) techniques are capable of inferring tissue composition, potentially contributing to such differentiation. In this study, we used magnetic resonance images in T2 multiecho sequence (RMT2m) processed using a quantitative technique known as relaxometry to differentiate between edema and tumor infiltration in high-grade gliomas. **Materials and Methods:** In this study, we report our initial experience using T2 multiecho relaxometry to differentiate perilesional edema from tumor infiltration in patients with high-grade gliomas. Patients who underwent RMT2m and with an anatomopathological diagnosis of brain tumor were retrospectively selected, divided into two groups: metastases/meningiomas, in which it is assumed from the literature that hyperintensity in RMT2m corresponds to vasogenic edema, and high-grade gliomas, where they are present both edema and tissue infiltrated by tumor cells. The areas of hyperintensity in RMT2m were manually delimited in

both groups and analyzed using the Relaxo LNI® software, developed in-house. In the group with high-grade gliomas, this analysis was subdivided into regions of interest in the center (close to the capturing lesion) and in the periphery of the tumors (far from the capturing lesion). **Results:** Ten patients were included in the group with metastases/meningiomas and twenty patients in the group with high-grade gliomas. The mean relaxation times in RMT2 were higher for the high-grade glioma group when compared to the control group ($p<0.05$). The times were also longer means of relaxation of central areas of high-grade gliomas (mean value of 498.68), where tumor infiltration is the most common component, in relation to peripheral areas (mean value of 136.13), $p<0.05$, where edema tends to be predominant. **Discussion/Conclusion:** Difference was statistically significant ($p<0.05$). Our results suggest that the LNI relaxo software could be a helpful tool to differentiate edema and tumor infiltration in patients with high-grade gliomas, allowing for a more efficient preoperative planning and postoperative assessment of tumor infiltration resection rate. Next steps include determining cut-off values for relaxation time where it is safe to assert the absence of tissue infiltrated by tumor cells, contributing to pre-operative planning and post-operative assessment of the extent of resection of these lesions.

EVALUATION OF EPILEPSY IN PATIENTS WITH SYNDROMIC CRANIOSYNOSTOSIS

D. A. Gulhote[1], M. P. Couto[2], F. Cendes[3], C. R. Amaral[4], E. Ghizoni.[5]
[1] SOBRAPAR, [2]Neurology Dept., FCM, UNICAMP.

Introduction: Syndromic craniosynostosis (SC) patients may develop epilepsy during craniofacial growth. The association between malformations of the brain parenchyma and changes in intracranial physiology may result in epileptiform disorders. There are no studies in the pertinent literature on the prevalence of epilepsy in the SC population, assessing type of epileptic syndrome, and the natural history of seizures. The objective of this study is to compare the rate of epilepsy in SC population and non syndromic patients. **Materials and Methods:** An observational retrospective study was performed on 127 consecutive patients with Apert, Crouzon, Pfeiffer, or Saethre-Chotzen syndromes, who underwent any type of craniofacial surgery or hand surgery between 2007 and 2022 at our Hospital. The International League Against Epilepsy (ILAE) Classification of the Epilepsies validated to Portuguese [1] questionnaire was handed out to all syndromic patients or families who completed at least one operation at our Institution. Demographic and clinical data about the seizures were collected. **Results:** Ninety-two SC families responded to the questionnaire, having 23.9% (n=22) of patients presenting at least one episode of crisis and are being investigated to have their diagnoses based on the classification proposed by the ILAE. **Discussion/Conclusion**: The prevalence of epilepsy seems to be profoundly higher in the SC population than overall population. Primary anatomic brain malformation or brain encephalomalacia following a variety of insults due to multiple craniofacial surgeries may result in epilepsy diagnosis.

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EVALUATION OF INTER-HEMISPHERIC COMMUNICATION AMONG HANDS DURING MOTOR TASK

D. A. Medeiros[1], T. Apolinário-Souza[1], G. M. Lage[2], L. A. Fernandes[3]
[1]Nneurom/GAIM, ESEFID. UFRGS [2]Nneurom, EEFFTO, UFMG [3]Nneurom/CoMNeuro, UFJF-GV.

Introduction: The corpus callosum plays a crucial role in facilitating communication between the cerebral hemispheres, enabling integration and coordination of bilateral brain activities. Its transmission of information is essential for cognitive and motor processes, influencing everything from perceptual skills to more complex functions such as language and motor learning. Previous studies have underscored the significance of the corpus callosum in hemispheric specialization and the efficiency of interhemispheric communication. This study aims to investigate the mechanisms of interhemispheric communication during the execution of a motor task, considering the influence of the corpus callosum through electroencephalography (EEG) evaluation and the motifs synchronization method. **Materials and Methods:** Sixty-one right-handed university students aged between 18 to 35 years participated in this study. The task employed was the serial reaction time task (SRTT), a task traditionally utilized in Motor Learning and Psychology studies. Participants were required to execute, as quickly and accurately as possible, the sequence ("f", "s", "d", "a") displayed on a computer screen. Each participant performed 16 trials with each hand. During the execution of the motor skill, scalp electrical activity was recorded using an electroencephalogram (EEG) device. EEG data were filtered into four bands of interest: theta, gamma, beta, low alpha, and high alpha. Motifs synchronization method was employed to estimate the level of communication between the hemispheres. This method involves counting the simultaneous occurrence of predefined patterns or motifs (of a certain length) in two temporal series. In this study, motifs of three points were used. Paired t-tests were utilized to compare each hand in each band. **Results:** Inferential analyses did not detect differences between hands in the theta [$t(60)=-0.65$, $p=0.51$], gamma [$t(60)=-0.42$, $p=0.67$], beta [$t(60)=1.78$, $p=0.08$], low alpha [$t(60)=1.29$, $p=0.20$], and high alpha [$t(60)=-0.41$, $p=0.68$] bands. **Discussion/Conclusion:** The results of this study reveal no significant differences between hands in the various frequency bands, indicating equivalence in interhemispheric communication during the execution of the SRTT task. This finding suggests efficiency in the integration of information between hemispheres, supporting the importance of the corpus callosum in coordinating brain activities and functional specialization of the brain.

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EVALUATION OF PARAMETERS AND PROGNOSIS FACTORS ASSOCIATED WITH BENIGN EVOLUTION OF MULTIPLE SCLEROSIS PATIENTS

Josué de Almeida David[1], Thomas Vieira de Paula[1], Alfredo Damasceno[1]
[1]FCM, UNICAMP.

Introduction: This study aims to analyze cognitive, clinical and neuroimage aspects of Benign MS patients, in order to understand more about this entity in general, as well as its development in the Brazilian reality [1]. **Materials and Methods:** We included 60 patients followed in a tertiary MS service, 30 having EDSS below 3.0 and at least 10 years of disease onset [28]. They underwent cognitive evaluation, assessment of mood and fatigue disorders, as well motor disorders. We analyzed the number of cerebral, infratentorial and medullary lesions in both traditional and benign patients [32][33]. **Results:** We found that the majority of BMS patients in this cohort were female, having low mean EDSS (1.9) and good performance on the T25FW and 9HPT motor tests. The prevalence of cognitive deficits was higher in traditional MS than BMS. The frequency of depression was similar in both groups. We also found that higher numbers of infratentorial and medullary lesions were indicative of worse prognosis. Furthermore, the use of a more stringent criteria did not show better clinical performance, neuroimage aspects or better cognitive performance. **Discussion/Conclusion**: In conclusion, this work corroborates previous epidemiological findings, regarding other countries [16], in the Brazilian reality as well. In addition, it shows the high prevalence of non-motor symptoms and cognitive impairment both in classical MS patients and the ones classified as "benign". Which suggest the need for a different analysis approach in this patient group [11]. However, the use of a more stringent criteria (EDSS < 3.0 and more than

Table 1. Comparison between neuroimaging findings of traditional and benign MS. Significance level used was $p<0,05$.

Mean variable value (Standard-Deviation)	BMS	Traditional MS	Signific.
EDSS	1,9 (0,80)	5,20 (1,33)	0,00
Medulla lesions	2,33 (2,74)	4,16 (3,06)	0,10
Thoracic medulla lesions	2,6 (1,77)	2,85 (2,11)	1,00
Cervical medulla lesions	2,05 (1,89)	2,72 (1,34)	0,126
Periventricular lesions	25,5 (19,07)	37,29 (24,62)	0,08
Juxtacortical lesions	16,65 (20,84)	24,20 (22,42)	0,10
Infratentorial lesions	5,76 (7,90)	7,79 (4,74)	0,029
Brain lesions	47,53 (45,24)	61,76 (47,76)	0,052

10 years of disease onset), did not show patients with better performance. Finally, the greater number of infratentorial and medullary lesions corroborates works in literature that shows a worse prognosis of this group of patients [32][33][37].

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EXPLORATORY PRENATAL ALCOHOL EXPOSURE CLASSIFICATION IN INFANTS USING BRAIN MR 3D CONVOLUTIONAL NEURAL NETWORKS ASSISTED BY DATA AUGMENTATION

K. T. N. Duarte[1], A. Das[2], C. Lebel[1,3] M. P. Bento[2,3]

[1]Department of Radiology, University of Calgary (UofC), [2]Department of Biomedical Engineering UofC, [3]Alberta Children's Hospital Research Institute UofC.

Introduction: Understanding the impact of prenatal alcohol exposure (PAE) in infants is crucial for early identification to mitigate potential developmental problems. Magnetic Resonance (MR) scans offer a non-invasive manner to seek for the detailed structure of the brain. Researchers can explore subtle anatomical variations associated with PAE[1], aiding in the identification of early biomarkers. Thus, the application of machine learning, particularly 3D Convolutional Neural Networks (CNNs), serves as a tool to identify the complex patterns within children's brains. Our goal is to generate a 3D CNN model able to discern patterns that differentiate individuals with PAE from unexposed children. **Materials and Methods:** The data comprises 122 children with PAE and 122 normal control participants, with sex equally divided and ages matched (2.5 to 8yo). The T1-weighted structural brain MR scans were acquired using the Fast Spoiled Gradient Echo BRAVO sequence, with flip angle of 12º, voxel size of 0.9mm^3 isotropic, 210 slices, a matrix size of 512 × 512, and a field of view of 23.0 cm. Data augmentation using MONAI increased our dataset by randomly adding: rotation, contrast enhancement ($\gamma = \{0.5\text{-}1.5\}$), and gaussian noise ($\alpha = \{0.1\text{-}0.4\}$). We use a 5-fold cross-validation to ensure generalizability. Our tested CNN architectures were defined as shown in Figure 1A. We adopted Accuracy and Binary Cross-Entropy as evaluation metric and loss function, respectively. We used a learning rate = . The model showing the lowest validation loss was saved. **Results:** Six CNN architectures over three rates of data augmentation (1x, 3x, 6x) were explored in our experiments. As shown in Figure 1B, adding data augmentation does significantly improve the validation accuracy (3x and 6x vs 1x,). However, no significant difference was found between augmenting by 3x and 6x. The lower number of layers seems to increase the accuracy of the model, whereas the increased number of layers decreased the validation accuracy. The testing set from Model A showed 83.2% accuracy, whereas the second best (Model B) reached 80.1% accuracy. **Discussion & Conclusion**: In conclusion, the lower number of layers in CNN helps to better generalize the model. Augmenting the number of scans helped the convergence of the models, showing a small difference between accuracy from training and validation. However, the small difference between augmenting 3x to 6x of the data possibly suggests a saturation of augmentation benefits. We

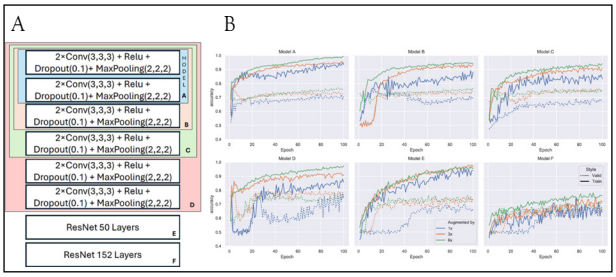

Figure 1. Model structure and performance during training step. A - Architectures (model name is in the right side). B - Importance of Data Augmentation - Learning curves.

varied the number of layers in this work, but adjusting the number of parameters might have a beneficial effect in the models. Future directions include preprocessing step (skull stripping, bias field correction, tissue and anatomical segmentation) and inserting an interpretability module to help identify brain differences among participants.

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EXPLORING ACADEMIC EXPERIENCES, DRUG USAGE, AND BULLYING: BAYESIAN NETWORK ANALYSIS OF STUDENT INTERVIEWS

A. C. P. Kulaif[1], R. Veroneze[1], L. F. R. de Souza Li[2], F. J. Von Zuben[1]

[1]LBiC, FEEC, UNICAMP, [2]Pediatrics Dept., FCM, UNICAMP

Introduction: Bayesian Networks (BNs) are powerful tools for representing and reasoning under uncertainty. BNs provide a structured way to model complex systems by capturing the probabilistic dependencies among variables. In a BN, nodes represent random variables, and edges represent probabilistic dependencies between them. These models allow for efficient inference, enabling predictions and decisions based on available evidence. BNs find applications in various fields, including medicine, finance, and engineering, where understanding uncertainty and making decisions based on uncertain information is essential. In this study, we generate a BN from a dataset comprising responses from interviews conducted with students attending a public school. These interviews cover a range of topics, including the students' academic experiences, patterns of drug usage, and encounters with bullying. We aim to investigate these variables' interactions by constructing a BN model. Through this analysis, we strive to gain insights into the complex relationships among academic experiences, drug usage behaviors, and incidents of bullying.

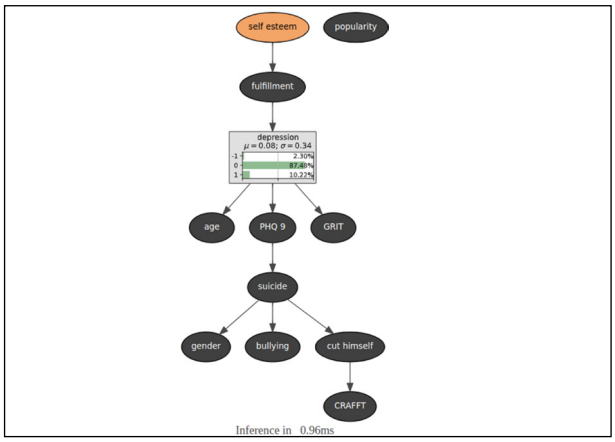

Figure 1. Bayesian Network.

EXPLORING DELETERIOUS *IL7R* GENE POLYMORPHISMS: A BIOINFORMATICS STUDY IN MULTIPLE SCLEROSIS

G. C. Silva[1], N. E. Bufalo[1,2,3], L. T. Rabi[3,4], and K. C. Peres[1,3]

[1]Max Planck University Center – UniMAX, Indaiatuba/SP; [2]Department of Medicine, São Leopoldo Mandic and Research Center, Campinas/SP; [3]Laboratory of Cancer Molecular Genetics, Faculty of Medical Sciences, State University of Campinas (UNICAMP); [4]Department of Biomedicine, Nossa Senhora do Patrocínio University Center – CEUNSP, Itu/SP.

Introduction: Multiple sclerosis (MS) is an autoimmune disease that affects the central nervous system, leading to the demyelination of axons and impaired nerve impulse transmission. This pathophysiology involves numerous reactive T lymphocytes that target the myelin sheath and trigger an inflammatory and destructive process. The *IL7R* gene encodes a protein crucial for binding to interleukin 7 (IL-7) and plays a role in the maturation of B lymphocytes and the activation of T cells. Previous studies have indicated that low expression of IL-7 results in immunodeficiency due to lymphopenia, whereas excessive signaling through this pathway may be associated with MS. Single nucleotide polymorphisms (SNPs) are single nucleotide exchanges that occur in DNA, and their presence can influence the production, size, and function of the encoded protein. Identifying SNPs in associated genes can be valuable for establishing individual genetic susceptibility and aiding the prognosis of clinical cases. **Materials and Methods:** We conducted a bioinformatic analysis of the *IL7R* gene using 11 different tools to assess the impact of SNPs on the structure, function, and stability of the protein. These tools included the UniProt and NCBI databases and PredictSNP1.0 [1], a consensus of seven tools providing information on the consequences of amino acid changes. Additionally, we used MuPRO [2] to determine the protein stability, HOPE [3] to report the size, charge,

conservation, and hydrophobicity, and gnomAD [4] to determine the clinical significance and frequency of the SNP in various population groups. **Results:** A total of 112 SNPs were evaluated. Twenty-one (21) SNPs were considered deleterious by 75% (n=112) of the computational tools, with particular emphasis on rs193922644, which was identified as deleterious by 100% of the tools. Post-translational analysis revealed increased protein stability in the presence of a new residue, and the HOPE tool explained that this improvement involved modifications in the new residue's size, charge, and hydrophobicity. Additionally, the gnomAD tool revealed a correlation between SNP rs201940568 and MS. **Discussion/Conclusion**: Genetic research has consistently linked *IL7R* and its polymorphisms with the susceptibility to MS. Variations in *IL7R* have been shown to modulate MS risk, underscoring its significance in the disease's pathophysiology [5]. Furthermore, the regulation of gene expression in rheumatoid synovial fibroblasts has implicated *IL7/IL7R* signaling in various autoimmune and inflammatory disorders, including MS [6]. In summary, our computational analysis revealed that 21 SNPs within the IL7R gene could potentially alter the protein's structure and function. Particularly, rs193922644 and rs201940568 have emerged as promising candidates warranting further investigation in individuals with MS.

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EXPLORING MULTIOMICS SIGNATURES IN MESIAL TEMPORAL LOBE EPILEPSY: PROTEOMIC PERSPECTIVES ON DRUG RESPONSE AND NEUROTRANSMITTER FUNCTION

Amanda M. do Canto[1,2], Jaqueline C. Geraldis[1,2], Alexandre B. Godoi[1,6], Fábio Rogério[2,3], Marina Alvim[2,4], Clarissa Yasuda[2,4], Enrico Ghizoni[2,4], Helder Tedeschi[2,4], Matthew MacDonald[5], José Luiz da Costa[1,6], Fernando Cendes[2,4], Iscia Lopes-Cendes[1,2]

[1]Department of Translational Medicine, FCM, UNICAMP, [2]Brazilian Institute for Neuroscience and Neurotechnology, Campinas, SP, [3]Department of Pathological Anatomy, FCM, UNICAMP, [4]Department of Neurology, FCM, UNICAMP, [5]Department of Psychiatry, University of Pittsburgh, PA, USA, [6]Analytical toxicology laboratory, CIATox, Campinas.

Introduction: Mesial temporal lobe epilepsy (MTLE) stands as the predominant form of focal epilepsy among adults, posing significant clinical challenges due to a substantial subset of patients resistant to conventional antiseizure medications [1]. Understanding the intricacies of synaptic transmission, including its processes and potential abnormalities, holds promise for unraveling the mechanisms underlying MTLE. Synaptosomes offer a unique window into synaptic function by encapsulating the essential machinery for neurotransmitter release, reuptake, and storage [2]. By delving into the proteomic and metabolomic profiles of synaptosomes isolated from the anterior temporal lobe and hippocampus, this study aims to illuminate the molecular landscape associated with pharmacoresistant MTLE and Hippocampus Sclerosis. Such insights hold the potential to advance our comprehension of MTLE pathogenesis and may pave the way for novel therapeutic avenues. **Materials and Methods:** Synaptosomes isolated from hippocampal and anterior temporal lobe tissue obtained during epilepsy surgery were analyzed, comprising samples from pharmacoresistant MTLE patients (N=20) and post-mortem controls (N=5). Proteomic data was acquired using an Orbitrap EclipseTM TribridTM mass spectrometer, while metabolomic data was obtained via an LCMS-9030 quadrupole time-of-flight (Q-TOF) Shimadzu instrument. Bioinformatics analysis utilized ProteomeDiscoverer and R software, supplemented by SynGO, STRING PPI, and ClueGO analyses to explore biological alterations. This methodology provided insights into synaptosome proteomic and metabolomic profiles, elucidating potential mechanisms associated with pharmacoresistant MTLE. **Results:** Significant protein and metabolite composition variations were observed among synaptosomes derived from distinct brain structures. Predominantly, the proteins identified in patient synaptosomes were associated with the presynaptic fraction, followed by the post-synaptic and synaptic membrane compartments. Our integrative analysis unveiled heightened hippocampal responses in serotonin and dopamine release cycles alongside notable alterations in NMDA receptor presentation and insulin receptor dynamics. Moreover, indications of heightened sensitivity to toxic substances suggested potential implications for drug metabolization within the hippocampus. **Discussion/Conclusion**: Our study delineates distinct protein and metabolite profiles within synaptosomes derived from various brain structures in patients with pharmacoresistant MTLE. Notably, the predominance of presynaptic proteins and observed alterations in neurotransmitter release cycles and receptor dynamics underscore the intricate molecular underpinnings of MTLE pathology. These findings provide valuable insights into potential therapeutic targets and avenues for further investigation in the pursuit of improved management strategies for pharmacoresistant MTLE patients.

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EXPLORING THE RELATIONSHIP BETWEEN PHYSIOLOGICAL AND INERTIAL CHARACTERISTICS IN INDUCED TREMOR EVENTS AMONG HEALTHY SUBJECTS

Caetano Ternes Coimbra[1], Giovani G. Martins[1], Bruno S. de Lima[1], Rickson C. Mesquita[1,2]

[1] Gleb Wataghin Institute of Physics, Universidade Estadual de Campinas - UNICAMP.
[2] School of Computer Science, University of Birmingham.

Introduction: Tremor is a well-known condition that can occur in various situations. Although it is commonly associated with diseases like Parkinson's and essential tremors, it can also happen naturally at rest or action in a milder form called physiological tremors. Factors like anxiety, stress, and muscle fatigue can enhance physiological tremors, serving as inducers in controlled environments. This study explores the relationship between physiological factors, such as muscle electrophysiology and oxygen tissue saturation (StO_2), and the inertial characteristics of tremors induced by muscle fatigue. **Materials and Methods:** We collected data from 11 healthy individuals (2 women, ages 19-35). The experiment protocol consisted of a one-minute wrist flexion isometric exercise using three weights with two series each. We collected inertial data from the wrist using a smartwatch (Galaxy Watch4, Samsung). At the same time, muscle electrical activity and StO_2 were obtained using an electromyography (EMG) armband (Myo Armband, Thalmic Labs) and a frequency-domain diffuse optical spectroscopy (FD-DOS) system (Imagent, ISS) in the forearm muscle. For this exploratory work, we extracted features of interest from EMG and accelerometer power spectral density, such as EMG peak power and tremor amplitude, along with their corresponding frequencies. **Results:** Our preliminary findings showed that both physiological and inertial sensors were sensitive to the tremor induced by the exercise at different loads, and the tremor frequency measured by the two variables was strongly correlated (). Additionally, we observed a moderate correlation between EMG peak power and tremor amplitude measured with the inertial sensors (). **Discussion/Conclusion:** These results provide initial insights into the relationship between physiological and inertial features during tremor events. A strong correlation between the frequency measurements reinforces the accuracy of wearable inertial sensors to detect physiological tremors. Therefore, extracting more information about tremor physiology from inertial sensors is possible, assuming an injective relationship exists between physiological and inertial measurements. To complete this study, we plan to investigate this relationship further and integrate StO_2 data into the analysis framework.

EXTENSIVE HIPPOCAMPAL SUBFIELD VOLUME LOSS ASSOCIATED WITH UNILATERAL TEMPORAL LOBE EPILEPSY REGARDLESS SIDE OF HIPPOCAMPAL SCLEROSIS

L. R. Pimentel-Silva[1], I. K. Aventurato[1], L. S. Silva[1], M.K.M. Alvim[1], F. S. Brancatti[1,2], F. Cendes[1], C. L. Yasuda[1]

[1]Laboratory of Neuroimaging, Department of Neurology, UNICAMP, [2]Faculdade de Psicologia, PUC-CAMPINAS

Introduction: The hippocampus plays a crucial role in the pathophysiology of temporal lobe epilepsy (TLE). Although hippocampal sclerosis (HS) has been largely addressed in TLE studies, both in- and ex-vivo, little is known about the effects of HS lateralization on hippocampal subfield volumetry. Here we aimed to evaluate hippocampal subfield volumetric changes in a large series of TLE patients and controls using automatic subfield segmentation. **Materials and Methods:** We included 3D T1-weighted images from 156 unilateral TLE-HS patients (67 right and 89 left-HS) and 305 age- and sex-matched controls, acquired in a 3T MRI scanner (Philips Achieva). Hippocampal subfield volumetry was performed using Hippunfold, a deep learning algorithm to automatically

segment hippocampal subfields. We applied generalized linear models with Sidak post hoc analysis to test HS side effects on ipsi- and contralateral subiculum, CA1, CA2, CA3, and CA4+dentate gyrus (CA4+DG) subfields volumes. For the control group, because there was minimal asymmetry between hemispheres (analyzed by paired t tests), we averaged left and right hippocampi subfields before group comparisons. **Results:** We found ipsi- and contralateral volume reduction in all subfields of TLE-HS group when compared to controls, except for contralateral CA3. However, left-HS showed smaller ipsilateral volumes than right-HS when compared to controls. When comparing patients, only CA1 contralateral volume was significantly reduced in right-HS when compared to left-HS (Table 1). **Discussion/Conclusion**: Here we described bilateral volume loss in TLE across all hippocampal subfields, except for unilateral volume loss in CA3, regardless side of HS. Nonetheless, left-HS patients presented with the most impaired volume loss ipsilaterally. This result is in line with findings of greatest brain abnormalities in left TLE. The only study investigating the effect of HS side on hippocampal subfield volumetry showed broader subfield abnormalities for right-HS, also failing to find overall differences between right- and left-TLE. However, this study collapsed CA2+CA3 subfields together and did not find differences in CA1 and subiculum, evaluating a small sample size. In conclusion, unilateral TLE-HS presented with broad, bilateral hippocampal subfields atrophy.

Table 1. Hippocampal subfield volumes (mm^3) descriptive statistics, overall tests and post hoc comparisons among the study groups.

		Test statistic*	Controls (mean ± SD)	Right-HS (mean ± SD)	Left-HS (mean ± SD)
Subiculum	Ipsilateral	$\chi^2_{(2)} = 467.5$ $p < 0.001$	597.19 ± 74.3	431.16 ± 79.9[a]	441.12 ± 76.7[a]
	Contralateral	$\chi^2_{(2)} = 36.4$ $p < 0.001$		559.37 ± 84.2[a]	547.25 ± 79.1[a]
CA1	Ipsilateral	$\chi^2_{(2)} = 932.3$ $p < 0.001$	832.71 ± 92.9	525.11 ± 107.7[a]	510.69 ± 139.3[a]
	Contralateral	$\chi^2_{(2)} = 37.9$ $p < 0.001$		753.19 ± 112.1[a,b]	795.61 ± 117.7[a]
CA2	Ipsilateral	$\chi^2_{(2)} = 382.5$ $p < 0.001$	139.35 ± 20.2	96.36 ± 23.2[a]	96.89 ± 27.6[a]
	Contralateral	$\chi^2_{(2)} = 51.8$ $p < 0.001$		123.45 ± 23.5[a]	125.96 ± 20.3[a]
CA3	Ipsilateral	$\chi^2_{(2)} = 274.9$ $p < 0.001$	223.83 ± 36.5	161.94 ± 42.9[a]	154.63 ± 51.5[a]
	Contralateral	$\chi^2_{(2)} = 2.8$ $p = 0.24$		217.09 ± 41.8	227.19 ± 38.8
CA4 + DG	Ipsilateral	$\chi^2_{(2)} = 689.6$ $p < 0.001$	406.83 ± 49.1	252.29 ± 68.7[a]	250.81 ± 84.2[a]
	Contralateral	$\chi^2_{(2)} = 26.4$ $p < 0.001$		383.84 ± 59.7[a]	376.33 ± 68.6[a]

FUNCTIONAL AND BEHAVIORAL EFFECTS OF BAICALIN PRE-TREATMENT ON THE ZEBRAFISH MODEL OF PTZ-INDUCED SEIZURES

Cintra, L.[1,2], Yanicostas, C.[3,4], Soussi-Yanicostas, N.[3,4], Maurer-Morelli, C. V.[1,2]

[1]Zebrafish Laboratory, Department of Translational Medicine, FCM, UNICAMP, [2]Brazilian Institute of Neuroscience and Neurotechnology, Campinas, Brazil, [3]NeuroDiderot, Inserm U1141, Université Paris Cité, Hôpital Robert Debré, Paris, France and [4]Department of Biochemistry, University of Paris, INSERM, T3S, 75006 Paris, France.

Introduction: Natural compounds have potential neuroprotective effects against inflammatory neurological diseases, including epilepsies [1,2]. Some flavonoids, when taken along with anti-seizure drugs can help reduce the likelihood of drug-resistant epilepsy [3]. Baicalin, a plant-based compound, has been shown to possess pharmacological properties such as anti-inflammatory, neuroprotective, anticonvulsant, and antioxidant activities [4]. Thus, we investigated the anti-seizure effects of BAI by using the Pentylenetetrazole (PTZ) induced-seizure model in zebrafish larvae model by analyzing locomotor behavior and neuronal Ca 2+ imaging. **Materials and Methods:** Locomotor behavior was monitored with an automated video tracking device (Zebrabox®, ViewPoint). At 4 dpf WT larvae were placed in a 6-well plate and treated with 7.5 μM baicalin or 0.1% DMSO for 24 h. At 5 dpf, larvae were treated and washed twice with E3 medium, placed individually in the wells of a 96-well plate and their activity was measured. Calcium activity was recorded using Zeiss LSM 880 laser scanning confocal microscope. At 4 dpf, Tg[HuC:GCaMP5G] were placed in a 6-well plate, and treated with 7.5 μM baicalin or 0.1% DMSO for 24 h. At 5 dpf, larvae were placed in the incubator of the Zeiss LSM 880 laser scanning confocal microscope at 28 °C for 15 min for acclimatization, and then placed horizontally. For the groups CTRL and BAI, calcium activity was recorded for 15 min, then 5 mM PTZ was added, and after 15 min of penetration calcium activity was recorded. The total exposure time to PTZ was 30 min. Statistical analyses were performed by one-way or two-way ANOVA test and then Bonferroni test using GraphPad v. 8.0 with significance ($p \leq 0.05$) **Results:** We did not find a significant difference between BAI-treated and CTRL animals in swimming behavior or neuronal calcium activity when they were exposed to the PTZ ($p > 0.05$). **Discussion/Conclusion**: Using rats as an animal model, Wang et al. (2008) and Yang et al. (2021) obtained results like ours. In the picrotoxin-induced seizure, BAI did not significantly alter the motor incoordination effect in the rotarod test [5]. In the kindling PTZ model, low concentration of BAI did not significantly alter the total distance [6]. It is essential to monitor the activities of the neuronal network to comprehend the seizure's onset and spread [7]. After administering BAI to animals, we noticed a slight decrease in the peak number of calcium activity. However, the statistical pattern of the BAI group closely resembled that of the CTRL or PTZ group. In conclusion, our results demonstrated that BAI does not have an anti-seizure effect in zebrafish larvae in the behavioral test and neuronal calcium activity, at least in the PTZ model and at the concentration and developmental stage parameters delineated by our experimental protocol.

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GENETIC STUDY OF MALFORMATIONS OF CORTICAL DEVELOPMENT

Laiz Luiza Miranda[1,2]; Luciana Cardoso Bonadia[1,2]; Fábio Rossi Torres[1,2]; Maria Augusta Montenegro[2,3]; Ana Carolina Coan[2,3]; Fernando Cendes[2,3]; Iscia Lopes-Cendes[1,2]

[1]Department of Translational Medicine, [2]Brazilian Institute of Neuroscience and Neurotechnology, [3]Department of Neurology; School of Medical Sciences, State University of Campinas (UNICAMP), Campinas, SP, Brazil.

Introduction: Human Cerebral Cortex development occurs through complex mechanisms, including three main stages: proliferation, migration, and cellular organization. Any alteration or discrepancy in one of these stages can result in malformation of cortical developmental (MCD), a condition characterized by variable clinical presentation, often associated with intellectual disability and epilepsy. With advances in molecular techniques, such as whole exome sequencing (WES), it has become possible to identify genetic variants in genes associated with monogenic diseases, including MCDs. Therefore, this study aims to investigate the monogenic causes of MCD in a large cohort of patients previously investigated from the clinical and neuroimaging point of view. **Materials and Methods:** We studied 96 patients who presented one of the following forms of MCD: lissencephaly, periventricular nodular heterotopia, polymicrogyria, and schizencephaly. We generated WES from all patients. Data was aligned and variant calling was carried out using the programs GATK 4.1.8.0, Picard 2.23.8, Samtools 1.14, and the BWA aligner version 0.7.17, with the GRCh38 version as the human genome reference. Variant data generated was subsequently analyzed using the Franklin variant interpretation platform [1]. Variants of interest were identified and classified according to the criteria proposed by the *America College of Medical Genetics and Genomics* (ACMG). **Results:** First, WES was analyzed using a bioinformatics panel composed of genes associated with MCD reported in the literature. After that, we used a secondary analysis to select candidate variants based on phenotypes, inheritance, biological pathways, variant frequency, confidence in variant call, and zygosity. Using both filters, we identified 407 variants in the 96 patients. Of these, we identified 17 variants that were more likely to be linked to the phenotype based on the ACMG variant classification. **Discussion/Conclusion**: Of the 17 variants, 3 are classified as pathogenic, 9 as likely pathogenic, and 5 as variants are currently considered of uncertain significance but leaning towards possible pathogenicity. Six of these variants are present in genes previously associated with MCDs [2]

(*DCX, FLNA, NSDHL, PIK3CA, and TUBA1A*). Eight variants were in genes associated with MCDs through the *Human Phenotype Ontology* (HPO) platform (*ARHGEF9, ASPM, COL4A2, DLL1, SHH e TP73*). We also found variants in *CACNA1A* and *SCN8A* which were classified as pathogenic by the ACMG criteria and are related to epileptic and developmental encephalopathies according to the *Online Mendelian Inheritance in Man* (OMIM). Furthermore, we a found variant in the *CCND2* gene, which was previously associated with focal cortical dysplasia (FCD) [3], a group of MCD. In conclusion, we could make a putative molecular diagnosis in approximately 18% of our patients with MCD.

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HAND DIFFERENCES IN AIMING TASK: A COMPLEMENTARY SPATIAL APPROACH AND ANALYSIS OF DYNAMIC BRAIN NETWORKS WITH EEG

L. A. Fernandes[1], T. Apolinário-Souza[2], G. Castellano[3], B. C. Fortuna[4], G. M. Lage[4]
[1]CoMNeuro, UFJF, [2]GAIM, UFRGS, [3] Gleb Wataghin Institute of Physics at UNICAMP, [4] NNeuroM, UFMG

Introduction: Left and right-hand exhibit differences in the execution of movements. Particularly, it has been shown that manual goal-directed aiming is more accurate with the right hand than with the left, which has been explained through the shorter time spent by the right hand in the feedback phase (FB). This explanation makes sense for the temporal aspects of the task; however, there is a lack of explanations for the spatial aspects. The present study hypothesizes that the right hand is more associated with the FB, while the left hand is more strongly associated with the pre-programming phase (PP). In addition, the present study aims to investigate differences between hands in functional brain connectivity (FBC). We hypothesize an increase in FBC of the right hand compared to the left hand. We hypothesize an increase in FBC of the right hand compared to the left hand. **Materials and Methods:** Twenty-two participants performed 20 trials of the goal-directed aiming task with both hands. All participants were right-handed university students whose mean laterality quotient on the Edinburgh Handedness Inventory (Oldfield, 1971). Participants placed the pen on the digitizing tablet at the corresponding position on the starting point (home position). Te B-Alert×10 sensor headset was used to acquire the electroencephalography data. The temporal and spatial measures of the motor task and functional brain connectivity were assessed. **Results:** Overall, the results confirm the study's hypotheses. Although the right hand stopped far from the target at the PP, it exhibited a lower final position error than the left hand. These findings imply that during the FB, the right hand compensates for the higher error observed in the PP, using the visual feedback to approach the target more closely than the left hand. Conversely, the left hand displayed a lower error at the PP than the right (Figure 1). **Discussion/Conclusion**: The study's results showed that, although the right hand had less time to use visual feedback, this use was more effective. Furthermore, our results indicate that increased inter-hemispheric inhibition may be one of the mechanisms associated with using visual feedback in the right hand. These findings may advance the understanding of the mechanisms of differences between hands already elucidated more than a century ago.

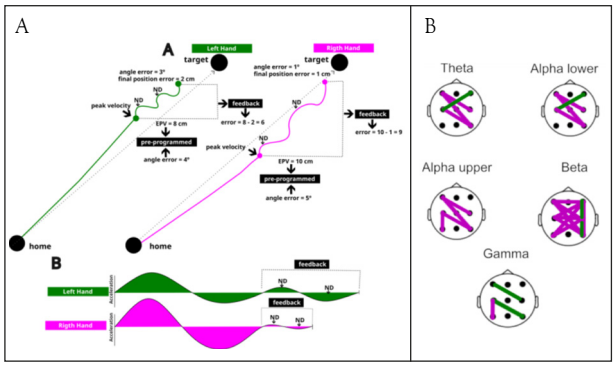

Figure 1. A. Measures of radial error and angle error at peak velocity and relation between the number of corrections and the radial errors of the feedback phase. B. Summarizes the results that exhibited significant differences or tendency related to functional connectivity. green = left hand. magenta = right hand.

HYPERSPECTRAL IMAGE RECONSTRUCTION FROM SMARTPHONE RGB + NIR IMAGES: AN APPLICATION TO TUMOR TISSUE ANALYSIS

A. C. C. Silveira[1], D. Carmo[1], L. Rittner[1]
[1]Medical Image Computing Lab., FEEC, UNICAMP

Introduction: Hyperspectral images (HSI) are composed of multiple spectral channels that extend beyond the visible range [1], providing a continuous spectrum and allowing the identification of tissues, materials, or substances based on spectral signatures of their chemical composition [2]. While HSI holds significant promise in medical applications, particularly in tumor delineation and segmentation, the cost and accessibility of hyperspectral cameras pose challenges for many hospitals. In this study, we aim to evaluate the accuracy of the novel architecture VITMST++ [3] in reconstructing the spectral signatures of brain glioma from simpler sub-sampled RGB + NIR images. Initially designed for skin reconstruction of smartphone applications, VITMST++ processes a 4-channel smartphone image and reconstructs a 61-channel hyperspectral image. **Materials and Methods:** In this study, the Brain HSI dataset from the HELICoiD project [4] was used, comprising 36 labeled hyperspectral surgical images with annotations for normal tissue, tumors, and hypervascularized tissue from 22 patients. The images were preprocessed to obtain 4 channels (RGB and NIR) which were used to reconstruct the 61 channels using the VITMST++ architecture trained for 500 epochs. The reconstructed intensity values were compared with the expected ones (ground-truth) in each channel for three tissues of interest: normal tissue, tumor and hypervascularized tissue (Fig A.I). Finally, five bounding boxes were extracted from each label to assess label intensity homogeneity (Fig B.I). **Results:** The VITMST++ model successfully reconstructed the hyperspectral image with 61 channels, starting from only 4 channels (RGB + NIR). Although the reconstruction accuracy varies along the different channels (wavelengths), the model output follows the ground-truth, preserving the tissue spectral signature (Fig A.II). Moreover, despite each tissue exhibiting relatively uniform intensities, distinguishing the specific label to which a pixel belongs becomes challenging when solely assessing RGB channels (Fig B.II), but easier considering the whole spectral signature (Fig B III). **Discussion/Conclusion**: VITMST++ shows promising results in reconstructing the spectral signatures from subsampled RGB images, potentially being able to assist surgeons in detecting hypersvascularized tissues and tumors with a common smartphone camera. The adoption of a spectral reconstruction model, such as the VITMST++, would allow the use of hyperspectral images

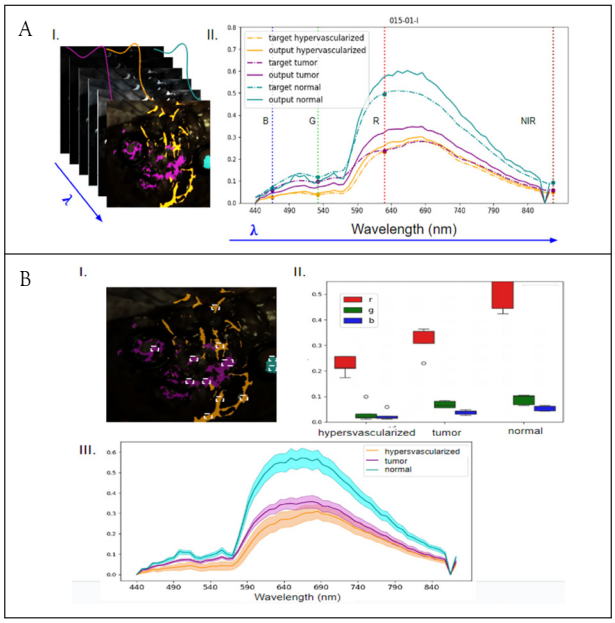

Figure 1. A - Spectral reconstruction of one case by VITMST++. I. Labeled target HSI: normal (cyan); tumor (purple); hypervascularized (orange). II. Normalized averages of channel intensity values generated through spectral reconstruction. Vertical lines correspond to RGB and NIR wavelengths. B - Characteristic tissue signature I. Bounding boxes selected in each tissue. II. Average channel intensity from selected bounding boxes. III. Spectral difference in each tissue. Filled areas correspond to intensity standard deviation within bounding boxes.

in hospital applications, overcoming financial constraints associated with traditional hyperspectral cameras.

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IMPACT OF EPILEPTIC SEIZURES ON THE IMMATURE BRAIN OF ZEBRAFISH: INVESTIGATING THE EFFECTS OF DIFFERENT CONVULSANT AGENTS ON LARVAL BEHAVIOR

P. Guimarães[1], L. C. Rodrigues[2], V. C. Fais[1], C.V.M. Morelli[1]

[1]Unicamp, School of Medical Sciences, Department of Translational Medicine, Zebrafish Laboratory [2]Unicamp, School of Medical Sciences, Campinas Poison Control Center (CIATox)

Introduction: In this study, we investigated the impact of epileptic seizures (both acute and status epilepticus) on immature brain. To achieve our goal, we used the zebrafish larvae model since it is an established model of epileptic seizure and has a wide range of behaviors already described and validated.[1][2] **Materials and Methods:** Wildtype zebrafish larvae at 6 days post-fertilization (dpf) were randomly divided into the following groups: 1. *Status epilepticus (SE)* – animals exposed to PTZ 15mM or PILO 30mM for 3 consecutive hours and 2. *Acute Seizure (AS)* - animals exposed to PTZ 15mM or PILO 30mM for 20 minutes. 3. *Control SE or AS* - animals handled in the same way as SE or AS but in aquarium water. Each group was composed of 12 larvae. Behavioral tests were carried out 24 hours after the convulsant treatment. All animals were tested for Thigmotaxis, Escape Response, Swimming Activity, and Light-Dark. Thigmotaxis and Swimming Activity were performed with the Danio Vision Equipment and the Ethovision Software (Noldus, Wageningen, Netherlands) using 5 minutes of lights on and 5 minutes off. The escape response was performed by applying a tactile stimulus to the animal's tail. Finally, the Light-Dark test perfomed in an arena adapted for larvae and was recorded using a smartphone camera and analyzed by two blind observers. Statistical analyses were performed with the Kruskal-Wallis test using GraphPad Prism version 10.0 (GraphPad Software, CA, USA). The significance level considered was $p < 0.05$. **Results:** According to our data, there was a significant increase ($p<0.05$) in thigmotaxis testing, which refers to the tendency of animals to move along the periphery of the arena. This suggests an increase in anxiety in animals treated with PILO SE and PILO AS, regardless of the lighting conditions, whether light or dark. In the swim activity test, we observed that the AS-PTZ Group exhibited higher swimming activity compared to the control group, but only in the dark; Regarding the escape test, which indicates motor response sensitization, animals in the SE-PTZ group took longer to achieve relaxation, while the SE-PILO group took less time, both compared to the control group ($p<0.05$). In the AS protocol, we found a reduction in relaxation time in the PILO group compared to the PTZ group ($p<0.05$). There was no difference in the light-dark test. **Discussion/Conclusion**: Our data showed that treatment with convulsant drugs PTZ and PILO in zebrafish larvae resulted in distinct behavioral changes. These changes persisted even after 24 hours of epileptic seizures. Animals treated with PILO in acute or prolonged exposure showed behaviors associated with anxiety. By conducting further behavioral analyses at different time points after seizure induction, we hope to gain more insight into the effects of these events on the developing brain and their long-term consequences.

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IMPAIRMENT OF INFORMATION PROCESSING SPEED IN PEDIATRIC-ONSET MULTIPLE SCLEROSIS

Vieira G.D.[1], Antônio F. F.[1], de Sá M. M. S.[1], Damasceno A.[1]

[1]Neuroimmunology Unit, University of Campinas, UNICAMP, Brazil.

Introduction: Pediatric-onset multiple sclerosis (PoMS) is defined as multiple sclerosis (MS) that started before 18 years old [1]. It generates a lot of physical disability, however, it can also generate significant cognitive impairment (CI), affecting about one-third of those patients, with the involvement of multiple cognitive domains [2]. This study aimed to evaluate cognitive aspects in pediatric patients. **Materials and Methods:** Ten pediatric MS patients were enrolled prospectively from the Clinical Hospital of the University of Campinas. Cognitive tests were conducted through The Brief Repeatable Battery of Neuropsychological Test and z-scores were obtained. It analyses 4 cognitive domains: verbal memory, visual memory, information processing speed (IPS) and verbal fluency. **Results:** Regarding the cognitive evaluation, we observed a reduced z-score in IPS tests (SDMT and PASAT, -1.54 and -1.72, respectively). Sixty percent of the patients had one cognitive domain impaired and another 40% had at least two domains affected. The IPS domain was the most frequently impaired (70%), followed by visual memory (40%). **Discussion/Conclusion**: Studies about cognition in the PoMs are scarcer, but they have taken on increasing importance, especially due to long-term cognitive impairment in these patients. Julian et al. [3] evaluated 231 pediatric patients, with a frequency of 35% of cognitive changes, having the most affected areas being motor coordination (54%) and visuomotor integration (50%), being these changes identified in the early stages of the disease. In conclusion, PoMS patients had significant impairment in the information processing speed.

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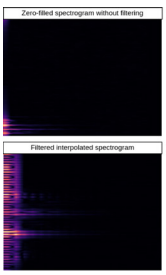
IMPROVING MAGNETIC RESONANCE SPECTROSCOPY FITTING WITH VISION TRANSFORMERS (VIT) AND SPECTROGRAMS THROUGH ENHANCED LOCALIZED PROCESSING

G. Dias[1], M. Oliveira[1], M. Almeida[1], S. Dertkigil[2], L. Rittner[1]

[1]Medical Image Computing Lab, FEEC, UNICAMP, [2]Radiology, FCM, UNICAMP.

Introduction: Magnetic Resonance Spectroscopy (MRS) offers a non-invasive approach to study the biochemical composition of brain tissue [1]. Deep learning (DL) methods have demonstrated superior capability to traditional MRS fitting methods in dealing with noisy signals, quantifying low-concentration metabolites, and addressing metabolites with overlapping characteristics [2]. This study advances the MRS fitting DL model by Almeida et al. [3], leveraging the strengths of the spectrograms representation of MRS signals by adding temporal and frequency filtering. **Materials and Methods:** The model utilizes a dataset featuring 13128 synthetic MRS signals from a short-echo time PRESS sequence with 21 metabolites and macromolecule contributions, and predicts 24 parameters, including the amplitudes of metabolites and macromolecules, as well as the signal's global damping, frequency, and phase shift. The spectrogram, which serves as the ViT [4] input, undergoes temporal filtering to retain only the first 60% of the signal's duration, since spectral entropy analysis indicates predominant signal decay and noise beyond this point. Additionally, the spectrogram is frequency-filtered to include only the 0 to 6 parts per million (ppm) region, focusing on the area containing the main metabolite information and excluding negative ppm values [1]. Finally, for compatibility with the ViT, upsampling is performed using bilinear interpolation instead of the zero padding used in the method by Almeida et al. (Fig.1). **Results:** The proposed model was evaluated against the models proposed by Almeida et al. and Shamaei et al. [5] using 128 test samples, presenting better results across 15 parameters for the R^2 score and 12 parameters for the Mean Percentage Error (MAPE) (Fig.1). **Discussion/Conclusion**: Spectrograms have shown to improve DL fitting performance by preserving both frequency and time information from



	New Model		Almeida et al.		Shamaei et al.	
Parameter	MAPE	R^2	MAPE	R^2	MAPE	R^2
Ala	**44.5516**	**0.6637**	55.6802	0.5772	87.8700	-0.0200
Asp	18.7545	-0.1303	**17.4783**	**-0.0292**	47.5200	-11.8000
Cr	**5.5058**	**0.8850**	6.4073	0.8641	6.0200	0.8800
Glc	14.8367	0.2508	**14.6556**	**0.3182**	32.9700	-4.7500
Gln	**10.9096**	**0.4602**	12.6337	0.3030	19.1100	-0.5300
Glu	6.7956	0.8119	**6.2045**	**0.8375**	8.8800	0.6800
Gly	**38.2396**	**-0.0237**	38.5757	-0.0527	41.6900	-2.4200
Ins	**5.1373**	**0.9159**	5.4842	0.9146	8.3000	0.7100
Lac	36.8086	0.1080	**36.6441**	-0.0556	41.3700	**0.4700**
NAA	3.9228	0.9518	3.8217	0.9493	**2.9600**	**0.9800**
PCho	21.3770	**0.6515**	23.4405	0.4820	**18.2200**	0.6200

Figure 1. Same spectrogram with zero padding and with the proposed localized processing (left). R^2 and MAPE on the test set for the most common metabolites. Best results in bold (right).

MRS signals. Moreover, the ViT showed improvement in both accuracy and quality of the fit compared to that proposed by Almeida et al., indicating that the filtered spectrogram provides better features for MRS fitting. Future experiments will focus on *in-vivo* data and comparison to popular MRS fitting softwares, such as LCModel [6].

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IN SILICO ANALYSIS OF *RELN* GENE POLYMORPHISMS: IMPLICATIONS FOR NEURODEVELOPMENTAL AND NEURODEGENERATIVE DISORDERS

Tereza Raquel Xavier Viana[1], Bruno Cateb Resende de Oliveira[2], João Pedro Perin[2], Karina Colombera Peres[3,4], Regiane Priscilla Ratti[1], Natássia Elena Bufalo[2,3,4], Larissa Teodoro Rabi[1,4,5]

[1]Department of Biomedicine, Nossa Senhora do Patrocínio University Center (CEUNSP), Itu/SP, Brazil; [2]Department of Medicine, São Leopoldo Mandic and Research Center, Campinas/SP, Brazil; [3]Department of Medicine, Max Planck University Center, Campinas/SP, Brazil; [4]Laboratory of Cancer Molecular Genetics, Faculty of Medical Sciences, State University of Campinas (UNICAMP); [5]Institute of Health Sciences, Paulista University (UNIP), Campinas/SP, Brazil.

Introduction: The *RELN* gene encodes a large extracellular matrix protein known as Reelin, pivotal in guiding neuronal migration and positioning during brain development[1]. Dysregulation or mutations in *RELN* gene have been implicated in various neurodevelopmental disorders, including schizophrenia, bipolar disorder, lissencephaly, and autism spectrum disorders (ASD). Experimental models have highlighted *RELN*'s essential role in synaptic activity modulation[2,3]. This emphasizes the importance of investigating the *RELN* gene to comprehend the genetic mechanisms underlying neuropsychiatric conditions. This study aimed to assess the potential utility of *RELN* gene polymorphisms as biomarkers for neurodevelopmental disorders. **Material and Methods:** This study conducted an in silico analysis of polymorphisms of *RELN* gene and their effects on protein structure, function, flexibility, and stability. For this purpose, a total of 12 bioinformatics tools were utilized: PredictSNP1[4] (including PredictSNP, SIFT, PolyPhen-1, PolyPhen-2, MAPP, PhD-SNP, SNAP, PANTHER, and nsSNPAnalyzer) and iStable[5] (comprising iStable, MuPRO, and I-Mutant). The selection of these tools was based on their capacity to predict the impact of genetic variations on proteins, enabling a comprehensive assessment of the consequences of amino acid alterations in proteins. **Results:** Twenty-three amino acid alterations (H545Y-rs371529135; R599C-rs369272208; R651H-rs144078760; R1010H-rs373089551; R1010C-rs375752077; R1198H-rs114655373; R1198L-rs114655373; C1422Y-rs192235848; P1703R-rs2229860; G1774R--rs141655702; W1970G-rs3025939; R2011C-rs374628146; G2153D--rs144387303; C2159Y-rs375440000; R2211H-rs374088118; G2233E--rs139819388; V2246M-rs201561165; G2255D-rs142573628; R2285C--rs144565023; D2309N-rs138978280; I2313T-rs141004002; R2639H--rs369735904; and G2876R-rs371264058) were considered deleterious by at least eight tools of PredictSNP1.0 consensus. In addition, 69,5% (n=16) of the amino acid alterations are capable of decrease protein stability. **Discussion/Conclusion**: Genetic investigations on *RELN* have demonstrated its correlation with lissencephaly and highlighted the necessity of exploring its involvement in neuropsychiatric disorders. In AD, the Reelin pathway (DAB1-RELN) is intricately associated with disease onset and progression, underscoring the complexity of the underlying mechanisms[6]. Similarly, in ASD, alterations in the *RELN* gene identified by the Autism Sequencing Consortium have shown strong associations with the condition, accompanied by elevated reelin levels in affected children. Polymorphisms within *RELN* may disrupt the production of reelin protein, which is essential for brain organization and neuronal migration, potentially compromising synaptic connectivity. In summary, *RELN* plays a crucial role in brain development and function, providing valuable insights into both neurodevelopmental and neurodegenerative disorders. Consequently, investigations involving patients with these disorders are essential to validate the potential utility of these polymorphisms as biomarkers.

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INITIAL ANALYSES OF A GENERALIZED SSVEP-BASED BCI USING A LINEAR CLASSIFIER

A. M. F. Martins[1], W. P. Fernandes[1,2], H. M. Leite[1], P. C. Fernandes[1], S. N. Carvalho[1], D. I. Alves[1]

[1]Division of Electronics Engineering, Bioengineering Laboratory, Aeronautics Institute of Technology (ITA), [2]Faculty of Medical Sciences of São José dos Campos Humanitas.

Introduction: Brain-Computer Interfaces (BCIs) utilize brain signals to control external devices and have shown great efficacy as assistive and rehabilitative technologies [1]. Due to its non-invasiveness, electroencephalography (EEG) has become a common technique for recording brain activity in BCI applications. Specifically, EEG-based BCIs can detect steady-state visually evoked potentials (SSVEP) and, for example, can restore the ability of "locked-in" patients to communicate with the external world [2]. The training and calibration phase of the BCI system involves collecting brain signal, which is time-consuming for patients. This study provides a preliminary analysis of the impact on the performance of SSVEP-based BCI systems when using brain signals from other subjects to train the system. **Methods:** We utilized a database with EEG recordings of 35 subjects [3]. Each subject participated in six trials (5 s each) involving 40 visual stimuli. A Common Average Reference filter was applied, and the Fast Fourier Transform magnitude was extracted at 10 Hz and 14 Hz from electrodes O1, O2, and Oz per 1-s window of each trial. The binary classification was conducted using a linear classifier based on the method of least squares in four scenarios: Scenario I (sI): an 80%/20% train-validation split within subjects. Scenario II (sII): validation performed with one subject, trained with the remaining 34. Scenario III (sIII): the validation set comprised subjects with less than 90% accuracy in sI, trained on others. Scenario IV (sIV): similar to sIII, with an 80% accuracy threshold. **Results:** Figure 1 shows the mean accuracy across stimuli for each subject from validation sets in scenarios sII, sIII, and sIV. For scenario sI, it illustrates the mean accuracy over 200 iterations. **Discussion/Conclusion**: Training the system with data from other subjects did not reveal a statistical difference ($p>0.05$) between the evaluated scenarios, although the average accuracy of sI remained slightly higher across tests. Subjects 14 and 16 demonstrated a performance decrease of over 10% between accuracies obtained in sI and sII. This could be due to the reduction of linear separability of their own

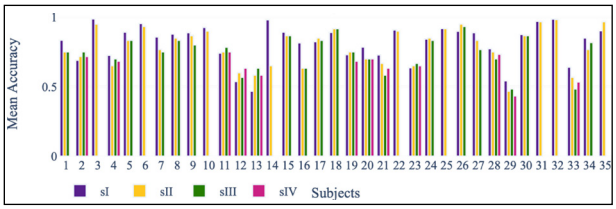

Figure 1. Mean accuracy for each subject from validation sets in scenarios sI, sII, sIII, and sIV.

data by incorporating data from others. However, for the remaining 33 subjects, the generalization of the BCI training either improved the system performance (Subjects 2, 11, 12, 13, 17, 18, 19, 23, 24, 26 and 35) or had no impact on it. Analyzing the average of the subject group, the removal of low-accuracy subjects in sI did not significantly impact the performance obtained in sIII and sIV. The consistent clustering of their data around the decision hyperplane in sI suggests that their absence would not affect hyperplane training. Consequently, similar accuracies were obtained across scenarios sII, sIII, and sIV for the subjects involved. In summary, our results indicate that it is feasible to conduct a generalized training of the SSVEP-based BCI, even using simple techniques such as the linear classifier.

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INSIGHTS INTO POST-COVID ANOSMIA: UNRAVELING NEURAL ALTERATIONS THROUGH 7T MRI AND DTI ANALYSIS OF OLFACTORY PATHWAYS

Mariana Lee Han[1], Felipe Carvalho Leão[2], Fábio de Rezende Pinna[2], Carlos Leandro Silva dos Prazeres[1] , Maria Concepcion Garcia Otaduy[1]

[1] LIM44, Instituto de Radiologia, Laboratório de Ressonância Magnética em Neurorradiologia, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR. [2] Departamento de Oftamologia e Otorrinolaringologia, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR.

Introduction: This study addresses the pervasive chemosensory alterations of smell (Alterações Quimiossensoriais do Olfato - AQO) emerging as prevalent symptoms in COVID-19, caused by the SARS-CoV-2 virus. Despite initial reports indicating a low incidence, AQO has become a prominent early symptom, affecting a significant percentage of cases. Understanding olfactory dysfunction in COVID-19 remains challenging due to the subjective and retrospective nature of many studies. This study focuses on the magnetic resonance imaging (MRI) evaluation of olfactory pathways, aiming to provide insights into persistent anosmiapost-COVID-19. **Materials and Methods:** Twenty subjects (14 post-COVID anosmia, mean age 32,8 years old, 6 controls, mean age 23,7 years old) underwent 7T MRI analysis with a 1Tx/32Rx headcoil. The protocol included T1 structural images and diffusion tensor imaging (DTI) for microstructural assessment. Data processing involved concatenating b-value and b-vector files, analyzing distortions with FSLeyes, correcting distortions with TOPUP and EDDY, conducting quality control and calculating FA maps with DTIFIT. Additionally, Tract-Based Spatial Statistics (TBSS) was performed to assess group-level differences in diffusion metrics, offering a comprehensive evaluation of microstructural changes among the fiber tracts skeleton. We also selected ROIs based on the JHU-ICBM-Labels-1mm template, and compared FA values for each defined tract for both groups. Statistical analysis included Saphiro-Wilk test to test the normal distribution and the U Mann-Whitney test to compare group differences. P-values smaller than 0.05 were considered statistically significant. **Results:** TBSS analysis did not reveal any significant difference among the groups. Analysis of the individual JHU-ICBM tracts revealed that the right anterior corona radiata ($p = 0.041$) and the right inferior cerebellar peduncle ($p = 0.033$) presented lower FA values than the control group. No other tract exhibited statistically significant differences. **Discussion/Conclusion:** Our 7T MRI study revealed lower FA values in regions such as the right anterior corona radiata andright inferior cerebellar peduncle among individuals with post-COVID anosmia compared to controls. These regions, traditionally associated with motor coordination, sensory integration, and the transmission of signals between the cerebral cortex and other brain areas, have not been directly implicated in anosmia. However, their involvement in broader neural networks suggests potential connections to the intricate mechanisms underlying olfactory dysfunction. The right anterior corona radiata, in particular, is known for its role in motor and sensory pathways, and alterations in this region may contribute to the complex interplay between sensory perception and motor responses. The findings highlight the need for further research to unravel the specific functional implications of microstructural changes in these regions concerning anosmia. Despite the study's limitations, including a small sample size, these unexpected results underscore the importance of exploring diverse brain regions to comprehensively understand the neurological manifestations of post-COVID anosmia. Future investigations, including an expanded patient sample and bootstrap analysis, aim to strengthen the robustness of our findings and contribute valuable insights to the evolving understanding of COVID-19-related neurological sequelae.

INVESTIGATING THE ROLE OF DELAYED INFORMATION IN FUNCTIONAL CONNECTIVITY FOR MOTOR IMAGERY HAND TASKS DISTINCTION

Pedro Felipe Giarusso de Vazquez[1,2], Carlos Alberto Stefano Filho[1,2], Gabriela Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN-FAPESP

Introduction: Motor imagery (MI) brain-computer interfaces (BCIs) aim at translating neurophysiologic activity (from movement imagination) into commands to control external devices. However, intra and inter-subject variability of brain responses has been a big challenge in the field, precluding BCIs to be adopted in clinical environments. This aim of this study was to explore the impact of delayed information on functional connectivity (FC) in the context of differentiating left and right-hand MI tasks. **Materials and Methods:** In this study, a male participant, aged 18, engaged in 12 MI sessions, recorded with a 16-channel electroencephalography (EEG) system. Each session comprised 5 runs, consisting of 8 MI tasks (4 per hand), in which the participant imagined opening and closing his hands while maintaining a tactile kinesthetic sensation. The task sequence was randomized and indicated through a cursor pointing left or right. The blocks followed a sequence of rest (8 s), preparation (2 s), and task execution (6 s). Pre-processing consisted of elimination of the 1st second of the signal, high-pass filtering at 0.5 Hz, ICA to remove blink artifacts and re-referencing to the common average. Task blocks were divided into non-overlapping 1 s windows and filtered in the mu (8-12 Hz) and beta (13-31 Hz) frequency bands. FC was assessed using the motif synchronization (MS) method [1] with delays ranging from 0 (no delay) to 8 (31.25 ms). Graph metrics (strength, eigenvector centrality, clustering coefficient, local efficiency, assortativity) were computed for each window and fed as a vector feature to an SVM classifier. **Results:** Table 1 shows the mean SVM accuracy across sessions. Overall the mean results were just above chance level (0.50), with the maximum test accuracy being 0.77 for the mu band at session 1/delay 4, and 0.67 for the beta band at session 7/delay 0 and session 8/delay 3. Interestingly, although mean training accuracies were mostly better than test ones, as expected, the maximum values were 0.67 for the mu band at session 0 and 0.66 for the beta band at session 6, both for delay 5. **Discussion/Conclusion:** Although the overall results were quite similar among bands and delays, the best mean training and test accuracies obtained were for the higher delays (6 to 8, i.e., ~23 to 31 ms). On the other hand, the maximum accuracy values obtained for both training and test occurred for a larger range of delays (0, 3 and 4 for test and 5 for training), and sessions (0, 1, 6, 7, 8). The first of those results could indicate a tendency for higher delays to better encode relevant FC information to distinguish between left and right MI. The last result simply reinforces the fact that many external variables can influence the MI EEG signal patterns, and therefore some days (sessions) were best than others to encode the information at a given metric. Future research should continue to explore the intricate dynamics of temporal information in neural connectivity to enhance the robustness and precision of motor imagery classification systems.

Table 1. Mean SVM accuracy across sessions for differentiating among right and left MI.

	Delays	0	1	2	3	4	5	6	7	8
Mean training accuracies	μ band	0.56	0.56	0.56	0.56	0.56	0.56	0.55	0.56	0.57
	β band	0.54	0.56	0.55	0.54	0.55	0.56	0.54	0.57	0.56
Mean test accuracies	μ band	0.50	0.49	0.51	0.50	0.52	0.50	0.53	0.51	0.50
	β band	0.51	0.49	0.51	0.53	0.51	0.50	0.50	0.54	0.50

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IORT MULTI-AGENT FOR ASSISTIVE HOMES: FIRST TEST

F. A. O. Mota[1], C. B. da Silva[1], E. A. B. Huayhua[1], B. M. Portela[1], E. Rohmer[1]

[1]Dept. Computer Engineering and Industrial Automation, FEEC, UNICAMP

Introduction: The deployment of a multi-agent solution consists of the joint action of agents in a specific environment. Agents must perceive the environment and act based on defined objectives, which determine their actions [1]. Allied with the definitions of Internet of Robotic Things (IoRT), the agents form an ecosystem with local and distributed intelligence, capable of acting on the environment while moving within it [2]. The current project is developed to be applied in assistive homes for the elderly or people with disabilities, and it delineates three types of agents: robotic, human, and IoT. Additionally, a normalization system is used to convert natural language into machine language. The objective of article is to present the structuring and validate the first test. **Materials and Methods:** A mobile robot P3DX was used for navigation in the laboratory with the assistance of three AXIS PTZ 214 cameras. The cameras act as IoT agents, while human agents are represented by objects with ArUco tags distributed throughout the space. Everything is managed by a REST server, with agents and the server following predefined standards for communication. The test involved detecting the position of the human agent and navigating the robot in response to the agent's requests. **Results:** The environment operates on a Wi-Fi network, where agents use a Large Language Model (LLM) to interpret requests. Actions are executed and visualized in real-time in a simulated environment (Figure 1). The server stores data divided into three databases: agents, rooms, and objects. Agents interact with each other, ob-

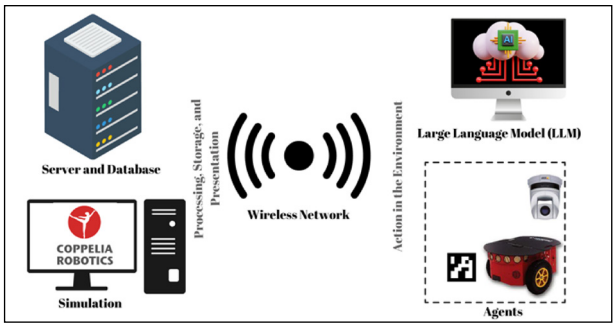

Figure 1. Organization of the First Test.

jects are targets of action, and rooms represent fixed areas. The server allows operations of querying, updating, inserting, and deleting in the database, with security restrictions applied to the rooms. To detect human agents, two cameras were used, positioned inside the room and in the hallway where the robot was. The system accurately detects and identifies agents, mapping their positions correctly in the simulator. The robot's navigation is facilitated by the LLM; upon receiving requests in natural language, the robot moves to the specified location, accurately reflecting the actions in the simulator. In both instances, the communication with the server remained stable. **Discussion/Conclusion**: The computational performance or device configuration has not been evaluated yet. However, the proposed framework managed to correlate all present agents and display their arrangement in relation to the environment. The simplified server communication structure facilitates scalable and interoperable work. Therefore, the future goal is to increase the number of agents and incorporate actions for object manipulation, expanding the possibilities for assisted domestic activities. References: [1] Gomez MA et al., doi:10.1016/j.robot.2018.05.001; [2] Batth RS et al., doi:10.1109/ICCS.2018.00033.

LONGITUDINAL ANALYSIS OF SEIZURES FREQUENCY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY ASSOCIATED TO HIPPOCAMPAL SCLEROSIS UNDER PHARMACOLOGICAL TREATMENT

Aline de Fátima Dias[1], Pamela Regina Henning[1], William Souza Martins Ferreira[1], Marina Koutsodontis Machado Alvim[1], Clarissa Lin Yasuda[1], Fernando Cendes[1]

[1]Laboratory of Neuroimaging, Department of Neurology, UNICAMP.

Introduction: Mesial Temporal Lobe Epilepsy (mTLE) is the most common focal epilepsy in adults and Hippocampal Sclerosis is the main cause [1]. Its treatment involves the use of anti-seizure medications which are associated with several side effects. Around 75% of patients will present pharmacoresistance [2]. Little is known about the clinical patterns of seizures frequency over a long period of follow-up, as well as the profile of anti-seizure medications used throughout the follow-up. **Objective:** To evaluate the lifetime seizure frequency in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (mTLE-HS). **Materials and Methods:** We studied 118 patients with mTLE-HS followed at UNICAMP. We reviewed the seizure frequency, age, duration of epilepsy, dosages and type of antiseizure medications (ASM) used. Patients were split into 3 groups: seizure-free (no seizures in the last two years or more of follow-up), fluctuating (seizure-freedom periods of one year or longer) or pharmacoresistant (never had a seizure-free period of more than one year). Pharmacoresistant patients did not undergo surgery either because they refused it or had contraindications. Patients who underwent surgery were not included in this study. **Results:** The mean age was 56.13 years and mean follow-up was 20.25 years (range 3-47, SD 9.83). 35.6% (n=42) had right-TLE, 50% (n=59) left-TLE and 14.4% (n=17) bilateral-TLE. Thirty-six (30.5%) were seizure-free, 39 (33.05%) had a fluctuating course and 43 (36.45%) were pharmacoresistant. There were no differences among groups in relation to the age they became seizure-free, age of epilepsy onset, epilepsy duration, epilepsy family history, number of ASM used over the years or number and type of ASM in use at the last follow-up ($p>0.074$). The most common ASM was carbamazepine. **Discussion/Conclusion**: Three clinical evolution patterns were observed among patients with mTLE-HS who did not underwent surgery: pharmacoresistant, fluctuating seizure control/pharmacoresistant, and seizure-free. We found no significant differences in the main clinical features among groups. Further studies are necessary to define the factors that could predict these three outcome profiles.

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LUNG LOBE SEGMENTATION USING PROBABILISTIC TEMPLATES AS A PRIORI INFORMATION IN CT IMAGES OF SEVERELY DISEASED LUNGS

Jean. A. Ribeiro[1], Diedre Santos do Carmo[1], Fabiano Reis[2], Leticia Rittner[1]

[1]Medical Image Computing Lab, FEEC, UNICAMP, [2]Radiology, FCM, UNICAMP.

Introduction: Lung lobe segmentation is considered an essential support tool for the diagnosis and treatment of lung diseases, but it is a challenging task in computed tomography (CT) images of the lung with diseases considered severe, due to pathological deformation and morphological changes in the pulmonary fissures. Although there are many methods in the literature, no good method or tool has been found that performs this task effectively [1]. This work aims to develop an approach for automatic segmentation of lung lobes using deep neural networks and a priori knowledge in CT images of lungs with anatomy severely altered by lung diseases. **Materials and Methods:** Our method uses the 3D U-Net [2] and probabilistic templates, integrated into the network as a priori knowledge, to learn the anatomical shape of the lungs. It trains a first UNet to do a coarse segmentation on a downsampled version of the CT volume, followed by 5 UNets, each one trained for refining the segmentation of each lobe separately. The template is used in conjunction with the loss of the first network and as a bounding box and post-processing in the second network. Probabilistic templates were generated by registering CT volumes manually labeled. Two public datasets were used to train the model. The first dataset is composed of 50 CT images from LUNA16 (cancer), with annotations of the lung lobes [4] and the second, composed of 8 CT images from Coronacases (COVID-19), with annotations of the lung lobes [5]. **Results:** In CT images with annotations for the lung lobes and well-defined fissures, dice values were considerably high, greater than 92% in all lobes. In cases with severe lesions or incomplete fissures, all methods struggled to achieve correct segmentation (Fig.1-B and E). However, errors caused by consolidation that our method made, were easily corrected with post-processing steps (Fig.1-C and D). Nevertheless, our method did not make errors that are difficult to correct, such as the wrong detection of pulmonary fissures, thanks to the use of a priori information in the network (Fig.1-D). Unlike our method, the Lungmask method was not as efficient in finding lung fissures, even with the inner region of the lobes correctly segmented (Fig.1-E). **Discussion/Conclusion**: Our approach combining UNet and a priori information, supplied by templates, was successfully employed to inform the target of the most likely lobe to be utilized

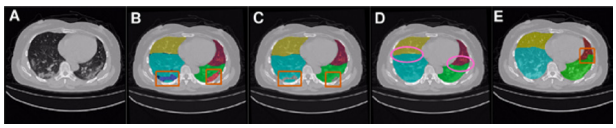

Figure 1. Qualitative assessment on a CT image (coronacases_010) with severe pathology: (a) ct ; (b) model output after choosing the largest connected; (c) largest connected component with lung template; (d) final post-processing by hole fillings; and (e) output by Lungmask model. Locations where the method got it right are represented by a circular region. Locations where the method made an error are represented by a rectangular region.

for filling gaps and find the fissures easily. Specially in severe cases, the inclusion of probabilistic templates was essential for the model to accurately segment lung lobes that exhibit lesions, opacities, and consolidations on CT images.

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"MATERNAL HIGH-FAT FEEDING STIMULATES CCR2 MONOCYTE MIGRATION INTO OFFSPRING'S HYPOTHALAMUS"

[1,3]Marin, N.P.,[2,3]Cavalheiro, I.V.S., [3,4]Alves, E.S.,[2,3]Guimarães, A.B.A.,[3,4]Velloso, L.A.,[1,3]Mendes, N.F

[1]Dept. Translational Medicine, FCM, UNICAMP; [2]University of São Francisco (USF); [3]Laboratory of Cell Signaling, OCRC, UNICAMP; [4]Dept. Pathophysiology, FCM, UNICAMP.

Introduction and Hypothesis: The inflammatory response triggered by a high-fat diet (HFD) in the hypothalamus involves a complex interaction among

proinflammatory cytokines and chemokines, along with the infiltration of peripheral immune cells, specifically CCR2 monocytes expressing the receptor for monocyte chemoattractant protein-1 (CCL2). Recent research by our research group has revealed a notable sexual dimorphism in the gene expression profile of hypothalamic CCR2 monocytes in HFD-fed mice. Based on this finding, we hypothesize that maternal diet plays a role in shaping the CCR2 transcriptome of offspring, thereby influencing their inflammatory and immune response. **Objective:** To evaluate the transcriptome of CCR2 monocytes from the offspring of female mice fed a standard diet (SD) and HFD during the pre-gestational, gestational, and lactation periods. **Materials and Methods:** We employed CCR2-RFP mice, which express a red fluorescent protein (RFP) sequence replacing the coding sequence of the Ccr2 gene. Six-week-old female CCR2-RFP mice were divided into two groups: one fed a standard diet (SD) and the other fed a high-fat diet (HFD) for four weeks and were subsequently bred with CCR2-RFP male mice. Offspring were weaned at post-natal day 21 (P21), separated by gender, and weighed. Glycemia was assessed after a 6-hour fast, and blood samples were collected for biochemical analyses. Offspring brains were designated for CCR2 monocyte visualization by confocal microscopy, while retroperitoneal white adipose tissue was harvested for adiposity assessment. **Relevance:** On P21, male and female littermates from HFD-fed dams displayed increased body and fat mass, along with higher plasma levels of total cholesterol and triglycerides compared to the offspring from SD-fed dams. There were no significant differences in fasting glycemia. Confocal microscope analysis revealed a substantial presence of CCR2 monocytes in the hypothalamic parenchyma and lining the third ventricle of male and female littermates from HFD-fed dams, which was not observed in the offspring from the SD-fed dams. Collectively, our data reinforce that maternal high-fat feeding triggers metabolic reprogramming of the progeny, affecting not only their energy metabolism but also accelerating the trafficking of CCR2 monocytes to the hypothalamus. In future analyses, we will explore the hypothalamic chemokine profile in these offspring and the transcriptome of CCR2 monocytes from their blood samples, aiming to identify key target genes and signaling pathways influenced by fetal metabolic programming.

MENINGIOMA REPRESENTATIVE METABOLITES IN LIQUID BIOPSY: THE POTENTIAL OF METABOLOMICS APPROACH

Estela de Oliveira Lima[1], Gabriel Araujo Kurokawa[1], Pedro Tadao Hamamoto Filho[1], Jeany Delafiori[2], Aline Faria Galvani[1], Arthur Noin de Oliveira[2], Flávia Luísa Dias-Audibert[2], Rodrigo Ramos Catharino[2], Marco Antônio Zanini[1], Adriana Camargo Ferrasi[1]

[1]Botucatu Medical School, São Paulo State University - UNESP, SP; [2]School of Pharmaceutical Sciences, University of Campinas - UNICAMP, SP.

Introduction: Meningiomas represent the most common primary tumor in the central nervous system, and they are classified into grades 1, 2 and 3, according to their malignancy [1]. The malignant meningiomas (grades 2 and 3) show high 10-year mortality rates, represented by 47% and 100%, respectively, and they can relapse even after therapeutical surgical resection [2,3]. The possibility of estimating relapses through a less invasive technique, in advance, such as liquid biopsy, would help to predict it and define the most effective therapeutic strategy. For that, it is necessary to find tumor representative biomarkers that could indicate meningioma presence. **Materials and Methods:** In this study, plasma samples from 50 healthy volunteers and 51 patients with meningioma were collected (n=43 - grade 1, n=5 - grade 2, n=3 – grade 3). Metabolites were extracted and submitted to mass spectrometry analysis into an ESI-LTQ-XL equipment, evaluating MS and MS/MS profiles. Statistical analysis was applied with PLS-DA and Fold Change. **Results:** Considering VIP score ≥ 2.5 and FC ≥ 2.5, differential metabolites were selected for meningioma cases (m/z ratios of: 172, 102, 1116, 931 e 143). They were used to build ROC curves intending to verify their ability to indicate the presence of tumor. Together, these five metabolites generated a ROC curve with area under the curve (AUC) of 0.99 (CI=95%). Using metabolomics databases (METLIN, LIPID MAPS and HMDB) and fragmentation profile, three of these five biomarkers were capable of being identified: 5-hydroxymethyluracil (m/z=143), sulfatide (m/z=931), and ganglioside (m/z=1116). These three metabolites, isolated from each other, were then tested through a ROC curve, and 5-hydroxymethyluracil showed the best accuracy (AUC=0.92). **Discussion/Conclusion**: Different studies support the hypothesis that 5-hydroxymethyluracil might indicate genomic instability, representing a tumoral biomarker [4]. In addition, sulfatide might indicate deregulation of ceramide metabolism [5], and ganglioside represents a molecule involved in immunomodulation, both processes increased in tumors [6]. In this scenario, these highlighted metabolites must be validated, but once it is done, they could be used to monitor patients after surgical resection using liquid biopsy. Their presence might represent tumoral molecular deregulation and indicate that the meningioma is back. These results highlight an opportunity to explore metabolites in liquid biopsy before and during therapy, helping to predict relapse and evaluate the response.

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METHOD FOR DIFFERENTIATING PREICTAL AND INTERICTAL STATES FROM LFP SIGNAL OF EPILEPTIC RATS

S. Y. Yamauti[1], G. O. S. Filho[1], E. Morya[1]

[1]Edmond and Lily Safra International Institute of Neuroscience, Santos Dumont Institute (ISD)

Introduction: The preictal and interictal states correspond to the phases before and between epileptic seizures, respectively. Characterizing and differentiating these states harness significant potential for developing predictive models for epileptic seizures, which is crucial for advancing responsive neurostimulation therapies [1]. **Materials and Methods:** Utilizing LFP data, provided by the Santos Dumont Institute through the Epilepsy Challenge on Kaggle (https://www.kaggle.com/competitions/ix-neuroengineering-symposium-epilepsy-challenge), from the motor cortex (M1) and ventral anterior nucleus (VA) in pentylenetetrazol (PTZ)-induced epileptic rats, this study delineates a methodology to characterize and classify the neurophysiological states through signal processing and machine learning strategies.Data pre-processing involved segmentation: 2-second window, with 1-second overlap in interictal condition, and 1.9s overlap in preictal condition; and bandpass filtering: 1-300Hz, Butterworth, order 4, to emphasize relevant frequency components. The difference in overlap size is a means to correct for the imbalance in the examples of interictal and preictal conditions. Feature extraction techniques included spectral and temporal feature extraction, and coherence analysis between M1 and VA electrodes. For predictive modeling and validation, various algorithms were evaluated, including Logistic Regression, Gradient Boosting, Random Forest, Support Vector Machine (SVM), and Multi-Layer Perceptron (Feedforward Neural Network). Hyperparameter tuning via grid search and cross-validation facilitated the selection of the most suitable model. The GradientBoostingClassifier emerged as the optimal model, achieving robust F1 scores on both public and private validation datasets. **Results:** The GradientBoostingClassifier model, fine-tuned through grid search and validation, achieved an F1 score of 0.60000 on the public leaderboard of the Kaggle competition. The model sustained its predictive power in the private validation phase with an F1 score of 0.59312. This stability in performance across data subsets shows the model's reliability and generalization capacity, and we believe this was the reason it got first place in the Epilepsy Challenge. **Discussion/Conclusion**: The developed methodology showcases the potential of predictive modeling in epilepsy management by characterizing and classifying neurophysiological states based on LFP signals. The robust performance of the GradientBoostingClassifier highlights its applicability in real-world scenarios, with implications for preemptive therapeutic strategies and personalized medicine in epilepsy care. While further optimization of the processing pipeline and exploration of alternative classifiers remain avenues for future research, this study supports the use of machine learning in epilepsy prediction, ultimately enhancing patient outcomes and quality of life.

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MODULATION OF IGF-1 RECEPTORS IN THE OLFACTORY BULB: A POTENTIAL THERAPEUTIC TARGET FOR OLFACTORY DYSFUNCTION IN PARKINSON'S DISEASE

L.S. Rodrigues[2], E.M. Azevedo[1], B.B.G. Santos[1], E.S. Mello[1], M.T. Lima[1], M. Fiori[1], A.S. Diniz[1], F.C. Mesquita[1], A.C. Braz[1], M.M.S. Lima[1]

[1] Federal University of Paraná, Neurophysiology Laboratory, Curitiba, Paraná, Brazil.

Introduction: The motor disturbances in Parkinson's disease (PD) result from extensive degeneration of dopaminergic neurons and dopamine depletion in the

nigrostriatal pathway. However, decades earlier, 90% of patients exhibit olfactory dysfunction, among other non-motor disorders. Adult cell proliferation in the subventricular zone, which produces dopaminergic interneurons in the olfactory bulb (OB), is regulated by factors such as IGF-1 receptors. This study aimed to analyze the modulation of IGF-1R in olfactory discrimination impairment. **Materials and Methods:** The experiments were approved by the Brazilian Committee of Animal Ethics of the Federal University of Paraná, under number 1517. To determine if the activation of IGF-1R in the OB by insulin could impair olfactory discrimination in adult male Wistar rats (N=12-18/group), we conducted a dose-response curve with three insulin doses (50mU, 100mU, and 150mU) in the OB cannulas and subjected these animals to an olfactory discrimination task (ODT). In the ODT, the animal explores the apparatus for 2 minutes during habituation and for 3 minutes during the test, in which the animal has to discriminate between two odors (familiar and non-familiar). To compare the behavioral data with a positive control, we performed an intranasal Zicam infusion (a substance containing gluconate and acetate of zinc) and subjected the animals (n=10) to the ODT. Subsequently, we evaluated the modulation of OB IGF-1 receptors by activation or blockade in an animal model of PD through intranigral infusion of the neurotoxin rotenone and submitted those animals to the ODT (N=9-12/group). Additionally, the expression pattern of p-IGF-1Rb in the OB was analyzed by Western blot (N=3-5/group). **Results:** We found that the activation of these receptors at the two highest doses of insulin generated olfactory discrimination impairment in the ODT, similar to the zicam group. In the PD animal model, we observed that the rotenone vehicle group exhibited impairment in the ODT, similar to the rotenone insulin and zicam groups. In contrast, both the sham vehicle group and rotenone BMS758407 (IGF-1R antagonist) group were able to discriminate between familiar and non-familiar odors. The expression pattern of p-IGF-1Rb in the OB supports the observed behavioral data, indicating a decreased expression in the OB of sham vehicle and rotenone BMS groups. **Discussion/Conclusion:** In conclusion, blocking OB IGF-1R may be related to the improvement and reversal of olfactory dysfunction in the animal model of PD, suggesting an important mechanism involved in the olfactory modulation of this disorder and, consequently, representing a significant therapeutic target for future studies.

NEUROIMAGING EVALUATION OF PATIENTS WITH GENETIC DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES

G. B. S. Ribeiro[1], A. C. Coan[1]

[1]Department of Neurology, School of Medical Sciences, University of Campinas (UNICAMP)

Introduction: The identification of consistent electroclinical phenotypes in patients with Developmental and Epileptic Encephalopathies (DEEs) of genetic etiology has enabled the development of precision therapies, as well as the prediction of prognosis and treatment of comorbidities. However, due to the plurality of phenotypic manifestations of a single gene mutation, there is still no specific imaging correlation in the majority of cases [1-3]. This study aims to describe the neuroimaging findings of patients with genetic DEEs, correlating with the genetic mutations, epileptic syndromes, and literature findings. **Materials and Methods:** We included individuals previously diagnosed with DEE and with prior identification of a genetic mutation related to the pathology. Patients with variants lacking phenotypic correlation were excluded. All patients were followed at the Clinical Hospital of the State University of Campinas (HC-UNICAMP), where imaging was previously performed for medical purposes. **Results:** Of the 25 patients included, 56% were female, and the average age at the onset of seizures was 19.14 months (SD: 27,68). Family history of epilepsy up to second-degree relatives was reported in 56%. The most frequent mutations were found in the KCNT1 and SCN1A genes (Fig. 1A), with autosomal dominant being the most observed zygosity. The most frequent phenotype was Early infantile developmental and epileptic encephalopathy (EIDEE) (Fig. 1B), and the most common neuroimaging abnormality (36%) was corpus callosum hypoplasia. Myelination delay was described in eight individuals, with the majority of cases (87.5%) showing terminal distribution. **Discussion/Conclusions**: In our analysis, 68% of patients with genetic DEE presented neuroimaging abnormalities, and the electroclinical phenotypes were consistent with previous reports in the majority of cases, yet new structural abnormalities were also observed. We believe that the descriptive assessment of neuroimaging patterns contributes to a better understanding and

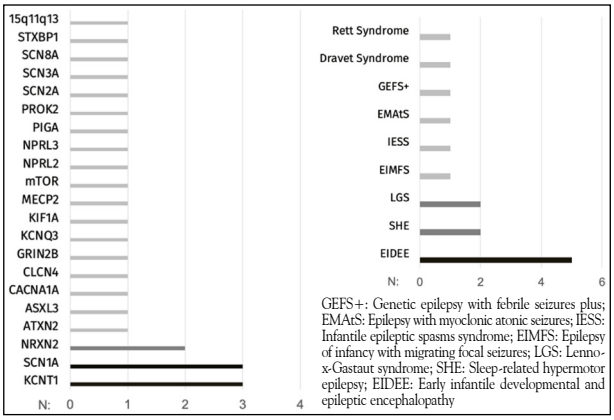

Figure 1. A – Mutations identified. B - Phenotypes.

categorization of structural brain alterations in this group of patients. The next steps include an increase in genetic testing and neuroimaging evaluation to expand the sample for assessment.

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NEUROIMAGING MARKERS IN HEALTHY BRAIN AGING: PRELIMINARY RESULTS FROM A SYSTEMATIC REVIEW

M. F. Socio[1], R.M. Loureiro[2], K. Schumacher[2], R. Frayne[3], A. J. M. Paulo[1,2], L. Rittner[4], J. P. Q. de Paiva[1,2]

[1]Brain's Institute, Hospital Israelita Albert Einstein, [2]Imaging Department, Hospital Israelita Albert Einstein, [3]Hotchkiss Brain Institute, University of Calgary, [4]Medical Image Computing Lab, University of Campinas.

Introduction: The process of aging is inherently linked to structural changes in the brain, consequently influencing cognitive functions across the lifespan of an individual. While much current research is focused on neurodegenerative diseases associated with aging, our study seeks to bridge a gap in other systematic reviews by identifying structural biomarkers that are associated with healthy brain aging. Our main objectives are to describe structural biomarkers derived from specific magnetic resonance (MR) imaging sequences, to enrich our understanding of healthy brain aging and, potentially, to facilitate the early detection of neurodegenerative conditions or therapeutic targets. Our review also examines the need for methodological rigor in neuroimaging processing protocols, offering a critical assessment of the reproducibility of existing studies to lay a firm groundwork for future research in healthy brain aging. **Methods:** This systematic review compiles studies from five primary bibliographic databases (Pubmed/MedLine, Embase, Lilacs, Scopus, and Web of Science). It focuses on structural MR sequences (*e.g.*, T1, FLAIR, and DTI) that examine brain changes in participants reported as healthy individuals aged over 60 years. A precise checklist, based on the Organization of Human Brain Mapping (OHBM) COBIDAS guideline [1], will be applied to assess the quality of neuroimaging processing protocols. The outcomes of this review will be reported in accordance with the PRISMA systematic review quality guidelines [2]. The full protocol of our study is documented on PROSPERO under registration CRD42023431376 [3] and is publicly available. **Results:** A total of 2,358 unique articles were identified using a validated search strategy. Following an initial screening, 131 articles were selected for inclusion. An additional 481 articles are currently under review for inclusion by a second experienced, blinded neuroradiologist. The process of independent peer review and validation by neuroimaging experts to ascertain eligibility of articles for this review is in its final phase. **Discussion and Conclusions**: Preliminary analysis has identified several common limitations within neuroimaging research, notably the absence of brain atlases tailored to the healthy elderly. This gap may affect analyses that require registration of regions of interest. Moreover, we commonly found a lack of detailed information regarding quality control and image preprocessing. Numerous studies failed to report correction for multiple comparisons in statistical evaluations or neglected to describe key demographic and physiological variables, including sex, age, or total intracranial volume. Importantly, the omission of clinical factors like hypertension, diabetes, depression, and obesity were missing. These factors can lead to structural brain change and confound image analyses, jeopardizing accuracy and

potentially causing misinterpretation. Such oversights may impact the validity and applicability of the findings, underscoring the need for more stringent and holistic approaches in neuroimaging studies focused on healthy aging. **Keywords:** Healthy Brain Aging; Aging Brain; Healthy Aging; Biomarkers; Magnetic Resonance Imaging; Structural Imaging; Neuroimaging; Neuroscience.

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OMEGA-3 FATTY ACIDS IN THE COGNITION AND BLOCKING OF MOLECULAR PATHWAYS ASSOCIATED TO ALZHEIMER'S DISEASE: A TRANSLATIONAL STUDY

Marcella Sant'anna[1,5], Kellen Cristina da Cruz Rodrigues[2,5] Leandro Pereira de Moura[2,5]; José Rodrigo Pauli[2,4,5]; Eduardo Rochete Ropelle[2,4,5]; Adelino Sanchez Ramos da Silva[6]; Marcio Luiz Figueredo Balthazar[3,5]; Dennys Esper Cintra[1,4,5]

[1]Nutritional Genomics Laboratory – LabGeN; [2]Molecular Biology of Exercise Laboratory – LaBMEx; [3]Neuroimaging Laboratory; [4]Nutrigenomics and Lipids Research Center – CELN; [5]University of Campinas – UNICAMP; [6]University of São Paulo – USP.

Introduction: Several studies have shown obesity as an extremely relevant component of Alzheimer's Disease (AD) predisposition. The accumulation of amyloid-beta (Aβ) and hyperphosphorylated TAU proteins is considered the hallmark of AD. In this translational study, the aim was to evaluate if the partial substitution of lard (rich in saturated fatty acids) for flaxseed oil (rich in omega-3 [alpha-linolenic fatty acid]) could block the molecular pathways associated with AD in diabetic and obese mice, as well the omega-3 concentration in the CSF (cerebrospinal fluid) of subjects with mild cognitive deficit. **Material and Methods:** Under ethical committee authorization (4973-1/2018), Swiss male mice were allocated to the following groups: Control (N=10), commercial diet for rodents for 16 weeks; Obese (N=10), under high-fat (HF) diet for 16 weeks; and Obese+ω3 (N=10), in which were fed with HF diet for 8 weeks and after another 8 weeks were fed with a HF diet with 1/3 of lard substituted for flaxseed oil. This oil was previously tested and contained 52% of alpha-linolenic fatty acid. The body weight and food intake were monitored constantly. The hippocampal bioinformatics were carried out. In the end, mice were submitted to insulin and glucose sensitivity and tolerance tests and learning and memory tests. Electronic microscopy, immunofluorescence, western blot, RT-qPCR, and lipidomics of the hippocampal tissue were carried out. Under the CAAE-09634412.5.0000.5404 ethical committee, 40 subjects with mild cognitive deficit were submitted to anthropometric tests and CSF analysis to detect the pro-inflammatory, TAU, and Aβ markers and the fatty acid profile, using lipidomic and metabolomic approaches. **Results:** Obese mice showed systemic and hippocampal molecular insulin resistance. In the hippocampus, inflammatory, endoplasmic reticulum stress, apoptotic, and AD proteins such as IL1β, TNFα, p-JNK, p-eIF2α, CHOP, BAX, βamyloid, and p-Tau were increased. The electronic microscopy has evidenced neurodegeneration and mitochondrial damage, which elicits cognitive impairment when compared with the control group. The omega-3 receptor, GPR120, was identified on several neuronal hippocampal cells from lean and obese mice and also showed in the bioinformatics, Western blot, and PCR approaches. Mice receiving flaxseed oil in the diet showed the presence of specific ômega-3 molecule, alpha-linolenic fatty acid incorporated in the hippocampal neurons. The molecular markers above described were significantly reduced in mice treated with a flaxseed diet. Interleukin IL1β and Aβ proteins in CSF were positively correlated with obese, but not lean subjects. Surprisingly, omega-3 appears in less concentration in the CSF of obese when compared with lean subjects. **Conclusion:** In conclusion, the diet containing flaxseed oil was able to control the inflammation advance and neurodegeneration, and reduced the AD predisposition induced by obesity in mice, preserving hippocampal functions. The obtained results in humans were sustained by experimental evidence and the omega-3 fatty acids show therapeutical possibility for its uses, reducing the risk of incidence of AD.

PATTERNS OF STRUCTURAL NETWORK ABNORMALITIES IN CHILDREN WITH DEVELOPMENTAL EPILEPTIC ENCEPHALOPATHIES OF GENETIC ETIOLOGY

Fernanda Germano de Azevedo[1], Maria Luiza Benevides[1], Helena T. Moraes[1], Luciana Bonadia[1], Brunno M. Campos[1], Fernando Cendes[1], Íscia Lopes-Cendes[1], Ana Carolina Coan[2]

[1]FCM, UNICAMP, [2]Child's Neurology Department, FCM, UNICAMP.

Introduction: This study evaluated the patterns of structural alterations in white and gray matter (WM and GM) in the brains of children with developmental epileptic encaphalopathies (DEEs) of genetic etiology. DEEs are conditions in which epileptic seizures occur alongside cognitive or behavioral changes determined by the underlying cause and/or ictal or interictal discharges [1]. Among the causes of DEEs, the genetic etiology is highlighted due to the increasing number of descriptions of involved genes [2]. **Materials and Methods:** Neuroimaging evaluation used voxel-based morphometry analysis with volumetric T1-weighted MRI sequences through SPM8 software. Eleven patients with DEEs of genetic etiology were included in the study. Analysis was conducted individually by comparing each participant with a group of age-matched healthy controls. Structural changes were classified into patterns: localized or diffuse (for WM and GM); juxtacortical or subcortical (for WM); and the anatomical distribution. **Results:** We observed that cerebral atrophy occurred in all patients. WM atrophy predominated in a diffuse pattern, both juxtacortical and subcortical. GM atrophy predominated in localized regions, with the following anatomical distribution: temporal and occipital lobes, fronto-temporal transition, left cuneus, and cerebellum. Children with distinct variants and clinical phenotypes despite the same gene mutation (*KCNT1* and *CLCN4*) demonstrated distinct patterns of atrophy. Two children with the same gene mutation and similar phenotypes (*NRXN2* gene) exhibited a similar pattern of GM and WM atrophy, in the parietooccipital regions. **Discussion/Conclusion**: In conclusion, it is clear that the genetic variant may influence the structural network abnormalities found in neuroimaging studies of children with DEEs. This study demonstrated that children with DEEs of genetic etiology present a diffuse pattern of GM and WM atrophy. The findings of atrophy were observed especially in areas associated with behavioral control and socioadaptive functions, wich may be correlated with brain anormalities and clinical phenotype.

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PHYSIOLOGICAL AND COGNITIVE CHARACTERIZATION OF STRESS INDUCED BY TIME-RESTRICTED MENTAL ARITHMETICS MEASURED WITH FUNCTIONAL NEAR-INFRARED SPECTROSCOPY

L. F. Bortoletto[1,3], Giovani G. Martins[1] and R. C. Mesquita[1,2,3]

[1]Institute of Physics, University of Campinas, Campinas, SP, Brazil. [2]School of Computer Science, University of Birmingham, Birmingham, United Kingdom. [3]Viva-Bem Hub, Artificial Intelligence Lab., Recod.ai, Institute of Computing, University of Campinas, Brazil.

Introduction and Hypothesis: Although stress is a normal and natural response to challenging situations, chronic or prolonged states of stress can contribute to mental health issues. Therefore, understanding the impact of stress on human physiology is valuable to prevent the onset of mental health disorders. However, there is still a lack of clinical assessments to provide accurate information about the individual's health under stressful conditions. Functional Near-Infrared Spectroscopy (fNIRS) is a noninvasive and versatile technique that can be used to study the underlying aspects of brain function using diffuse optics. For this work, we hypothesized that stress induced by time-restricted mental arithmetics would evoke neural and systemic changes that could be quantitatively assessed with fNIRS and peripheral physiological monitors. **Materials and Methods:** Fifty neurologically healthy participants (27 females; mean (standard deviation): 26 (8) years) were enrolled in this study. The setup process involved a NIRS system (NIRScout, NIRx Medical Systems) covering the frontal and parietal lobes bilaterally, a peripheral vascular monitor (Finometer, Finapres), and a noninvasive capnograph (G3C patients monitor, General Meditech). The experimental protocol consisted of a block-design stimulation composed of randomized 20 to 30 seconds of simple arithmetic followed by 30 to 45 seconds rest, repeated 20 times. In the initial 10 blocks, the participants were free to perform the calculations without any time restriction; the average time for each block was evaluated and used as the time limit for the remaining 10 blocks, consisting of a time-restriction task. Functional brain images were obtained through fNIRS data using the standard GLM framework, and maximum evoked physiology during each block was extracted from the independent physiological data. **Results:** Arithmetic performance was higher for unlimited time, reaching 90% (8), in contrast to time-restricted condition, where performance was at 57% (8), ($p<0.001$). In both conditions, arithmetics elicited brain activation bilaterally in the prefrontal and parietal cortices. However, brain functional maps were more specialized during time restriction, significantly reducing the recruitment of surrounding regions (Figure 1). During the restricted protocol,

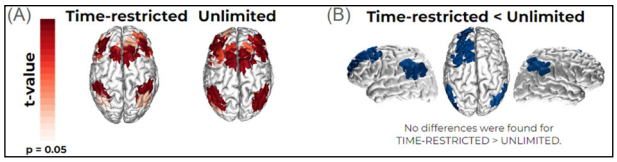

Figure 1. Brain activity maps. (A) Unlimited time condition and time-restricted, and; (B) difference between both conditions, regions painted in blue represents decreased time-restricted activity.

we observed an increase in mean arterial pressure (MAP), heart rate (HR) and respiratory rate (RR) of 3.8 (0.8) mmHg, 4 (1) bpm and 2.7 (0.4) cpm when compared to baseline. These changes were higher than the ones observed with unlimited tasks for MAP ($p<0.001$), HR ($p=0.026$) and RR ($p=0.008$). **Discussion/Conclusion:** Overall, the higher increase in systemic physiology is consistent with a stronger activation of the sympathetic branch of the autonomic nervous system, which is typical of stressful situations, and the more local brain maps obtained with fNIRS potentially reflects the lower task compliance and periods execution, due to higher mistakes fraction under time restriction.

POSTERIOR CINGULATE CORTEX CONNECTIVITY PATTERNS AND ITS INTERACTIONS WITH MEMORY PERFORMANCE IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

B. A. Martins[1], C. F. Tessler[1], L. R. Pimentel-Silva[1], M. H. Nogueira[1], B. M. de Campos[1], C. L. Yasuda[1], Fernando Cendes[1]

[1]Laboratory of Neuroimaging, FCM, UNICAMP

Introduction: Patients with mesial temporal lobe epilepsy (MTLE) have cognitive dysfunctions not fully explained by the temporal seizure focus. Several pieces of evidence indicate the impairment of disruptions in the PCC connectivity in MTLE. Abnormal functional connectivity in the Posterior Cingulate Cortex (PCC), an essential node to Default Mode Network (DMN) appears to be related to these cognitive impairments. Studies showed PCC connectivity abnormalities in MTLE, but most combined patients with hippocampal sclerosis (HS) with other underlying etiologies. **Materials and Methods:** We enrolled 96 MTLE patients (matched for age, sex and education years) divided into right-HS (n=28), left-HS (n=49), and MRI-negative MTLE (n=19) who underwent resting-state fMRI. Functional connectivity between PCC and ipsilateral and contralateral hippocampus was analyzed with a seed placed at the PCC using Uf2C toolbox. In addition, patients underwent neuropsychological testing using the Wechsler Test, visual, verbal, delayed and general memory z-scores were obtained. The effects of the variables were analyzed using SPSS, outlining a Mann-Whitney U Test to access the significance of the differences in connectivity between PCC versus Hippocampus ipsilateral and contralateral ($p<0.05$) as well as a ANOVA study ($p<0.05$) to access the difference between memory in each group. **Results:** The difference in connectivity were significant between PCC versus Hippocampus ipsilateral and contralateral (significance level of 0.003) and more perceivable in the ipsilateral Hippocampus, evidencing the dysfunction of the epileptogenic focus. For verbal memory, there was a significant difference between MRI-negative versus right-HS. For general memory, between MRI-negative versus right-HS. And for delayed memory, between MRI-negative versus right-HS as well as MRI-negative versus left-HS (all $p<0.05$). This differences may clarify the effect of lateralization on memory performance. We found no correlations between memory z-scores and PCC connectivity to ipsi and contralateral hippocampus. **Discussion/Conclusion**: The relative reduction of functional connectivity between PCC and the hippocampus ipsilateral to the seizure focus and HS is in line with the epileptogenic dysfunction. Consistent with previous studies, the group with left HS had worse verbal, general, and delayed memory performance. The lack of correlation between functional connectivity and memory z-scores may be related to the small sample size.

PRECISION MEDICINE FOR *CHRNA4*-RELATED DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY WITH SLEEP HYPERMOTOR SEIZURES: WHEN CAN NICOTINE SUCCESSFULLY CONTROL SEIZURES?

Maria Luiza Benevides, M.D., Ph.D[1], Claudio Gusmão, M.D[2], Katia MRS Schmutzler, M.D.[1], Ph.D., Laura Moriyama, M.D., PhD[2], Paula Thaís Bandeira Elias, M.D.[1], Giovana Barros e Silva Ribeiro, M.D.[a]; Luciana C. Bonadia, Ph.D.[3], Íscia Lopes-Cendes, M.D., Ph.D.[3,4], Ana Carolina Coan, M.D., Ph.D[1,4,5]

[1]Child Neurology Service, Department of Neurology, University of Campinas (UNICAMP), Campinas - São Paulo (SP), Brazil; [2]Movement Disorder, Department of Neurology, University of Campinas (UNICAMP), Campinas - SP, Brazil; [3] Department of Translational Medicine, UNICAMP, Campinas - SP, Brazil; [4]Brazilian Institute of Neuroscience and Neurotechnology, BRAINN, at UNICAMP, Campinas, SP, Brazil; [5]Neuroimaging Laboratory, UNICAMP, Campinas - SP, Brazil.

Introduction: *CHRNA4* gene variants are associated with autosomal dominant sleep-related hypermotor epilepsy (ADSHE) and developmental and epileptic encephalopathy (DEE). The pathophysiology of nAChR-related epilepsy makes precision treatment with nicotine promising for pharmacoresistant cases. We described a case of *CHRNA4*-related early onset DEE and sleep hypermotor seizures successfully treated with nicotine, and reviewed the literature of nicotine use in epilepsy. **Materials and Methods:** We searched in PubMed the keywords: *CHRNA4* AND nicotine AND epilep*; *CHRNA4* AND nicotine AND sleep-related hypermotor epilepsy; *CHRNA4* AND nicotine AND SHE; transdermal nicotine AND epilep* [All Fields]. **Results:** A female patient presented with DEE with sleep hypermotor seizures related to an unreported heterozygous variant of uncertain significance in *CHRNA4* gene (c.860T>G; p.Val287Gly; NM_000744.6). At 19 years old, seizure control was achieved due to nicotine patch treatment. She progressed with spontaneous paroxysmal kinesigenic dyskinesia (PKD). In literature review, the median age of seizure onset was 7.5 years old, and the use of nicotine patches started at the median age of 19, at a median dose of 7mg per day. All cases responded to nicotine patches, and 50% remained seizure-free. Patients with the p.Ser280Phe variant had lower chances of seizure freedom. **Discussion/Conclusion**: This study supports the use of nicotine patches in *CHRNA4*-related epilepsy and presents a new variant associated with PKD.

PRELIMINARY ASSESSMENT OF DIFFUSION MODELS IN BCI-SSVEP

G. M. K. Pereira[1], G. V. Vargas[2], H. M. A. Leite[3], S. N. Carvalho[3]

[1]Institute of Exact and Applied Sciences-UFOP, [2]School of Electrical and Computer Engineering-UNICAMP, [3]Aeronautics Institute of Technology (ITA).

Introduction: The implementation of a steady-state visually evoked potential-based brain-computer interface (BCI-SSVEP) requires the collection of brain signals to calibrate the system. This step is crucial for achieving optimal performance by customizing parameters tailored to each individual using the BCI. However, the exclusive collection of brain signals for parameter calibration poses a burden. In this study, we assessed the diffusion model as an emerging technique for generating synthetic brain data and examined its impact on system performance when incorporating synthetic data during the calibration stage. This evaluation opens up new possibilities to enhance the efficiency and accuracy of interactions between the human brain and machines. **Methods:** The diffusion process involves a direct pass, , wherein Gaussian noise is step-wisely added to the original signal up to steps, , and it is escalated by a noising schedule. If we define and , we can obtain the noised version at any time step from , according to the equation in the Forward Diffusion in Fig.1. The reverse process involves predicting the added noise, enabling a trained model to generate new samples from a fully noised instance [1]. Our analyses utilized the electroencephalography (EEG) signals from 10 subjects from a public database [2]. Data from the Oz electrode, with a 1-second window and 4 stimulation frequencies (6, 10, 12, and 15 Hz), were used. The database offers 30 samples for each stimulus. Partitioning the dataset, 24 samples per stimulus were used to train the diffusion model. These same 24 samples were employed to calibrate the BCI-SSVEP, alongside synthetic signals, creating three scenarios with different ratios between real and synthetic EEG data: **Baseline** (only 24 samples of real EEG signal), **Scenario1** (24 real and 4 synthetic EEG samples), and **Scenario2** (24 real and 10 synthetic EEG samples). The remaining 6 samples per stimulus were used just to evaluate the BCI with a Support Vector Machine classifier. **Results:** Table 1 shows the average performance for each subject considering the 3 scenarios. The values represent a mean of 50 iterations, considering different random splits. Our results indicate that, for 7 out of 10 subjects, there was a tendency of improvement in BCI performance with the inclusion of synthetic EEG signals for the BCI calibration.

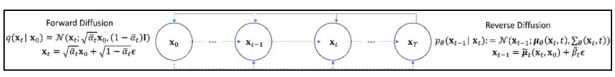

Figure 1. Diffusion process involving T Markovian steps. The dotted line represents the forward pass.

Table 1. BCI-SSVEP performance (%) considering different combinations of real and synthetic EEG signals.

Subject	1	2	3	4	5	6	7	8	9	10	Mean± Std.
Baseline	0,46± 0,11	0,29± 0,09	0,21± 0,05	0,24± 0,07	0,19± 0,09	0,15± 0,04	0,19± 0,06	0,65± 0,10	0,34± 0,09	0,39± 0,09	0,311± 0,08
Scenario1	0,48± 0,10	0,31± 0,10	0,22± 0,06	0,18± 0,07	0,20± 0,11	0,17± 0,05	0,18± 0,07	0,65± 0,09	0,31± 0,11	0,40± 0,10	0,310± 0,09
Scenario2	0,47± 0,10	0,31± 0,09	0,20± 0,08	0,18± 0,07	0,22± 0,11	0,15± 0,05	0,20± 0,06	0,65± 0,07	0,31± 0,11	0,37± 0,10	0,306± 0,08

Conclusion: The diffusion models demonstrate the capability to reproduce EEG signals with evoked potential, offering valuable support in the calibration stage of BCI-SSVEP. This noteworthy outcome holds significant promise for advancing brain-computer interfaces and their practical applications. Future investigations are essential to assess the scalability by increasing the number of channels and evaluating the system's ability to generalize BCI calibration, thus reducing the need for individualized configuration without compromising the overall performance of the BCIs.

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QUALITY CONTROL OF CORPUS CALLOSUM SEGMENTATION IN MAGNETIC RESONANCE IMAGES: TRAINING A VISION TRANSFORMERS (VIT) MODEL WITH SHAPE SIGNATURES

S.S. Silva[1], J. Rodrigues[1], P.R. Julio[2], S. Appenzeller[2], L. Rittner[1]

[1]Medical Image Computing Lab, FEEC, UNICAMP, [2] Rheumatology, FCM, UNICAMP.

Introduction: The Corpus Callosum (CC) is crucial for the transfer and integration of sensory, motor, and cognitive information [1]. Its analysis using magnetic resonance imaging (MRI) starts usually by segmenting the structure with an automated segmentation algorithm, however the only way of assessing the accuracy and reliability of these methods [2] is through visual inspection. Although the literature shows efforts in the development of automated and semi-automated Quality Control (QC) methods [3], there is still no method agnostic to different MRI scanner sequences and segmentation methods. With this in mind, we propose a Vision Transformer (ViT) model [4] trained with CC shape signatures to identify correct and incorrect segmentations. **Materials and Methods:** A total of 1524 MR volumes were used to acquire midsagittal CC segmentations. The segmentation methods included techniques specifically designed to segment CC by Rittner et al. [5], Niogi et al. [6], and Rodrigues et al. [7] using Fractional Anisotropy (FA) maps, and the FreeSurfer software [8] working on T1-weighted images, in addition to manual segmentations, resulting in 4584 binary masks. Segmentation results were visually inspected and labeled as *correct*, *partially correct* and *incorrect*. From each binary mask 36 curvature profiles were extracted as shape signatures, using a resolution ranging from 0.15 to 0.40 (step parameter) [9], and used as input images (Fig.1) for the ViT model. The classification performance was evaluated using the area under the curve (AUC) of the ROC curve for different ViT configurations. **Results:** The ViT model achieved an AUC of 99% in the test set (304 masks), indicating a high degree of accuracy in classifying CC segmentations as *correct*, *partially correct*, or *incorrect*. The good performance can be attributed to the combination of detailed shape signatures with the capacity of the ViT network's self-attention mechanisms, which proved effective in capturing the complexities and variations inherent to the CC profiles. **Discussion/Conclusion**: The potential and effectiveness of the CC shape signatures and ViTs in Quality Control were confirmed. The model can distinguish between correct and incorrect segmentations, independent of segmentation method and MR sequence used. Due to the use of CC shape signature in several resolutions, the method is able to account for anatomical differences and inter-method variability. However, it still faces challenges when CC segmentations result in two separated components or isolated pixel errors, as the curvature profile requires a continuous contour of the CC for accurate evaluations.

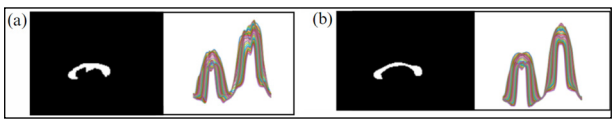

Figure 1. Segmentation examples and respective shape signatures: (a) partially correct; (b) correct.

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RELATIONSHIP BETWEEN SUBTYPES OF AURAS AND CORTICAL AND SUBCORTICAL EXTRA-HIPPOCAMPAL ATROPHY IN PATIENTS WITH TEMPORAL LOBE EPILEPSY ASSOCIATES WITH HIPPOCAMPAL SCLEROSIS

G. O. Giovanna[1], C. Fernando[1], R.P.S. Luciana[1]

[1]Faculty of Medical Sciences and Neuroimaging Laboratory – UNICAMP.

Introduction: Mesial temporal lobe epilepsy (MTLE) is highly prevalent, often originating in the hippocampus, entorhinal cortex, amygdala, or parahippocampal gyrus [1-3]. Auras, focal aware epileptic seizures, commonly precede MTLE. This study aims to investigate hippocampal and extrahippocampal structural changes in MTLE patients with and without auras, comparing them with a control group. **Materials and Methods:** The study involved 129 MTLE patients with hippocampal atrophy on MRI images and followed up on an outpatient basis at HC-UNICAMP, with review of medical records and collection of demographic and clinical data. Patients were grouped into: (1) presence of exclusively autonomic auras, (2) presence of other auras (cognitive, emotional and sensory), with or without associated autonomic auras, and (3) no auras. In the control group, MRI images and information from 205 healthy people were selected. The images were acquired on a 3T Achieva MRI machine, with high-resolution T1-weighted 3D sequences in the sagittal plane being selected. They were processed by the Freesurfer 6.0 software [3, 4]. Subcortical volume and cortical thickness in temporal regions and insula were evaluated. Clinical, demographic and MRI data for each participant were tabulated and analyzed using the statistical software SPSS Statistics version 26. Data distribution and exploration were performed using the Shapiro-Wilk test and Levene's test of homogeneity of variances. Categorical data were evaluated using the Chi-square test. Continuous data were compared between aura and control groups using a generalized linear model (MLGz) with identity link function for normal distribution and sequential Sidak post hoc. Subcortical volumes were analyzed, including total intracranial volume as a covariate (a representative measure of cranial size). **Results:** The p-value indicated no significant age or gender differences between patients and controls. Group 3, without auras, had auras lasting 7.96±2.98 years longer than Group 2. Subcortical volume analysis revealed ipsilateral (IPL) thalamus reduction in all patients, with Group 3 displaying additional reduction compared to Groups 1 and 2. Contralateral (CTL) thalamus was reduced in Groups 1 and 2 compared to controls, and in Group 3 compared to Group 2. IPL hippocampus reduction was consistent across all groups, with Group 3 showing further reduction compared to Group 1. In the IPL amygdala, Group 3 exhibited reduction compared to controls and Group 2. Cortical thickness reduction occurred in IPL mean temporal gyrus for all groups, and Group 1 also showed CTL reduction compared to controls. IPL superior temporal gyrus reduction was observed in all three groups, with Group 3 also showing CTL reduction. IPL reduction occurred in inferior temporal gyrus (Group 3 vs. controls), parahippocampal gyrus (Group 3 vs. controls and Group 1), and insula (Group 3 vs. controls). **Discussion/Conclusion:** Group-specific structural changes were identified. Group 1 exhibited ipsilateral hippocampal and superior temporal gyrus reduction, and the thalamus and middle temporal gyrus was reduced bilaterally. Group 2 showed ipsilateral hippocampal atrophy and thinning of middle and upper temporal gyrus. Group 3, with the longest epilepsy duration, displayed extensive ipsilateral reductions (hippocampus, amygdala, parahippocampal, insula, inferior and middle temporal gyrus), along with bilateral thalamic and superior temporal gyrus atrophy. This group exhibited significant structural reductions compared to other MTLE patients. In conclusion, patients without auras showed more profound extrahippocampal damage, emphasizing potentially greater overall impairment.

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ROBOTIC LOWER LIMB EXOSKELETON: A CONTROL SOFTWARE

C. M. S. Freitas[1], V. A. Author[1] , E. Rohmer[1]
[1]Dept. Computer Engineering and Industrial Automation, FEEC, UNICAMP.

Introduction: Robotic exoskeletons are designed to assist people with gait abnormalities in their locomotion, increase physical capabilities, or rehabilitate patients after surgery or patients suffering from various neurological disorders, such as spinal cord injury. [1]. The system is composed of several subsystems such as electrical, mechanical, digital network, and embedded control software. The main purpose of the control software is to drive an exoskeleton along the trajectory, providing the correct activation of the electric motors and ensuring the safety of the users [2]. The current project depicts embedded software for robotic exoskeletons to understand back-end and front-end functionalities. A graphical interface is provided to the user to facilitate interaction with the hardware and enable quick system diagnosis. To manage the movement and safety functions, embedded control software was developed to perform the necessary control functions and manage the system's communication network. **Materials and Methods:** A physical prototype of a robotic exoskeleton was used for the development and testing of the control software, 4 BLDC motors model RMD-X were used as actuators, two motors drove the hip joints, and two motors drove the knee joints. The embedded software was developed with the Python language using the flet graphical framework and the CAN (Controller Area Network) communication bus. The central processing unit used is a Jetson Nano card from Nvidia. The system also has a 20A/h 48Vdc rechargeable lithium battery. **Results:** The control software is capable of controlling each motor by sending actuation angle, speed, and torque commands, it is also possible to read motor data such as temperature, electric current, voltage, current angle, and adjustment data from the motor's PID controller. The graphical user interface is fully functional, enabling quick access to data and enabling remote configuration and startup of the system. **Discussion/Conclusion**: Although the tests were conducted without the application of exoskeletons on human legs, it was possible to conclude that the development of the embedded control software allowed the correct control of leg movements and also opened up wide options for testing and operational analysis. Allowing the onboard control software to send tuning data from the motor PID controllers. The control software also allows the collection of data for later analysis or even for training neural networks in order to expand its functionalities and improve the system's response.

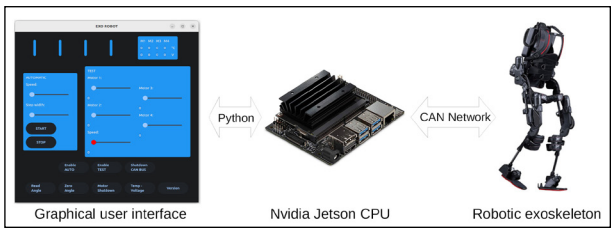

Figure 1. Organization and interaction between embedded control software and hardware.

References: [1] Kapsalyamov A et al., doi: 10.1109/ACCESS.2019.2928010 [2] Ristiana Ret al., doi: 10.1109/ICWT55831.2022.9935372

ROBOTIC STRUCTURING OF AN ASSISTIVE HOME: EXPERIMENTAL TEST

C. B. da Silvar[1], F. A. O. Mota[1], E. A. B. Huayhua[1], B. M. Portela[1], E. Rohmer[1]
[1]Dept. Computer Engineering and Industrial Automation, FEEC, UNICAMP.

Introduction: This study aims to design an assistive living environment and implement a system capable of automatic localization, mapping, and dynamic evaluation. Agents with diverse capabilities can contribute information, fostering the creation of a collaborative map, thereby enabling distributed intelligence and multi-agent decision-making. The current project is specifically crafted for implementation in assisted living environments, catering to the needs of the elderly or individuals with disabilities. The robotic structuring seeks to establish an autonomous robotic system capable of adapting to various environments. This adaptability facilitates the incorporation of different information, whether conveyed through voice or activated by displaying a map through a User Interface (UI). This article's objective is to introduce the agents used in this system and illustrate how this structural framework enhances its application [1]. **Materials and Methods:** A mobile robot P3DX was employed for navigation within a laboratory setting, assisted by three AXIS PTZ 214 cameras, aimed at detecting both the robot and human subjects. Initially, human agents were represented by objects equipped with ArUco tags strategically placed throughout the space. All operations were managed through a dedicated REST server responsible for storing crucial map data. The conducted test focused on accurately identifying the position of human agents and guiding the robot in response to their requests, primarily initiated through voice commands. The map stored in the REST server is seamlessly integrated into a CoppeliaSim simulation, offering additional utility as a Human-Machine Interface (HMI). he command is communicated in natural language to the Large Language Model (LLM), which then translates it into action planning. **Results:** The experimental test involved validating the system's ability to coordinate map coordinates and information derived from both the cameras and the robot. This information is gathered, organized, and made accessible for consultation by the Large Language Model (LLM) to facilitate action planning. In the preliminary phase, the sole action considered is movement. For instance, with the command 'Take me to person 1,' the robot, after consulting the map, discerns that person 1 is located in the laboratory, specifically in the corridor. Consequently, the system generates an action plan directing the robot to navigate to the laboratory, effectively executing the assigned task. **Discussion/Conclusion**: As an initial step in this project, the system successfully executed tasks by collating information from diverse sources. It demonstrated real-time updates, establishing a platform that facilitates seamless translation from the Large Language Model (LLM) to machine language. n the subsequent phases, the system will advance to include automatic detection of human agents and objects. Additionally, it will incorporate a probabilistic fusion method for information, aiming to enhance autonomy and efficiency. This capability, in turn, simplifies the implementation of various User Interface (UI) interfaces

References: [1] Zhang, W. et. al. https://doi.org/10.48550/arXiv.2303.10089

SEED-BASED FUNCTIONAL CONNECTIVITY CHANGES IN ELDERLY SUBJECTS PLAYING SERIOUS GAMES

V. A. Oya[1], R. F. Casseb[2,4], F. Ota[3], S. Hirata[3], L. M. Li[2,4], G. Castellano[1,4]
[1]Neurophysics Group, IFGW, UNICAMP, [2]Neuroimage Lab, FCM, UNICAMP, [3]ISGAME, [4]BRAINN.

Introduction: Serious games (SG), also known as applied games, are interactive experiences that allow players to engage in activities aimed at honing skills and attaining goals beyond mere entertainment. SG have been shown to promote cognitive decline prevention [1]. However, there are few studies that have analyzed functional connectivity (FC) changes resulting from elderly subjects playing SG. The aim of this study was to evaluate FC changes in older individuals who played SG, using fMRI. **Materials and Methods:** Seventeen subjects (age range 53-76, 2 men/15 women) participated in this study. They played an SG named Active Brain on a smartphone, for 1h 30min, once a week, for 3 to 5 months. Resting state fMR images were acquired before (t1) and after (t2) the intervention. The fMR images were processed using SPM12 and UF2C [2]. Six regions of interest (ROIs) commonly associated with logical reasoning and attention were selected from the AAL atlas [3] for performing a seed-based FC analysis: 5: Frontal Superior Orbital Left, 10: Frontal Middle Orbital Right, 33: Cingulum Middle Left, 34: Cingulum Middle Right, 59: Parietal Superior Left and 61: Parietal Inferior Left. FC maps for each seed were then compared among instances (t1 and t2). **Results:** We found a decrease in connectivity for ROI 5 with the supplementary motor area (SMA) and ROI 10 with the right (close to the hand) motor area (M1) after the intervention (Figure 1). **Discussion/Conclusion:** The orbitofrontal cortex (OFC, which encompasses ROIs 5 and 10) serves as a central hub for integrating sensory information, regulating autonomic responses, and engaging in processes of learning, anticipation, and decision-making related to emotions and rewards [4]. SMA has been attributed the functions of postural stabilization, coordination, and control of voluntary movements [5]. The observed decrease in FC between the OFC and SMA, as well as between the OFC and M1, following the SG intervention, indicates significant alterations in neural networks related to motor control, sensory integration, emotional processing, and reward mechanisms. More studies with a larger sample are needed to refine these conclusions.

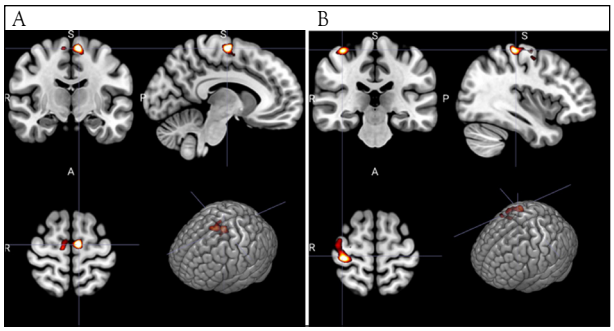

Figure 1. Maps showing FC values for which t1 was significantly larger than t2, for seed placed on A – ROI 5; B – ROI 10.

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4), PIBIC-CNPq.

References: [1] Sokolov AA et al., doi: 10.1097/WCO.0000000000000791; [2] Campos BM et al., doi: 10.1016/j.softx.2020.100434; [3] Tzourio-Mazoyer N et al., doi: 10.1006/nimg.2001.0978; [4] Kringelbach ML, doi: 10.1038/nrn1747; [5] Matsuzaka Y et al., doi: 10.1152/jn.1992.68.3.653.

SOLVING FIBER CROSSING AND ENHANCING TRACTOGRAPHY FROM 32 DIRECTIONS SINGLE-SHELL DIFFUSION-MRI ACQUISITIONS USING DEEP LEARNING

M. O. Silva[1], C. P. Santana[1], D. S. Carmo[1], L. Rittner[1]

[1]School of Electrical and Computer Engineering, Universidade Estadual de Campinas, Campinas, Brazil.

Introduction: Diffusion-Weighted MRI is crucial for understanding brain white matter structure, but traditional models such DTI fails to represent complex fiber orientations. Although advanced Spherical Deconvolution (SD) methods, particularly effective in High Angular Resolution Imaging, have shown to significantly improve results, the ideal multi-shell HARDI data is often unavailable clinically. Some solutions have been proposed to improve the resolution of Fiber Orientation Distribution (FOD) from single-shell DWI data, such as FOD-Net [1], a single-shell to multi-shell reconstruction algorithm and SS3T [1], which proposes reconstructing multiple fibers using only single-shell data. In previous work we presented FOD-SWIN-Net [2], a deep learning approach to improve the resolution of FOD from single-shell 32 directions diffusion acquisitions. While its superior performance, when compared to FOD-Net and SS3T, has been demonstrated using the Angular Correlation Coefficient, its effectiveness on enhancing tractography still needs assessment. **Materials and Methods:** The FOD-SWIN-Net model was trained on down-sampled data from the Human Connectome Project [3], using the ADAM optimizer over 80 epochs and focusing on optimizing against a multi-shell MSMT CSD[4] target via Mean Square error. For qualitative assessment, tractography was done using the deterministic algorithm of MRtrix3 [5], focusing on the Corpus Callosum and the Corticospinal Tract. **Results:** Tractography results (Fig.1) demonstrate that the FOD-Net model (d) effectively crosses fibers while minimizing the generation of spurious fibers around the corticospinal tract (blue), unlike the SS3T method (b), which, despite accurately reconstructing some crossing fibers, generates numerous non-existent fibers around them. Results from the FOD-SWIN-Net model (c) stands out by balancing this dynamic, accurately solving crossing fibers without creating false ones. **Discussion/Conclusion**: The FOD-SWIN-Net employs a transformer and patch-based encoder-decoder architecture, and effectively enhances single-shell FODs to match the quality of multi-shell acquisitions with 288 directions (HARDI), being able to solve fiber crossing and other complex fiber configurations.

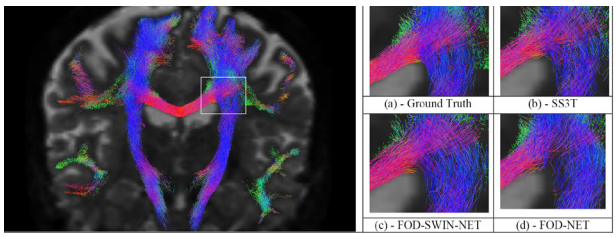

Figure 1. Resulting tractography based on data reconstructed by the proposed method (c) resembles the ground truth, maintaining the integrity of the corpus callosum fibers and Corticospinal tract (red lines) without introducing spurious fibers.

References: [1] Zeng R et al., doi:10.1016/j.media.2022.102431; [2] Oliveira et al., doi: https://doi.org/10.48550/arXiv.2402.11775; [3] Van Essen DC et al., doi:10.1016/j.neuroimage.2013.05.041; [4] Jeurissen B et al., doi:10.1016/j.neuroimage.2014.07.061; [5] Tournier J. et al., https://doi.org/10.1002/ima.22005

SPATIAL PATTERNS DYNAMICS OF MOTOR IMAGERY TRAINING

J. A. S. Meireles[1,2], C. A. Stefano Filho[1,2], G. Castellano[1,2]

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

Introduction: Brain-computer interfaces (BCIs) represent a paradigm shift in human-computer interaction, providing direct connections between the human brain and external devices. Through complex interactions between neurobiology, signal processing, and machine learning algorithms, BCIs have the potential to transform fields from healthcare to gaming and assistive technology to cognitive development, but these devices' accuracy is still low for practical application. The aim of this work was to develop a BCI model for extracting spatial information from the neurological signals and using it to improve the model's accuracy over time and better understand the underlying biological mechanisms. **Materials and Methods:** Electroencephalography signals from 10 healthy participants (mean age 25±4, 70% males) were collected during Motor Imagery (MI) tasks [1]. Prior to analysis, the signals underwent preprocessing steps to mitigate noise and eliminate potential artifacts, using PCA and band pass filters. Features were then derived using Common Spatial Patterns (CSP) filters, along with computing the average power across frequency bands associated with MI. These features served as input to a Support Vector Machine (SVM) classifier. Since the algorithm maximizes the discrimination between the classes of MI, the vector potentials, i.e. the weights of the columns of the CSP projection matrix, indicate how much an electrode is correlated to a MI class. The spatial patterns from CSP as well as the electrodes from which features were selected were calculated individually for each user on every session. Both spatial patterns and number of features per electrode were plotted as topographic plots for analysis of possible changes in their distributions and how they relate to the MI training. The CSP patterns were compared to the Event Related Potentials (ERPs) of each session in order to eliminate artifacts and other unrelated information from the spatial patterns. **Results:** The overall mean group results showed an increase in the CSP weights in frontal regions, specially premotor regions (Figure 1.A). This increase indicates a higher correlation of these areas with each MI task. Responders had a bigger spread of regions correlated with MI, with not expected electrodes showing in both CSP potentials and ERPs (Figure 1.B). Classification results showed a continuous increase in accuracy, with group averages reaching (75±8)% while responders (3/10) achieved accuracies over 80%. **Discussion/Conclusion**: The observed results of the spatial distributions' evolution may be related with how the subjects' brains learned to modulate MI to better perform on the tasks. Previous results using functional Magnetic Resonance Imaging showed that participants with greater ease in MI tasks had higher neurological activity in premotor areas [2].

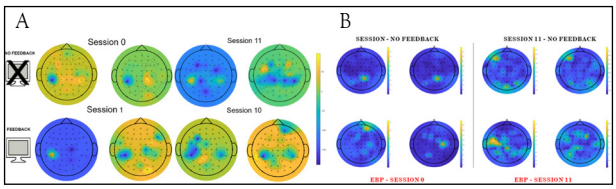

Figure 1. A: CSP patterns for group (averaged over all subjects) and B: example responder.

Furthermore, the different regions observed in responders may indicate how user individualities may affect the learning process for both the subject and the BCI.

References: [1] C. A. Stefano Filho et al., doi: 10.1007/978-3-030-36636-0_17. [2] A. Guillot et al., doi: 10.1016/j.neuroimage.2008.03.042.

STRUCTURAL BRAIN CHANGES IN PEDIATRIC MULTIPLE SCLEROSIS

Vieira G.D.[1], Antônio F. F.[1], de Sá M. M. S.[1], Damasceno A.[1]

[1]Neuroimmunology Unit, University of Campinas, UNICAMP, Brazil.

Introduction: Pediatric-onset multiple sclerosis (POMS) affects 5% of all multiple sclerosis (MS) patients, beginning before 18 years old [1]. Clinically, it is similar to adult disease, but with a more inflammatory pattern. This study aimed to

evaluate neuroimaging and functional aspects in pediatric patients. **Materials and Methods:** Ten pediatric MS patients were enrolled prospectively from Clinical Hospital of the University of Campinas. The diagnosis was confirmed according to 2017 McDonald criteria. Functional were realized, such as the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk Test (T25-FW) and the 9-Hole Peg Test (9HPT). For neuroimage and clinical comparisons, 16 healthy controls were selected. Magnetic resonance imaging (MRI) was performed on a 3.0T scanner. Brain volume evaluations were performed on volumetric T1 images using FreeSurfer v7.0. The structures analyzed were: Cerebral Cortex, estimated Total Intracranial Volume, Thalamus, Choroid plexus, Caudate, and Putamen. To compare volumetric data between groups (MS vs HC groups), the General Linear Model (GLM) was used. The study was approved by the ethics and all participants provided written informed consent. **Results:** None of them presented severe physical disabilities. In group, there was a lower thalamic volume (POMS group 12.09 cm^3 vs HC 13.4 cm^3, $F = 4.88$, $p = 0.038$) and higher CP volume (POMS group 2.9 cm^3 vs HC 2.3 cm^3, $F = 7.48$, $p = 0.012$) in POMS compared to controls. Correlations between clinical, imaging, and cerebrospinal fluid parameters were performed, however, there were no significant results. **Discussion/Conclusion**: Some studies in adults have shown an increase in the CP volume in MS, mostly in adults. For example, Bergsland et al. [2] found higher CP volumes when compared to HC and an association with disability progression and reduction of thalamic. However, there is only one recent comparative study showing this increase in the pediatric population [3]. Regarding thalamus atrophy, its relationship with cognitive decline is known, especially with others' reduced GM subcortical volumes [4]. In conclusion, we found an enlargement of the CP in patients with POMS, suggesting a role in the pathophysiology of MS and being a possible inflammatory marker of the disease, in addition to the difference in thalamic volume, being associated with cognitive involvement.

References: [1] Absinta M et al. Association of Chronic Active Multiple Sclerosis Lesions With Disability In Vivo. JAMA Neurol. 2019 Dec 1;76(12):1474-1483, 2019; [2] Bergsland N et al. Association of Choroid Plexus Inflammation on MRI With Clinical Disability Progression Over 5 Years in Patients With Multiple Sclerosis. Neurology; 28:100(9): e911-e920, 2023; [3] Margoni M et al. Choroid plexus enlargement in paediatric multiple sclerosis: clinical relevance and effect of sex. J Neurol Neurosurg Psychiatry; 94(3):181-188, 2023; [4] Till C., Ghassemi R., Aubert-Broche B., et al. MRI correlates of cognitive impairment in childhood-onset multiple sclerosis. Neuropsychology;25(3):319–332, 2011.

SUCCESSFUL SINGLE-CELL RNA SEQUENCING LIBRARY FROM PERIPHERAL BLOOD MONONUCLEAR CELLS: A PROTOCOL POINT OF VIEW

P.A.O. Ribeiro[1#], J. Geraldis[1#], L.C. Bonadia[1], D. Bruno[1], T.C. Oliveira[1], I. Lopes-Cendes[1]

[1]Department of Translational Medicine School of Medical Sciences, University of Campinas (UNICAMP); and the Brazilian Institute of Neuroscience and Neurotechnology, Campinas, SP, Brazil.

Introduction: Single-cell omics techniques allow for the analysis at an individual cell level and can accurately identify diverse cell populations and their transcriptome landscape. A key issue in single-cell experiments is the viability of cells, especially in single-cell RNA sequencing experiments (scRNASeq). Isolating PBMC cells from fresh whole blood is a challenge because the thawing process reduces final cell concentration considerably, which may hinder scRNA-Seq. In this context, we developed and standardized an experimental protocol for isolating and preserving PBMCs from fresh whole blood for scRNASeq. **Materials and Methods:** We used 30 whole blood samples (3mL each) from control individuals collected in EDTA-containing vials. Histopaque®-1077 was used to recover PBMCs from blood. Subsequently, we used a modification of the previously published 10X preservation protocol [1] with the following steps: for cryopreservation (a) centrifugation of the fresh PBMC isolated for 5min, at 300rcf and 4 °C; (b) resuspension at Resuspension Medium to achieve 20x10e6 cells/mL and; (c) 2X Freezing Medium to achieve 10x10e6 cells/mL; (d) transfer of the cell suspension to a pre-cooled cryovial; (e) placement of the cells in a -80 °C freezer for at least 4h and, then, transfer to liquid nitrogen. For thawing, (f) the frozen samples are placed in a water bath at 37°C for 3min maximum; (g) followed by three sequential washing steps with medium and 1X PBS + 0.04% BSA solution; (h) centrifugation for 5min, at 300rcf; (i) resuspension and counting the viable cells using trypan blue in a Countess II Automated Cell Counter (ThermoFisher). The single-cell RNA sequence library followed 10X protocol [2], with an input cell amount of 1.200 cell/uL, a target recovery of 3.000 and samples were handled in three batches with eight and the last with six samples. **Results:** Cell viability was 87% on average. We also observed little presence of clumps and cell debris, which did not affect scRNASeq experiments. We obtained 17ng of cDNA library on average with a quality control curve like the standard present in the protocol. **Discussion/Conclusion**: In research workflows, cryopreservation is a frequently used technique for the processing of tissues; however, it needs to be adequately addressed in scRNASeq protocols. We also obtained excellent cell viability, cell membrane stability, and reduced clumps and debris, enabling the subsequent use of the cell suspension for cDNA library. The choice of target recovery and cell concentration input is also a critical point for successful library experiments once they can modify enzyme activity. For the next steps, sequencing will be done with 30X deep coverage.

Supported by: Fundação de Amparo à Pesquisa do Estado de São Paulo, FAPESP, Brazil.

References: [1] 10X Demonstrated protocol "Fresh Frozen Human Peripheral Blood Mononuclear Cells for Single Cell RNA Sequencing" (CG00039.RevE); [2] "Chromium Next GEM Single Cell 3' Reagent Kits v3.1 (Dual Index)" (CG000315.Rev E)

SUPPRESSION OF MU RHYTHM IN CHILDREN USING A LOWER LIMB EXOSKELETON

Bruna M. Carlos[1,2], Benjamin Norman[3], Elizabeth G. Condliffe[3,4], Gabriela Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, BRAINN, [3]Clinical Neurosciences, Alberta Children's Hospital, [4]Department of Pediatrics, Cumming School of Medicine, University of Calgary.

Introduction: Robotic-assisted gait training (RAGT) is a promising tool for improving gait rehabilitation, however, while studies emphasize RAGT benefits in adults, a deeper understanding of its effects in developing brains is still needed. Electroencephalography (EEG) plays a crucial role in providing neurophysiological information during RAGT, revealing suppressed mu and beta rhythms and increased gamma oscillations in sensorimotor areas [1-3]. In this sense, this study aims to identify EEG biomarkers in children during grounded RAGT that can provide robust means to analyze training progress and form a basis for EEG exploration in brain-machine interface controlled exoskeletons for children. **Materials and Methods:** A typically developing child (female, 5 years old) (TD) and a child diagnosed with Rett syndrome (female, 11 years, gross motor function classification system level 4) (RS) underwent one session of RAGT using the Trexo robotic gait trainer, a lower limb robotic walker. They walked for 1 to 3 minutes in both active (partial assistance) and passive (full assistance) modes, and EEG was acquired for 90 s before the beginning of the session, while standing in the Trexo, and during walking. The initial 10 gait cycles were divided into stance and swing phases, and the 90 s of rest were segmented into periods equal to the full gait cycles. Power spectral density (PSD) was computed in the mu band for electrodes C3, Cz and C4 (motor cortex) for all segments, and significant differences were tested. **Results:** Figure 1 depicts PSD distributions for the first 10 steps of each mode and rest periods. In Cz, significant differences were observed between rest and walking in stance, swing, and full gait cycles, and greater desynchronization during active compared to passive walking in the TD child. The participant with RS exhibited significant differences in C3, also indicating higher desynchronization during walking.

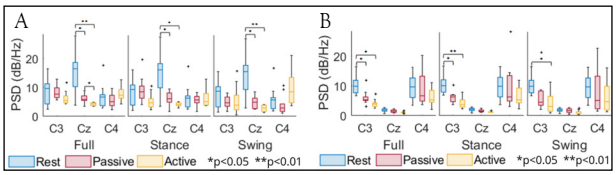

Figure 1. PSD distributions of the TD (a) and RS (b) participants.

Discussion/Conclusion: Suppressed activity in Cz (typically associated with lower limb functions) during RAGT aligns with similar findings in adults [2], that also present greater desynchronization during active compared to passive walking [1]. Notably, the participant with mobility impairment exhibited a leftward shift in this desynchronization, indicating individual and diagnostic-specific alterations in brain organization. In summary, these results highlight the uniqueness of individual brain responses to RAGT and lay the foundation for future research questions.

Acknowledgments: Work partially supported by FAPESP (2013/07559-3, 2022/14788-8) and CNPq (304008/2021-4).

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THE EFFECT OF IMPULSIVITY ON MOTOR AND COGNITIVE ASPECTS IN DIFFERENT CONDITIONS OF AN AIMING TASK: AN EEG ANALYSIS

Luisa Veiga da Rocha[1], Bárbara de Paula Ferreira[1], Tércio Apolinário-Souza[1,2], Guilherme Menezes Lage[1]

[1]NNeuroM Group, EEFFTO, UFMG, [2]GAIM Group, ESEFID, UFRGS.

Introduction: Despite impulsivity being widely reported in its dysfunctional aspect by the literature, there is evidence that non-pathological impulsivity has positive effects on motor behavior in certain contexts. Based on previous studies, it is speculated that motor tasks that require less cognitive effort and high space-time pressure may favor the motor performance of individuals with higher impulsivity. Conversely, motor tasks that demand higher cognitive effort and low temporal pressure may favor the performance of individuals with lower impulsivity. In order to investigate this possible relationship, the present study aimed to investigate the effect of impulsivity on motor control and cognitive effort in different aiming tasks. **Materials and Methods:** We had an initial sample of 109 right-handed participants of both sexes, with a mean age of 23.35 ± 3.33 years. The BIS-11 scale was used to classify the level of impulsivity. Participants who did not meet the scoring criteria to be allocated to the more impulsive group (GI+) or less impulsive group (GI-) were excluded from the final sample. The participants from the GI+ group (n= 31) and GI- group (n= 32) performed two conditions of an aiming task that required lower and higher cognitive demand. To assess the level of cognitive effort demanded by the task conditions, an electroencephalogram was used. Variables related to time, accuracy, kinematics, and inhibitory control were analyzed to infer motor performance and control, and cognitive variables were analyzed to infer the level of cognitive effort. **Results:** The results indicated that motor performance and kinematic profile were similar between groups in both task conditions. In the cognitive variables, the GI+ group showed a higher workload index than the GI- group in both conditions. The GI+ group showed higher level of errors in inhibition condition. **Discussion/Conclusion**: From the results, it is possible that the increase in cognitive effort is used as a compensatory mechanism by individuals with higher impulsivity. This possible compensatory mechanism can be considered functional since it allows individuals with higher impulsivity to achieve similar motor performance levels to those of individuals with lower impulsivity in unfavorable practice contexts.

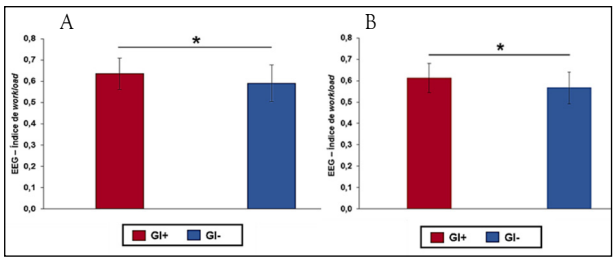

Figure 1. Mental workload in both aiming conditions. A) Lower cognitive demand. B) Higher cognitive demand.

THE EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON NEUROMUSCULAR AND MOTOR RECOVERY OUTCOMES OF STROKE SURVIVORS

C. V. Ruas[1,2,3], B. M. Carlos[1,2], M. V. N. Silva[1], S. S. Feitosa[1], P. F. G. Vazquez[1,2], L. L. Pontes[1], J. H. A. F. Silvestre[1], A. F. Brandão[1,2,4], S. Almeida[1,2], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN; [3]Edith Cowan University, Australia; [4]PUC-Campinas.

Introduction: Stroke is one of the leading causes of motor disability worldwide [1]. In particular, neuromuscular disfunction such as abnormal levels of surface electromyographic (sEMG) activity have been found in the paretic muscles of stroke survivors [2], and reductions in maximum joint range of motion (ROM_{max}) have also been reported [3]. Rehabilitation methods that include transcranial direct current stimulation (tDCS) and virtual reality (VR) exercises are known to improve clinical outcomes of stroke patients [4], but the neuromuscular mechanisms underlying these improvements are not fully understood. The aim of the present study was to examine the specific effects of tDCS applied during VR exercises on neuromuscular and motor recovery outcomes of stroke survivors. **Materials and Methods:** Seventeen stroke survivors (10 females, 58.8±14.6 y, 28.6±22.8 months post-stroke) were recruited for the study and allocated to a tDCS or Sham group. The tDCS group received anodal tDCS (2 mA current) and the Sham group received sham tDCS, respectively, on the ipsilesional primary motor cortex (M1) while performing a 10-session full body rehabilitation program consisting of VR exercises (30 minutes/session). Before the start of session 1 (baseline), sEMG activity (root mean square over 250 ms) was recorded from participants' paretic deltoid and rectus femoris muscles during maximal voluntary isometric contractions (MVICs) in four different joint movements: 1) shoulder abduction, 2) shoulder flexion, 3) hip flexion and 4) knee extension using a Neuro-EMG-Micro-4 system (sampling rate = 2 kHz). In this session, sEMG during MVICs was recorded twice: without and with the use of tDCS. Participants' shoulder abduction and hip flexion active ROM_{max} were also measured in sessions 1, 5 and 10 with a Kinect® v2 device system. In addition, the timed up and go (TUG) functional test was assessed before and after the rehabilitation. **Results:** sEMG activity was greater during hip flexion when participants received tDCS (89.8±64.7 mV) than without tDCS (44.5±16.3 mV) in the baseline session (p=0.04). Hip flexion ROM_{max} of the paretic limb increased at sessions 5 and 10 compared to baseline for the tDCS group (p<0.03) but not for the Sham group (p>0.05) (see Fig.1). Participants from the tDCS group also showed ~11% faster results in the TUG test from before to after the rehabilitation program (p<0.05). No between group or limb differences (p>0.05) in the other measures were observed. **Discussion/Conclusion**: Improvements in the paretic hip flexion ROM_{max} and TUG were observed only for the tDCS group from before to after the rehabilitation program. sEMG activity of the paretic limb was also greater when stroke participants received tDCS than without receiving tDCS (measured at baseline). It seems that the anodal tDCS was more focused on the ipsilesional M1 representation of the quadriceps, which potentiated muscle activity in the paretic rectus femoris muscle, and resulted in greater motor recovery in hip flexion movements for the tDCS group than for the Sham group.

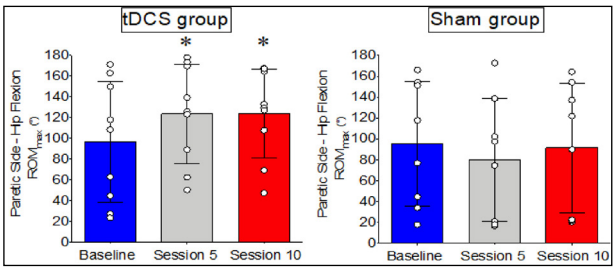

Figure 1. Mean±SD of paretic limbs' hip flexion ROMmax (circles represent individuals). *Denotes significant difference compared to baseline (p<0.05).

Acknowledgments: FAPESP (2013/07559-3), CNPq (304008/2021-4), FAPESP (2022/08057-0).

References: [1] Hu X *et al.* J Neural Eng 12(6):1-11, 2015; [2] Andrews AW *et al.* Phys Ther 69(9): 768-72, 1989; [3] Llorens R *et al.* J Neuroeng Rehabil. 18(1):108, 2021.

TIMING INVESTIGATION OF EEG FUNCTIONAL CONNECTIVITY CHANGES DURING A MOTOR IMAGERY TASK

G. C. de Melo[1], G. Castellano[1]

[1]Neurophysics Group, IFGW, UNICAMP.

Introduction: In electroencephalography (EEG) signal analysis, many Functional Connectivity (FC) research assume stable connections within a trial [1]. Others that do consider the variation usually focus on very specific frequency bands [2]. The characterization of FC changes related to the motor-imagery (MI) timing can provide features to be used in real-time detection of MI. In this paper we characterized the FC variation pre and post MI initiation across a broad frequency band (0-50 Hz). **Materials and Methods:** A public dataset [3] with MI-EEG data from four subjects (A, B, F, G) was used. Sampling was at 100 Hz and the electrodes resulted in 1711 channel pairs for FC computation. Subjects performed multiple trials of a left-hand MI task. FC was calculated using the imaginary part of coherency (iCoh) [4] across the entire 0-50 Hz frequency spectrum. We divided the data into two intervals: a 2-second period

before the MI cue (interval 1) and the first 2 seconds after the MI cue appeared on the screen (interval 2). The iCoh absolute values in each interval were obtained, then the difference from interval 2 and interval 1 () was calculated for the analysis. **Results:** FC changes were found to be dependent on frequency, channel, and subject (Fig. 1). The largest variations were -0.33, 0.19, -0.32, 0.61 for subjects A, B, F, and G, respectively. Frequency regions associated with larger changes can be visually identified. Notable positive changes are seen near 10 Hz for A, below 5 Hz and between 40 and 50 Hz for B, slightly below 10 Hz for F, slightly below 40 Hz for G. Notable negative changes, in turn, are near 10 Hz and between 25 and 40 Hz for A, close to 0 Hz in a few cases for B, between 30 and 45 Hz for F, and were absent for G. **Discussion/Conclusion:** The analysis shows that there are important changes in the FC before initiating the MI and after the cue is presented (likely when MI begins). These changes vary among subjects and appear to be more closely linked to frequency than channel pairs, although the latter also influence them. Notably, high values above the beta band (<30 Hz) are observed, warranting attention. While these may relate to muscle artifacts [1], iCoh typically isn't sensitive to such corruption. Further investigation is needed for a more thorough analysis.

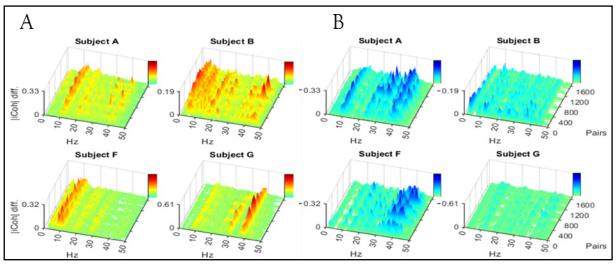

Figure 1. Values of $|iCoh_2| - |iCoh_1|$. The axis named "Pairs" refers to the channel pairs. A) Positive values (increase in the FC). B) Negative values (decrease in the FC).

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4), FAPESP (2023/12422-9).

References: [1] Nentwitch M. et al., doi: 10.1016/j.neuroimage.2020.117001. [2] Yu H. et al., doi: 10.3390/brainsci12020194. [3] Blankertz B. et al., doi: 10.1016/j.neuroimage.2007.01.051. [4] Nolte G. et al., doi: 10.1016/j.neuroimage.2007.01.051

TOURETTE SYNDROME CLASSIFICATION VIA SUPPORT VECTOR MACHINE AND TEXTURE ANALYSIS BASED ON GRAY LEVEL RUN LENGTH MATRIX IN BRAIN MRI

M. C. Barros[1], K. T. N. Duarte[2],C. J. Hsu[3], W. T. Lee[4], M. A. G. Carvalho[1]

[1]Computing Visual Laboratory, School of Technology - UNICAMP, R. Paschoal Marmo, 1888 - Jd. Nova Itália, 13484-332 - Limeira, São Paulo, Brazil,[2]Department of Radiology, University of Calgary (UofC), [3]Department of Pediatrics, National Taiwan University (NTU) Children's Hospital, [4] NTU Hospital Hsinchu Branch, Hsinchu, Taiwan.

Introduction: Tourette Syndrome (TS) is a genetically inherited condition characterized by neurobehavioral disturbances that result in involuntary motor and vocal tics. These symptoms typically emerge in childhood, becoming more pronounced between the ages of 4 and 6. Clinical diagnosis often relies solely on physician evaluation, sometimes overlooking crucial additional information, such as brain imaging using Magnetic Resonance (MR) scans. Subtle changes in texture patterns within anatomical regions may be indicative of TS. Thus, Machine Learning (ML) techniques come into play to discern these intricate patterns and distinguish TS from healthy normal (HN) children. The goal of our study is to compose a technique combining texture features and ML to classify TS from HN individuals. **Materials and Methods:** A total of 68 individuals were equally divided into two groups: TS and HN, with each group comprising 34 participants. Structural T1-weighted MR scans were obtained for each participant using the SIEMENS Triotrim scanner, following standard protocols. We preprocessed each subject scan using standard Freesurfer 6.0.0 processing pipeline, involving intensity normalization, bias field correction, skull stripping, and anatomical parcellation using the DTK-atlas (maintaining 86 brain regions). We employed the Gray Level Run Length Matrix (GLRLM) to extract the texture features within each region. Later, these texture features served as input for individual (one per region) Support Vector Machine (SVM) models for classification. We used a Majority Voting of the five best anatomical region models (5-MV) to enhance classification performance. **Results:** The evaluation of results was conducted using accuracy metric, with a primary focus on accuracy values. The right rostral middle frontal cortical region exhibited the highest accuracy, reaching 69.05%, followed closely by the mid-posterior corpus callosum region, which achieved an accuracy of 66.43%. Additionally, the right precuneus cortical region demonstrated an accuracy of 66.19%. The lowest accuracies were the left pericalcarine cortical and left thalamus regions, with 61.67% and 61.43%, respectively. The 5-MV achieved an overall accuracy of 85%. **Discussion/Conclusion:** In conclusion, we explored individual ML classification models to identify which regions are prone to identify TS patients. As expected, limbic regions showed higher performance, aligning with current literature on TS [1]. The high accuracy in the rostral middle frontal region

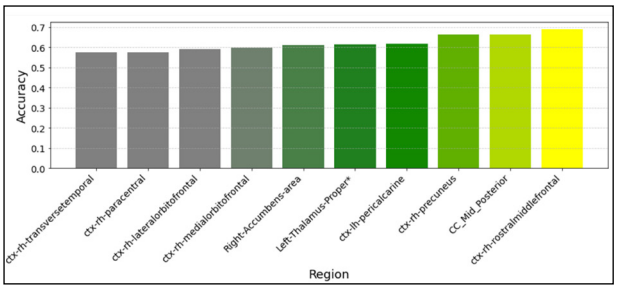

Figure 1. Accuracy of TS classification for the top 10 anatomical brain regions.

emphasizes its significance in capturing regions responsible for cognitive and emotional aspects, while the corpus callosum's involvement highlights neural network complexity. Addressing limitations such as data scarcity and scanner variations is crucial for future experiments. Potential strategies to overcome these limitations include incorporating additional scans or data augmentation. Using 3D Convolutional Neural Networks with augmented data can automate pattern extraction, providing a comparison to our current results.

References: [1] Perani *et. al.*, doi: 10.1002/mdc3.12648

TOWARDS A COMPREHENSIVE MULTIMODAL CELL ATLAS OF THE CHILDHOOD BRAIN

Isabella C. Galvão[1], Manuela Lemoine[1], Lauana Andrade[1], Steven Hebert[2,3], Bhavyaa Chandarana[2,3], Tomas Vega Waichman[2,3], Fabio Rogerio[4], Fernando Cendes[5], Claudia Kleinman[2,3], Iscia Lopes-Cendes[1], and Diogo F. T. Veiga[1]

[1]Department of Translational Medicine, Universidade Estadual de Campinas, Campinas, SP, Brazil. [2]Department of Human Genetics, McGill University, Montreal, Quebec, Canada. [3]Lady Davis Research Institute, Jewish General Hospital, Montreal, Quebec, Canada. [4]Department of Pathology, School of Medical Sciences, Universidade Estadual de Campinas, Campinas, SP, Brazil. [5]Department of Neurology, Universidade Estadual de Campinas, Campinas, SP, Brazil.

Introduction: Focal Cortical Dysplasia (FCD) II is a malformation of cortical development characterized by disrupted cortical lamination and abnormal cell types. It is a major cause for intractable epilepsy in children, often requiring surgical resection of the affected area as treatment. This study aims to construct a multimodal cell atlas of the childhood brain by performing joint single-cell open chromatin and transcriptome profiling of three distinct brain regions of histologically normal surgical tissue. Our focus will be on delineating the cell populations and regulatory networks that participate in the early stages of neuronal development. This resource will address the need for a comprehensive multimodal reference of the pediatric brain, as well as the underrepresentation of Brazilian admixed populations in existing reference datasets. **Materials and Methods:** Pediatric brain tissue samples were collected during epilepsy surgery from three specific regions (cortex, hippocampus, amygdala) of donors aged 3 to 15 years old. These samples were meticulously examined by an experienced pathologist and classified into FCD IIb or control tissue. FCD IIb tissue displayed abnormal cell types and cortical dyslamination, while control tissue from the adjacent area displayed no histological abnormalities. Nuclei extraction was carried out using the 10X dissociation kit, followed by comprehensive sequencing (scMultiome seq - ATAC, RNA, and whole-genome sequencing) for all samples. Data integration and analysis were performed using Seurat v.5.0.1[1], Signac v.1.12[2], Harmony v.1.2[3]., escape v.1.4[4], and scDblFinder v.1.8[5]. **Results:** Phase I (kit and tissue validation) consisted of multimodal profiling of

matched FCD IIb and normal tissues. We obtained 6,633 cells from 2 donors and found all major brain cell types: astrocytes, upper and deeper-layer excitatory neurons, subtypes of inhibitory neurons, endothelial cells, microglia, oligodendrocytes, and oligodendrocyte precursor cells. FCD IIb lesions exhibited a loss in upper-layer excitatory neurons and an increase in oligodendrocytes when compared to matched control tissue. Pathway analysis also revealed hallmarks of the disease, such as mTOR signaling pathway hyperactivation and severe astrogliosis. Phase II involved the construction of a multimodal reference atlas of the childhood brain created with histologically normal samples. We obtained 93,591 cells from 6 donors totaling 13 unique samples, with 51,803 cortical, 15,091 amygdala and 26,687 hippocampal cells. **Discussion/Conclusion**: In conclusion, FCD lesions and their matched control tissues display clear differences in cellular, transcriptomic, and epigenetic profiles. Therefore, histologically normal tissue obtained from epilepsy surgery can serve as the foundation for creating a comprehensive reference multimodal cell atlas of the developing childhood brain. Next steps involve detailed annotation and integrative analysis of cortex, amygdala, and hippocampus datasets.

References: [1] Hao, Y et al. , doi:10.1016/j.cell.2021.04.048; [2] Stuart, T et al., doi: 10.1038/s41592-021-01282-5; [3] Korsunsky, I et al., doi: 10.1038/s41592-019-0619-0; [4] Borcherding N et al., doi:y ; [5] Germain, P.-L et al., doi:10.12688/f1000research.73600.2.

VARIATIONS OF MOTOR PROGRAMS AND PARAMETERS: DIFFERENCES IN BEHAVIOR, COGNITIVE CONTROL AND BRAIN DYNAMICS TRANSITIONS

T. Apolinário-Souza[1], B. P. Ferreira[2], N. G. H. M. Nogueira[2], L. A. Fernandes[3], G. M. Lage[2]

[1]Nneurom/GAIM, ESEFID. UFRGS, [2]Nneurom, EEFFTO, UFMG [3]Nneurom/CoMNeuro, UFJF-GV

Introduction: The Generalized Motor Program (GMP) concept, introduced by Schmidt in 1975, is an abstract memory structure underlying responses within specific movement classes or patterns. Invariant features within a GMP, such as relative timing and force, coexist with the adaptability of movement patterns through parameterization (total timing). The variation during practice can be thought of in terms of GMP's variations or parameters' variation of one GMP (Magill & Hall, 1990). The processes involved in motor programming may differ between variations of GMPs and variations of parameters, in which the parameterization can be considered a more superficial feature of motor programming (Shea & Wulf, 2005). Thus, processing involving GMP variations demands a higher cognitive control, mainly in working memory load, than processing parameter variations. The study proposes to investigate cognitive control and brain dynamics during variations in GMPs and parameters using electroencephalographic (EEG) analyses. Different EEG frequency bands (theta, delta, and alpha) are suggested for assessing cognitive load and rule processing. The recurrence quantification analysis (RQA) is introduced as a method to analyze signal complexity in brain dynamics during GMPs and parameter variations, with the expectation that GMP variations would exhibit higher cognitive load and complexity across all analyzed frequency bands. **Materials and Methods:** This study included a sample of 22 undergraduates (18 to 40 years of age). The Motor Task required the participants to sequentially press four keys (2, 8, 6, and 4) on the numeric keypad. The study consisted of two conditions: parameter and GMP. In each condition, participants performed 60 trials with EEG data acquisition. During the parameter condition, which varied the parameters (total time). The GMP condition had a variation of the GMPs (relative time). The signal was decomposed through a discrete Fast Fourier transform from 2 to 30 Hz with a resolution of 1 Hz. The quantitative analysis of complexity (entropy) is performed from a dynamical systems theory perspective, inspired by the recent investigation of EEG data in motor behavior through recurrence quantification analysis. The recurrent behavior of these trajectories is encoded into a recurrence matrix, where the elements indicate whether two trajectories are close within a threshold. The recurrence plot is a graphical representation of this matrix. The complexity of brain dynamics in each EEG band is quantified using Shannon entropy, which considers the number and length of diagonal lines in the recurrence plot. The entropy is used because it correlates with the largest Lyapunov exponent and provides more consistent results than other entropy measures. For each participant, recurrence quantification analysis (RQA) variables are averaged over the first and last ten trials, and the difference (ΔS) in entropy between these blocks is calculated. ΔS reflects the direction of change in the complexity of overall brain activity dynamics. **Results:** In behavioral terms, the GMP condition exhibited more errors than the parameter condition. In the spectral power analysis, the GMP condition displayed higher spectral power than the parameter condition, and some channels showed differences between blocks, particularly in the theta band. The alpha band results indicated consistent differences between conditions across various channels. For Recurrence Quantification Analysis (Entropy), the theta band, a significant difference between conditions was identified, indicating that the GMP condition exhibited a greater entropy than the parameter condition. **Discussion/Conclusion**: Our results support these expectations. PMGs variation produced (a) a higher level of relative timing error, (b) higher levels of cognitive load in several electrodes analyzed, in the three analyzed bands, and (c) more complexity during the brain dynamics transitions. An exception was the non-difference observed in the level of absolute errors.

A COMPARATIVE ANALYSIS OF DIFFERENT IMAGE PROCESSING METHODS IN ARTERIAL SPIN LABELING (ASL) TECHNIQUE

Magalhães Junior, Hermes de Souza[1]; Paschoal, André Monteiro[1]

[1]LOAM Lab, Institute of Physics Gleb Wataghin, University of Campinas

Introduction and Hypothesis: Arterial Spin Labeling (ASL) is a perfusion weighted MRI technique, in which exogenous contrast agents are not necessary to quantify the cerebral blood flow (CBF)[1]. The images are acquired through the magnetic labeling of the arterial blood, whose hydrogens serves as an endogenous tracer. For labeling, a radiofrequency pulse (RF) is applied to change the magnetization of the arterial blood spins, compared to the spins in the static brain tissue. Although the ASL method has become more popular in recent years, it presents some limitations, such as a low signal to noise ratio and the need of a complex pipeline for post-processing and CBF quantification, that hinder the use of this method in clinical practice. In recent years, the Open Science Initiative for Perfusion Imaging (OSIPI) organized the first ASL challenge[2] aiming to standardize the processing pipelines and to identify the best practices. Thus, this study will compare the results obtained with the main softwares for processing ASL data available in the literature. **Objective:** This study aims to compare different post-processing pipelines for the ASL images, using previously collected data, to investigate which of the following pipelines will present less statistical fluctuation and providing a better accuracy in the measurements of the quantitative perfusion related parameters. **Materials and Methods:** This project will utilize publicly available data used in the ISMRM--OSIPI ASL Challenge, shared trough a repository on the OSF platform. The dataset consists of a population-based data and 9 synthetic data simulated using the ASLDRO platform, with the acquisition parameters shown in table 1. For the data processing, it will be considered the following softwares, that are more frequently mentioned in the literature as well as a different combination of processing steps in the pipeline:

- BASIL: developed by the University of Oxford, this method consists of large number of tools to quantify the cerebral perfusion and analyze ASL images.
- ExploreASL: an open-source program, developed as part of a multicenter, that focuses on processing ASL data and on its statistical fluctuation.
- Quantiphyse: consists of an analysis and visualization tool for MRI imaging. It presents various functionalities for different MRI techniques, including ASL.

Relevance[1]**:** At the end of this research, it is expected that a more efficient method of post-processing data is determined, in a way that statistical fluctuation is reduced the accuracy of the quantitative measures compared to the ground-truth are improved. With this analysis, we expect to assist professionals

Table 1. An overview of population-based acquisition and synthetic parameters for use in analysis.

A: Population based data:		B: Synthetic data:	
Sequence	2D PCASL	Sequence	3D PCASL
Echo Time	10.4 ms	Echo Time	10.4 ms
Repetition Time: ASL/MO	4800/10,000 ms	Repetition Time: ASL/MO	4800/10,000 ms
Initial Post Label Delay	2025 ms (range across slices: 2025-3310 ms)	Initial Post Label Delay	1800 ms
Labelling Duration	1650 ms	Labelling Duration	1800 ms

in health centers to deliver a more precise diagnostic, and facilitate professionals in research fields, with more accurate data.

References: [1] D. C. Alsop *et al.*, "Recommended implementation of arterial spin-labeled Perfusion mri for clinical applications: A consensus of the ISMRM Perfusion Study group and the European consortium for ASL in dementia," *Magn. Reson. Med.*, vol. 73, no. 1, pp. 102–116, 2015, doi: 10.1002/mrm.25197./ [2] U. Anazodo *et al.*, "The Open Source Initiative for Perfusion Imaging (OSIPI) ASL MRI Challenge," in *Proceedings of the 29th Annual Meeting of the International Society of Magnetic Resonance in Medicine*, Virtual Meeting, 2020, pp. 1–3.

ANALYSIS OF THE ROLE OF GLIAL CELLS IN THE DEVELOPMENT AND MAINTENANCE OF CHRONIC MUSCLE PAIN AND ITS PREVENTION THROUGH PHYSICAL EXERCISE

Gomes, B.B., [1]Rodrigues, H.L. [1], Santos, T.S. [1], Dorta, E. [1], Oliveira, M.C.G[1]

[1]Laboratory of Pain and Inflammation Research - FCA/ UNICAMP

Introduction and Hypothesis: Chronic musculoskeletal pain is a worldwide public health problem. However, little is known about the mechanisms underlying the transition from acute to chronic pain. Glial cells, mainly astrocytes and microglia has been associated with the development and maintenance of chronic pain [1,2] we demonstrated that these cells are involved in muscle pain of inflammatory origin through the intrathecal administration of fluorocitrate and minocycline, respectively. Glial cells may have phenotypic changes [3] it is known that and these changes can be modulated by physical exercise [4,5]. The hypothesis is that the activation of glial cells are important processes for the development and maintenance of chronic muscle pain and that physical exercise modulates the phenotype of these cells and the migration of immune system cells to the dorsal horn of the spinal cord. **Objective:** Evaluate whether there is activation, polarization of microglia and astrocytes and the contribution of immune system cell infiltration during chronic muscle pain and its prevention through exercise. **Materials and Methods:** C57BL/6 male mice (2 months old) will be used. Carrageenan (Cg, 100μg) will be injected into gastrocnemius muscle to induce acute muscle hyperalgesia and, 10 days later, PGE_2 (1μg) will be injected at the same local to reveal the state of chronic muscle hyperalgesia. The treadmill running protocol consists of 50-minute sessions, progressively increasing speed over the 3 weeks of exercise [5]. Mechanical muscle hyperalgesia was quantified by Randall Selitto test at different time points of the acute and chronic period. The involvement and phenotypic changes of microglia and astrocytes will be assessed immunofluorescence of the dorsal horn, using the markers Iba1+/TMEM119+ (microglia) and GFAP+ (astrocytes), the anti-inflammatory profile with the CD206 and pro-inflammatory CD16/32. The infiltration of cells of the immune system will be evaluated through intrathecal injection (L5-L6) of RS504393 (a highly selective CCR2 chemokine receptor antagonist, 10μg 30 minutes before the cg or PGE_2 injection) and SB225002 (a potent nonpeptide inhibitor of chemokine receptor CXCR2, 10μg 30 minutes before the cg or PGE_2 injection), Furthermore, we will analyze the expression of the chemokines CXCL1 and MCP-1 and their respective receptors using the Western Blotting technique. To confirm the results, we will use C57BL/6 $CCR2^{RFP/RFP}$ transgenic animals, which express fluorescence in the CCR2 protein. Statistical analysis will perform by Two Way ANOVA with Tukey's test, the significance level adopted it is $p<0.05$. **Relevance:** Understanding the mechanisms of exercise-induced hypoalgesia can support therapeutic strategies that associate the use of more efficient drugs with lower dosages with regular physical exercise. Furthermore, a better understanding of the mechanisms of chronic muscle pain brings benefits to individuals with it, caregivers and family members, and society in general. This is because pain-free and/or healthier individuals make less use of the healthcare system and consume fewer medications, therefore reducing the economic impacts of this disease.

References: [1] Lundquist AJ et al., doi: 10.1002/jnr.24430/ [2] Mee-Inta O et al., doi: 10.3390/cells8070691/ [3] Tu H et al., doi: 10.1016/j.tice.2020.101438/ [4] Xu et al., doi: 10.2147/JPR.S213112/ [5] Zhang J et al., doi: 10.1152/jn.00680.2016/

CARTOGRAPHY AND COGNITIVE NEUROSCIENCE: HOW DO ELEMENTARY SCHOOL STUDENTS READ THEMATIC MAPS?

M. B. Rizzo[1], J. R. Sato[1]

[1]Postgraduate Program in Neuroscience and Cognition, Center for Mathematics, Computing and Cognition, UFABC

Introduction and Hypothesis: The map is a language capable of presenting itself autonomously in communication [1], becoming a typical information model. Mastering cartography will give us support to analyze, question, criticize and act in our environment. When reading the map, especially the thematic type, the reader should make assumptions about reality's phenomenon, investigate and explain it. We have the following hypotheses: 1) mapping and analyzing how students read thematic maps can bring new directions for a more efficient teaching of this language; 2) reading the map in a targeted way will bring greater efficiency to the task. **Objective:** To analyze the strategies used by students, duly enrolled in the 4th year of Elementary School I, in the cognitive task of reading, analyzing and interpreting thematic maps, in addition to developing, applying and validating a methodology that improves their skills that results in greater competence in the task. **Materials and Methods:** There will be four thematic maps used together with the Gazepoint-HD 150Hz Eye-Tracker (ET) tool. The first map will appear with some interpretation questions; in the following two maps the methodology developed to increase the efficiency of the task will be used; finally, the last map will appear with some interpretation questions to assess whether there has been a change in ocular exploratory behavior. In addition, two questionnaires will be introduced: the Likert Scale will assess cognitive overload, and the other on affinity with maps to assess whether the student's background can have an influence in the efficiency of the task. To record the data, it will be used the Gazepoint Analysis Software to generate maps of fixation points (Fig.1) and duration time (Fig.2), in addition to comparing the AOI - Area Of Interest of the activity (Fig.3). Variables such as gender, correct and wrong answers, also fixation time will be analyzed and compared. The preliminary data obtained allowed adjustments to the methodology described above. **Relevance:** Aware of the importance of students mastering cartographic language, this work proposes two points not yet observed in previous research [2, 3, 4]: the use of ET, to investigate how the map reading process occurs; and to inquire into with a group of 9 and 10 year olds, as other studies carried out research with adolescents and adults.

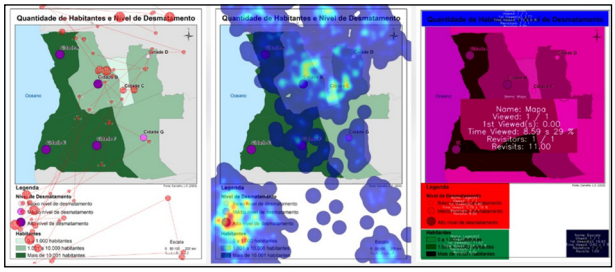

Figure 1. Figure 2. Figure 3.

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DATA ANALYSIS FOR MOTOR DISABILITIES REHABILITATION OF THE UPPER LIMBS USING A VIRTUAL REALITY DEVICE AND AUGMENTED REALITY

Gutierres. P.[1] ,Jurioli, M.. [2], Brandão A. [3], Toledo. C. F[4]

[1]PPG-CCMC, University of São Paulo,[2] University of São Paulo, [3],BRAINN., IFGW, PUC-CAMPINAS, [4]CeMEAI., ICMC, University of São Paulo.

Introduction: A rehabilitation process is a challenge for both the patient and the therapist, from the point of view of the process itself and the data evaluation. This work aims to provide a tool to analyze patient's data, assisting the health professional's assessment process. **Materials and Methods:** The present work proposes a dashboard to inspect the collected data, showing meaningful insights for the physician or therapist. Dashboards provide users the ability to create an automatic report, track patients' performance, and set estimates and targets for the treatment. The proposed architecture will use a client-server model, a database, and an application to show the data to the user. The main goal is to help the physiotherapist to evaluate if the patients are following the prescribed recovery program, and allow them to have a more accurate prognosis analysis. **Results:** The application produces a rich set of patients data, which is uploaded to a server, automatically processed and displayed in a dashboard, showing statistical data, and useful information for the therapist. The implementation of the system's dashboard has been conducted, showing data analytics for some

Figure 1. A. Main widget. B. Details widget.

augmented reality games, processing and delivering information in a predictive analytics dashboard, using a single file or comparing between sessions.

Conclusion: This study is very promising because it adds an automatic data analysis in a dashboard and sends data from the game developed by Brandão's to a cloud server or a local network. It can use statistical methods and other metrics established by the health professional.

Data analysis can be extended beyond this project by adding metrics and resources to make it more dynamic and efficient.

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DYNAMIC FUNCTIONAL CONNECTIVITY IN PATIENTS WITH SCHIZOPHRENIA

M. H. A. Belarmino[1], H. F. B. Ozelo[1]

[1]Data Modelling and Analysis Laboratory, DCNME/CCA, UFSCAR

Introduction and Hypothesis: FMRI resting-state networks might be used to increase our understanding about brain disorders. In particular, higher-order networks such as the default mode network (DMN) are frequently disrupted in patients with schizophrenia [1][2]. Most rs-fMRI studies have employed static connectivity methods to examine the functional organization of the brain, assuming a stationary condition throughout the scanning session. However, there is evidence that functional connectivity changes over time, showing that subjects are likely to engage in slightly different mental activities at different instances in time [3][4]. We hypothesize that dynamic analysis of these networks can provide connectivity variations that may occur at different times and that would not be revealed in static methods. For this purpose, we will use the sliding time window approach, where functional connectivity (FC) is calculated for consecutive portions of the scan period and this process is repeated until the last fMRI volume. Then, the FC matrices from these windows are grouped by similarity in order to form a set of "connectivity states". Each connectivity state is formed by a set of brain regions, whose temporal pattern over time describes the functional organization of the brain. **Objective:** The objective of this work is to quantify variations in functional connectivity over time in order to verify whether it is possible to use them to discriminate between healthy controls and patients with schizophrenia. **Materials and Methods:** Data analysis will be applied to a subset of UCLA Consortium for Neuropsychiatric Phenomics LA5c Study[1]. It comprises 122 healthy controls (HC) and 50 patients with schizophrenia (SZ), both with age-range of 21-50 years. fMRI data were acquired in a 3T Siemens Trio scanner with an EPI protocol (slice thickness=4mm, 34 slices, TR=2s, TE=30ms, flip angle=90°, matrix 64×64, FOV=192mm, oblique slice orientation). During the rs-fMRI scan, the participants were instructed to relax and keep their eyes open. Additionally, a T1-weighted MPRAGE image was collected (TR=1.9s, TE=2.26ms, FOV=250mm, matrix=256×256, sagittal plane, slice thickness=1mm, 176 slices) and defaced for subject anonymity. Data analysis will be performed using FMRIB Software Library FSL. Standard preprocessing will include: slice timing, motion correction, removal of non-brain tissues, normalization to MNI152 template, high-pass filtering, spatial smoothing, resampling, ICA decomposition with automatic dimensionality and signal denoising using FMRIB's ICA-based Xnoiseifier (FIX). Cleaned rs-fMRI data from all subjects will be temporally concatenated and submitted to MELODIC ICA with limited dimensionality (70 ICs). The resulting group-level components will be correlated with a reference study [5] and the significant RSNs (Pearson's $r > 0.25$) will be used as predictors to derive individual-level component timeseries and associated spatial maps by dual regression approach. The time courses of the identified components will be analyzed in the GIFT Dynamic FNC Toolbox. **Relevance:** Several studies have used static methods to detect differences in FC between SZ and HC. However, there is no consensus on its findings due to an intrinsic non-stationarity. This work hopes that taking into account the dynamic characteristic of connectivity fluctuations can provide more accurate biomarkers for schizophrenia.

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EFFECT OF CAFFEINE SUPPLEMENTATION ON THE DEVELOPMENT AND MAINTENANCE OF CHRONIC MUSCLE PAIN: POSSIBLE INVOLVEMENT OF THE PGC-1α/ PPARγ PATHWAY

Dorta, E,[1] Rodrigues, H.L,[1] Gomes B.B,[1] Oliveira, M.C.G[1]

[1]Laboratory of Pain and Inflammation Research - FCA/ UNICAMP

Introduction and Hypothesis: Pain is a public health problem with a major negative impact on the social and economic spheres. Its treatment consists of the use of drugs and the prescription of regular physical exercise, but in patients with chronic muscle pain, exercise with moderate and high intensity may not be the best strategy, because it may increase pain sensitivity and fatigue. One strategy is caffeine supplementation, due to its analgesic role in some pain conditions [1]. Considering we have previously shown that the prevention of chronic muscle pain by exercise is modulated via PPARγ receptors [2]; that PGC-1α of these receptors can modulate the anti-inflammatory effects of exercise [3]; and that caffeine can act on PGC-1α [4], we hypothesized that caffeine supplementation reduces chronic muscle pain via this pathway. The pilot experiments (Figure A, B e C) showed that supplementation with caffeine reduced the development and maintenance of chronic muscle hyperalgesia as hypothesized. **Objective:** To assess whether the reduction on the development and maintenance of chronic muscle hyperalgesia induced by caffeine supplementation is modulated by the PGC-1α/ PPARγ signaling pathway. **Materials and Methods:** Six-week-old male C57BL/6 mice obtained from CEMIB/UNICAMP (6331-1/2023) will be used. Acute muscle hyperalgesia will be induced by injecting Cg (100μg) into the right

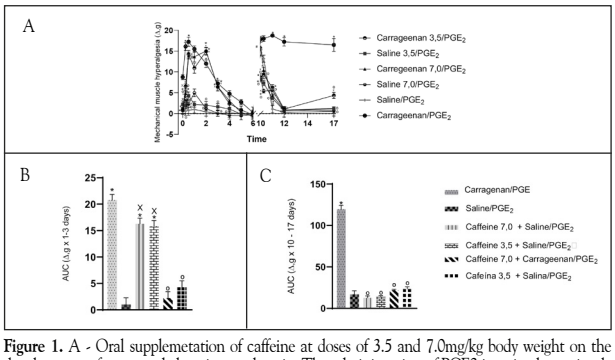

Figure 1. A - Oral supplemetation of caffeine at doses of 3.5 and 7.0mg/kg body weight on the development of acute and chronic muscle pain. The administration of PGE2 in animals previously sensitized by carregeen (Cg) induces chronic mechanical muscle hyperalgesia when compared to the control group treated with saline+PGE2. The animals that received caffeine supplementaion in both doses showed a reduction in the hyperalgesic response in the period evaluated (1 to 6 days after carrageenan and 10 to 17 days after carrageenan), when compared to the animals not supplemented with caffeine and injected with carrageenan. B - Area under the curve of the acute period)1-3 days) confirming the data obtained in the line graph ($p<0.05$, One Way ANOVA and Turkey's post-test). The symbols indicate "x" difference between saline+caffeine and carrageenan+caffeine groups, "*" saline+PGE_2, "○" carrageenan+PGE_2, and "#" diffeence between doses fo caffeine groups. C - Area under the curve of the acute period (1-3 days) which confirms the data obtained in the line graph ($p<0.05$, One Way ANOVA and Turkey's post). The symbols indicate "x" difference of saline+caffeine with the carrageenan+caffeine groups. "*" saline+PGE_2, "○" carrageenan+ PGE_2 and "#" difference between the doses of the caffeine groups.

gastrocnemius muscle and, ten days later, Prostaglandin E_2 (1μg) will be injected into the same site to induce the development of chronic muscle hyperalgesia. Caffeine will be administered by gavage (supplementation) at doses of 3.5 mg/kg/ and 7.0 mg/kg body weight [5], for 17 days which will be concomitant with the muscle hyperalgesia protocol. Muscle hyperalgesia will be quantified using the Randall & Selitto test at different times 17 days), gastrocnemius muscle samples will be collected and sent for rtQPCR. Analysis statistical analysis will be performed by ANOVA with Tukey's test, the Area Under the Curve will be used to evaluate the chronic period of muscle hyperalgesia, the significance level adopted will be set at $p < 0.05$. **Relevance:** Understanding the mechanisms involved in the chronicity of muscle pain is essential for developing efficient treatment strategies. The present study may provide scientific support for the use of caffeine as a therapeutic strategy for controlling the chronic muscle pain.

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EMPLOYING BAYESIAN NETWORKS TO INTEGRATE ASSOCIATION RULES AND DOMAIN EXPERTISE FOR CAUSAL REASONING

A. C. P. Kulaif[1], R. Veroneze[1], L. F. R. de Souza Li[2], F. J. Von Zuben[1]
[1]LBiC, FEEC, UNICAMP, [2]Pediatrics Dept., FCM, UNICAMP

Introduction and Hypothesis: Determining genuine causal relationships is a cornerstone in developing effective interventions across various domains, including medicine. In many cases where randomized control trials are not feasible, the challenge of deriving causal insights from observational data arises. This is where the fact that correlation does not mean causation becomes particularly pertinent. Hence, it becomes imperative to differentiate between events that cause specific outcomes and those that merely exhibit correlations. Association rules (ARs) [1] are powerful tools for identifying relationships and dependencies between variables within a dataset. However, they do not provide evidence of a causal relationship, i.e., association does not imply causality. ARs are based on correlations and cannot account for confounding variables, temporal sequences, or the underlying mechanisms that establish causation. Therefore, when interpreting an AR, it is crucial to exercise caution and consider additional evidence and domain knowledge when concluding cause-and-effect relationships. Notwithstanding, we assume that association rule mining (ARM) is a powerful tool for generating hypotheses for further investigation. Beyond that, we hypothesize that it is possible to employ structural causal models based on Bayesian networks (BNs) [2] to integrate ARs and domain expertise for leveraging causal reasoning. **Objective:** ARM methods often yield a plethora of rules, yet many of these merely reflect spurious associations. The first goal of this project is to create a framework based on domain expertise and BNs for selecting interesting rules (i.e., rules that potentially exhibit cause-and-effect relationships). This framework would be grounded in a step-wise procedure. First, the rules are mined. Next, the rules are selected. Yet, based on a step-wise procedure, the second goal is to use domain expertise to guide the ARM and use structural causal models to measure the strength of the rules regarding cause-and-effect relationships. Lastly, considering resource efficiency and robustness, the next goal is to develop a more advanced framework for integrating structural causal models based on BNs and domain expertise into ARM. **Materials and Methods:** This study will use publicly available datasets from the UCI repository. Additionally, we will use a dataset obtained by the Pediatrics department of the School of Medicine of the University of Campinas, comprising interviews with 411 students from the State school *Barão Geraldo de Rezende*. The interviews regard their academic experiences, drug usage, and encounters with bullying, totalizing 177 variables. This study will use ARM methods, BNs, and other Probabilistic Graphical Models (PGMs). We will use the Charm-L algorithm [3] for mining the ARs since it mines only non-redundant rules. For the BNs and PGMs, we will use the *pyAgrum* Python Library [4]. **Relevance:** The work addresses the challenge of deriving causal insights from observational data where randomized control trials are not feasible. By integrating ARs with structural causal models, the work provides a framework for leveraging causal reasoning and advancing understanding of complex phenomena. The approach allows researchers to explore cause-and-effect relationships more effectively, contributing to the pursuit of further studies and the development of effective interventions across various domains.

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EVALUATION OF CEREBRAL BLOOD FLOW CHANGES IN PATIENTS WITH HEALTHY HUMAN AGING AND VASCULAR DEMENTIA USING ARTERIAL SPIN LABELING

Lucas Grava[1], André M. Paschoal[1]
[1]LOAM Lab, Gleb Wataghin Institute of Physics, University of Campinas

Introduction and Hypothesis: The human brain is highly dependent on oxygen and nutrients supply for a proper functioning. Several studies have reported that human aging is associated with a decrease in the cerebral blood flow (CBF)[1], which is related to an impairment of brain capacities and may be a risk factor for diseases, like vascular dementia. A noninvasively technique of magnetic resonance imaging (MRI) that can be used to study CBF is the Arterial Spin Labeling (ASL), which can provide quantitative measure of CBF using blood water molecules as an endogenous tracer. This method, which is increasingly being studied, can be used for both diagnosis and monitoring of diseases associated with changes in cerebral perfusion[2]. **Objective:** The primary objective of this study is the investigation and evaluation of the effects of normal aging in the cerebral blood flow through analysis with ASL method. That analysis involves processing ASL images taken from elderly subjects and comparing them with images taken for subjects at a younger age. It is expected that this analysis, in addition to providing quantitative values, will also provide data on the areas that are most severely affected by the decrease in CBF. This analysis will then be extended to vascular dementia patients. **Materials and Methods:** The data to be analyzed belongs to the database human connectome for lifespan aging (https://www.humanconnectome.org/study/hcp-lifespan-aging), collected in a Siemens Magnetom Prisma. The ASL images were collected with the pseudocontinuous approach (pCASL) with a labeling duration of 1500 ms and post-labeling delay (PLD) of 1642 ms. T_1-weighted images will be used for anatomical references. The respective acquisition parameters can be found in the table below. The images will be analyzed with the FSL software, which is an MRI image processing tool, including the BASIL, a toolbox that allows us to create perfusion-weighted images, providing important hemodynamics parameters as the CBF. **Relevance:** What makes ASL different from other techniques is that it provides quantifiable CBF measurement and does not require intravenous contrast, allowing for an efficient mapping of brain perfusion. Therefore, we can more accurately study regions most affected by healthy aging, which make ASL a more reliable tool for the assessment of changes in cerebral hemodynamics. Furthermore, compared to other techniques, ASL is more repeatable and useful in conditions for which the contrast agent is contraindicated, including but not limited to studies with debilitated patients, making it the most effective method. Therefore, we expect to have a better understanding of the hemodynamic changes in the brain during the process of aging.

Table 1. Data acquisition parameters.

Parameters	FOV	Voxel size	TR	TE
ASL image	215 x 215 mm^2	2.5 x 2.5 x 2.3 mm^3	3580 ms	19 ms
Structural	256 x 240 mm^2	0.8 x 0.8 x 0.8 mm^3	2500 ms	3.6 ms

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EVALUATION OF FUNCTIONAL NETWORKS OF PEOPLE UNDER THE INFLUENCE OF AYAHUASCA TEA

M. Tisoc[1], I. Wiessner[2], F. Palhano-Fontes[2], D. B. Araújo[2], G. Castellano[1,3]
[1]Neurophysics Group, IFGW, UNICAMP; [2]Center for Advanced Medical Psychedelics, Instituto do Cérebro, UFRN; [3]BRAINN-FAPESP

Introduction and Hypothesis: Throughout ancient history, the use of psychoactive plants for medical and ceremonial purposes has been a recurring theme. An example is the Ayahuasca brew containing N,N-DMT used by the indigenous people of the Amazon to heal the body and mind [1]. The use of this drink was so important that it extended to the Andes; indeed, mass spectrometry methods identified the presence of harmine, the second main compound in Ayahuasca, in hair samples from Andean mummies dated between 500 and 1000 AD [2]. Although its medicinal uses have been known for years, it has recently been found that Ayahuasca treatments help treating depression, anxiety and addictions [3]. However, beyond its clinical applications, Ayahuasca

has been used as a tool to explore altered states of consciousness, which modify brain activity and functional connectivity (FC) of brain regions associated with self-perception, introspection, cognition, and emotion [4]. **Objective:** The aim of this study is to determine the changes in FC induced by Ayahuasca, using electroencephalography (EEG) data. **Materials and Methods:** EEG data (BrainProducts equipment, 32 electrodes, 1 kHz sampling frequency) were collected from 50 healthy subjects (age 32±10, 31% men) in three stages: before Ayahuasca ingestion, after 2 hours and after 4 hours of ingestion. Also, each EEG measure was divided in two moments: eyes open and eyes closed. Half of the participants took Ayahuasca (experimental group) and the other half took a placebo brew (control group). Groups had similar mean age and similar percentage of male/female participants. This is a triple-blind study, in which neither the researchers who collected the data, nor the analysis crew know who is part of which group. The data will be preprocessed using EEGLAB [5] in the MATLAB environment. FC will be computed using the motifs synchronization (MS) method [6], and graph measures will be extracted to compare the different stages and different groups. **Relevance:** Neuroscientific research on the effects of Ayahuasca may provide new insights into the nature of the human mind and the underlying mechanisms of subjective experience. Also, the FC analysis will improve knowledge on the Ayahuasca effects on the brain which may help its application for the treatment of other neurological diseases.

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4), CAPES (finance code 001).

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EVALUATION OF SLEEP AND CSF BLOOD BIOMARKERS IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT AND SUBJECTIVE COGNITIVE DECLINE

E. R. Hurtado[1], T. A. Marchiori[2], L. Rizzi[3], I. C. Ribeiro[1], I. K. Aventurato[1], M. C. R. Silva[1], B. C. Gonçalves[1], E. R. Guimarães[1], M. L. F. Balthazar[1,2]

[1]Laboratory of Imaging and Biomarkers in Cognitive Disorders, School of Medical Sciences, UNICAMP, [2]Neurology Dept., School of Medical Sciences, UNICAMP, [3]Memory and Aging Center, University of California San Francisco, San Francisco, CA, USA.

Introduction: Sleep and circadian rhythm disorders are known markers of neurodegenerative diseases and have emerged as potential biomarkers of Alzheimer's disease (AD). The present work intends to investigate the possible association of sleep with milder stages of cognitive impairment, Mild Cognitive Impairment (MCI), and Subjective Cognitive Decline (SCD), part of the Alzheimer's continuum. **Materials and Methods:** This is a quantitative observational cross-sectional study, part of a broader project already approved by the ethics committee (JP2 Fapesp 2018/15571-7). 74 individuals were included in this investigation (30 individuals without positive biomarkers in control group and 44 individuals in the AD continuum, according to A/T/N classification). We evaluated the scores in quality assessment questionnaires of sleep and daytime sleepiness (Pittsburgh Sleep Quality Index – PSQI, and the Epworth Sleepiness Scale - ESS, respectively) and the level of CSF biomarkers amyloid beta, total tau, and phosphorylated tau. Elecsys® immunoessays kits were used to measure CSF proteins, with the following cutoff values: tTau > 300 pg/mL, pTau > 27 pg/mL and β-Amyloid (1-42) ≤ 1000 pg/mL. For statistical analysis we apply a Mann-Whitney test and a Spearman's correlation due to the non-normal distribution of the sample. The software used was IBM SPSS Statistics v.29. The significance was considered in $p<0.05$. **Results:** There were no differences in sex, age and education. In comparison with a Mann-Whitney test, the diagnosis (normal or within the Alzheimer's continuum) influences the score on the Epworth Sleepiness Scale ($p<0.001$), but it was not significant for the Pittsburgh Sleep Quality Index ($p=0.825$). Spearman's correlation shows that there is a positive and weak correlation between the ESS score and the CSF amyloid ($\rho=0.273$; $p=0.02$). **Discussion/Conclusion**: The results suggest a relationship between sleep, biomarkers, and AD, in accordance with what other studies have shown. Individuals with Alzheimer's pathology had higher ESS scores, and this appears to be related to CSF amyloid level. Future research, with longitudinal design, objective sleep metrics, and larger sample may better elucidate this bidirectional pathophysiology between sleep and Alzheimer's disease.

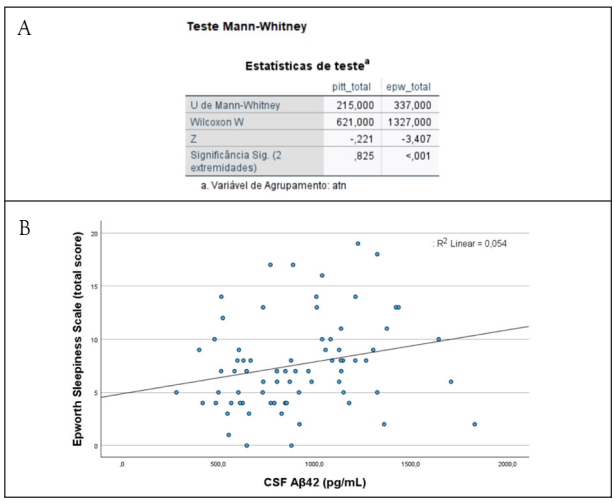

Figure 1. A. Mann-Whitney test shows that the diagnosis influences the score on Epworth Sleepiness Scale. B. Bivariate correlation shows positive and weak correlation between the ESS score and the CSF amyloid.

EXPLORING BRAIN ENTROPY AS BIOMARKER IN ALZHEIMER'S DISEASE: A RESTING-STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING APPROACH

N. C. Santos[1,2], L. L. da Silva[1], G. Gambaro[1], P. H. R. da Silva[3], R. F. Leoni[1]

[1] InBrain Lab, FFCLRP, USP; [2] Instituto de Física de São Carlos, USP; [3] Instituto de Psiquiatria, HCFMUSP

Introduction and Hypothesis: Dementia, particularly Alzheimer's Disease (AD), presents a significant challenge to public health, adversely affecting an individual's cognition and functionality. With the increasing life expectancy, early and accurate detection of AD signs becomes essential. Brain entropy (BEN), a measure quantifying the degree of disorder in biological systems, emerges as a promising perspective in understanding brain states and their alterations in neurological conditions. Specifically, employing this methodology in resting-state functional magnetic resonance imaging (rs-fMRI) has been explored to identify brain activation and investigate potential markers of brain diseases. Research indicates that brain entropy tends to decrease during reduced consciousness states and is associated with aging, suggesting its potential as a brain health indicator [1]. We hypothesize that analyzing BEN via rs-fMRI could serve as a sensitive marker for early AD detection and provide valuable insights into changes in neural system complexity during aging and mild cognitive impairment. **Objective:** Investigate BEN in patients with AD using rs-fMRI to gain a deeper understanding of the changes in brain entropy related to the disease and contribute to advancements in the diagnosis, monitoring, and treatment of this condition. **Materials and Methods:** All images, acquired with 3T Siemens scanners, were obtained from Open Access Series of Imaging Studies 3 (OASIS-3), a free database with 1098 participants, including patients with various stages of cognitive impairment, including AD, aged 42 to 95 years. Resting-state fMRI with blood oxygenation level-dependent contrast (rs-BOLD-fMRI) were acquired with the following parameters: slice thickness = 4 mm, spacing between slices = 4 mm, TE = 27 s, TR = 2,2 s, flip angle = 90°, matrix = 64 x 64 cm^2, 164 volumes. T1-weighted images were acquired with the clinical sequence parameters of the respective scanners: Triotim - slice thickness = 1 mm, TE = 316 s, TR = 2,4 s, flip angle = 8°, matrix = 256 x 256; Biograph_mMR - slice thickness = 1,2 mm, TE = 295 s, TR = 2,3 s, flip angle = 9°, matrix = 256 x 256. Clinical Dementia Rating (CDR) and Mini-Mental State Examination (MMSE) scales were used to select patients of interest. For the AD group, patients diagnosed with AD and CDR > 1 were selected (27 male and 18 female, 75 ± 8 years old, MMSE = 22 ± 4). For the control group, participants without AD and CDR = 0 were selected (26 male and 14 female, 77 ± 7 years old, MMSE = 29 ± 1). All selected patients had acquired rs-BOLD-fMRI and T1W images less than six months apart from the clinical diagnosis, and they will be used to evaluate BEN and for anatomical reference, respectively. Images will be processed in SPM12 (Statistical Parametric Mapping, University College London, UK). BENtbx (Brain Entropy Mapping Toolbox) will be used for BEN quantification. **Relevance:** The World Health

Organization estimates that more than 55 million people are living with dementia, and this number is expected to almost triple in 2050 (139 million) [2]. Therefore, the need for early AD diagnosis is evident, as well as a better understanding of its neurophysiology.

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INVESTIGATION OF EEG FUNCTIONAL CONNECTIVITY DURING READING AND RECALLING TASKS

Márcio Vinícius N. Silva[1], Gabriela Castellano[1,2]
[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN-FAPESP

Introduction and Hypothesis: It is yet unclear how brain regions that process sensory inputs, such as visual stimuli and sounds, contribute to working memory. To investigate this, Dimakopoulos et al. measured brain electrical activity of people with epilepsy, as they read, heard and mentally replayed short letter sequences (up to 8 letters) [1]. For this, they used implanted, surface (i.e., electrocorticography) and scalp (i.e., electroencephalography, EEG) electrodes. They found a flow of brain signals from the auditory cortex to the hippocampus when participants read the letters, that was reversed when they recalled the letters [1]. However, they did not investigate the functional connectivity (FC) among EEG electrodes during those processes. Although EEG cannot measure signals from deep structures such as the hippocampus, it is a non-invasive and therefore widely used technique for measuring brain signals, and it is particularly relevant for epilepsy studies. Therefore, it would be interesting to find out if and how FC patterns reflect those different tasks. **Objective:** The aim of this work is to compute FC from the EEG signals obtained in the tasks of reading and recalling letter strings and verify if and how this reflects the information flow found in [1]. This project is a Scientific Initiation and as such, it also aims to introduce the student to concepts related to EEG signal processing and analysis, FC methods for EEG and graph theory. **Materials and Methods:** We will use only the scalp EEG signals from the database related to the study [1] and available at the OpenNeuro platform, called "Dataset of intracranial EEG, scalp EEG and beamforming sources from human epilepsy patients performing a verbal working memory task" [2]. The EEG data will be pre-processed using EEGLAB [3]. FC will be computed using the motif synchronization (MS) method [4], which consists on counting the appearance of patterns or motifs in two time series simultaneously or with a predefined lag. Three-point motifs will be used in this work, as illustrated in Figure 1. The MS will be programmed using the Python language. **Relevance:** EEG is the gold-standard method to investigate several brain disorders, such as epilepsy and sleep disorders. Compared to other techniques, EEG has the advantage of being non-invasive and more affordable. Therefore, studying this type of signals can bring advances to society with a lower cost. Furthermore, the investigation of FC in the reading and recalling tasks will bring further insights into the relation between sensory brain regions and working memory, without the need for a surgical procedure.
Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4).

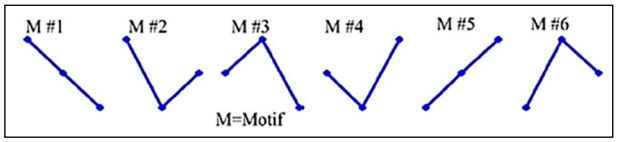

Figure 1. Pattern possibilities for three-point motifs [4].

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INVOLVEMENT OF THE INFLAMMATORY CYTOKINE IL-1B IN MAINTENANCE OF THE CHRONICITY OF MUSCLE PAIN AND ITS PREVENTION THROUGH PHYSICAL EXERCISE

H.L Rodrigues[1], B.B Gomes[2], E.O Dorta[2], M.C.G Oliveira[1]
[1] Laboratory of Studies of Pain and Inflammation Research– LABEDI, FCA-UNICAMP

Introduction and Hypothesis: Recently, our research group demonstrated that acute and chronic inflammatory muscle hyperalgesia are characterized by an increase in IL-1β cytokine in the acute phase and by pro-inflammatory macrophages in both phases [1]. Considering these findings, we hypothesized that the increase in IL-1β during acute muscle hyperalgesia is involved in the development and maintenance of chronic muscle hyperalgesia. Pilot experiments showed that the injection of IL-1ra, an IL-1 receptor antagonist, after the inflammatory stimulus reduced the development and maintenance of chronic muscle hyperalgesia in male and female mice (Figure 1), confirming our hypothesis. **Objective:** We aimed to better explore the involvement of IL-1β in development and maintenance of chronic muscle pain. **Materials and Methods:** C57BL/6 mice, 6-7 weeks, from CEMIB-UNICAMP (5973-1/2022), will be used. Carrageenan (Cg, 100μg) will be injected into the gastrocnemius muscle to induce inflammatory pain, and 10 days later, PGE_2 (1μg) will be injected at the same site to reveal the state of chronic hyperalgesia. The IL-1ra (500ng/muscle) will be injected before or 48h after Cg. Mechanical muscle hyperalgesia will be quantified by the Randall Selitto test at different time points (0-17 days). Gastrocnemius muscle and sciatic nerves from mice will be collected after euthanasia for analyzes of IL-1B, IL1-ra and IL1R1 by *Western Blotting*. Statistical analysis will be carried out by Two-Way ANOVA, with a significance level set at $p < 0.05$. **Relevance:** Chronic muscle pain is a worldwide public health problem. Therefore, the studies related to mechanisms underlying the chronification process have scientific, social and economic relevance. In addition, the findings of the present study will reinforce the importance of exercise as a strategy of treatment for chronic muscle pain.

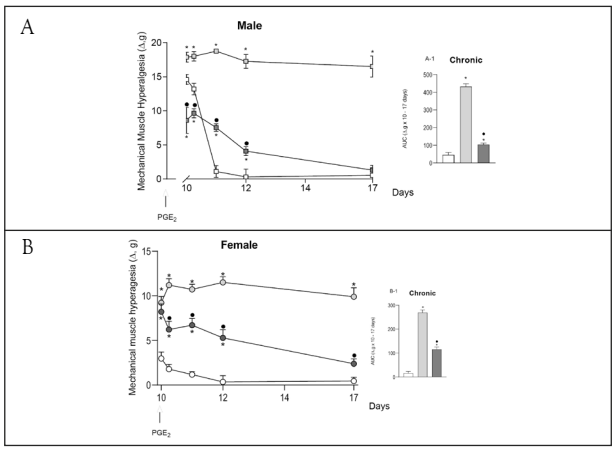

Figure 1. Muscle IL-1ra administration reduce the development and maintenance of chronic muscle pain in mice previously sensitized by cg. A and B. Timeline graph showing male and female mice respectively that received IL-1ra reduced the development and maintenance of chronic muscle ($p<0.05$, Two Way ANOVA, post Tukey's test) compared to Carrageenan group. A-1 and B-1. Area Under the Curve (AUC) graph ($p<0.05$, One Way ANOVA, post Tukey's test). The symbols "*" indicates difference to control saline group, "•" indicate difference to carrageenan group.

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MITOCHONDRIAL ANCESTRALITY IN THE BRAZILIAN POPULATION AND ITS PHARMACOGENOMICS EFFECTS

Vinicius Garcia Rodolfo[1,2], Thais C. de Oliveira[1,2], Rodrigo Secolin[1,2], Iscia Lopes-Cendes[1,2]
[1]Department of Translational Medicine, School of Medical Sciences, University of Campinas (UNICAMP), Campinas, Brazil, [2] The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, Brazil

Introduction and Hypothesis: Pharmacogenomic studies have made headway in the precision medicine scenario alongside population genetics, creating a multidisciplinary interface between pharmacology and genomic sciences[1]. Within the context of population genetics, it is possible to study mitochondrial genetic variants and their relationship in the response to certain medications. This is especially interesting in admixed populations, such as the Brazilian population. Given that populations with distinct ancestry may display inter-ethnic genetic differences that can affect mitochondrial activity. Therefore, these differences must be considered from the perspective of individualized pharmacotherapy in a unique way[2,3]. **Objective:** The overall objective of this project is to evaluate the impact of ancestry (Europeans, Africans, and Native Americans) on mitochondrial genes that have pharmacogenetic effects.

Specific aims are: i) analyzing the relationship between genotypes related to distinct ancestry with genes of pharmacological relevance (pgx) in mitochondrial genes; ii) evaluating the frequency of risk genotypes in the autosomes of Brazilian individuals that may be related to pharmacogenomics; iii) if needed, creating a model that adjusts the relationship between pgx genes and admixed genotypes. **Materials and Methods:** We are studying 203 exomes of control individuals from southwestern Brazil, available in the Brazilian Initiative on Precision Medicine database (BIPMed) [4,5]. The SNP Array data obtained with the Genome-Wide Human SNP Array Platform 6.0 (Affymetrix Inc, Santa Clara, CA) are being processed from the observed fluorescent signals using the CRLMM 69 package in the R software, followed by conversion to the variant call file format. The sequences produced will be aligned using the BWA algorithm, using the GRCh38 human reference genome as a reference. Single nucleotide variants (SNV), insertions, and deletions (indels) will be called for each individual using the HaplotypeCaller algorithm, and new variants will be called for the data cohort using the JointGenotyping algorithm, both present in GATK4. The variants will be annotated in relation to pathogenicity using the ANNOVAR algorithm and VEP (Variant Effect Predictor). All these analyses will be carried out using advanced computational parallelism systems, including WDL and Cromwell on dedicated servers. We will evaluate which drugs confer resistance, toxicity and/or increased efficacy and that have been related to genes present in the mtDNA. Haplotypes will be determined using Haplogrep software using VCF files as input. In addition, publicly available mtDNA sequence data from different ethnic origins (1000 genomes project) will be used as references for comparison with the mtDNA haplotypes from Brazilian individuals. Finally, we will look for potential associations between ancestral haplotypes and SNPs found in mtDNA genes involved in response to different medications, using advance bioinformatics. **Relevance:** The effects of ancestry on the mtDNA haplotypes of Brazilians have not been fully elucidated. Therefore, with this project we aim to identify the frequency of mitochondrial genes of pharmacological interest in the Brazilian population, thus contributing to the implementation of precision medicine in Brazil and worldwide.

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MOTOR IMAGERY CLASSIFICATION WITH DEEP LEARNING AND RIEMANNIAN GEOMETRY

A. H. Matias[1], L. H. dos Santos[2], D. G. Fantinato[3]

[1]School of Electrical and Computer Engineering, UNICAMP, [2]Mathematics, Computation and Cognition Center, UFABC, [3]School of Electrical and Computer Engineering, UNICAMP

Introduction and Hypothesis: Brain-Computer Interface (BCI) systems might use electroencephalographic (EEG) signals to control devices/applications. Among the main components of the BCI system, the classifier is responsible for pattern recognition from EEG signals, in which we highlight the use of the machine learning framework, in particular, the SPDNet. This artificial neural network takes advantage of the fact that covariance matrices, obtained from EEG signals, are symmetric positive definite (SPD) and lie on the Riemannian manifold. The properties of Riemannian Geometry (RG) have shown to be efficient for both representation and manipulation of EEG covariance matrices, such that current state-of-the-art and many emerging classifiers are based on RG. The usual Riemannian perspective, however, is focused on the use of spatial information through the covariance matrices, which lacks temporal information. Since the temporal behavior in EEG signals might be crucial for a classifier, we intend to additionally exploit the temporal statistics in order to improve classification accuracy. **Objective:** Our objective is to propose a Deep Riemannian Network (DRN) architecture that takes into account the temporal information obtained from a set of covariance matrices calculated for different time delays of the EEG signals. With a focus on the Motor Imagery paradigm, incorporating extra temporal information is expected to enhance the efficiency of classification. **Materials and Methods:** This project will use publicly available EEG datasets accessible through Python libraries like MOABB, pyRiemann, and MNE. These libraries enable straightforward integration into the code. In the process of obtaining covariance matrices, our approach involves adapting the conventional sample estimator by introducing the use of delayed EEG signals. After calculating multiple covariance matrices, they will be consolidated into a unified tensor as input to the SPDNet, as illustrated in Fig. 1. **Relevance:** BCI systems, widely applied, especially in medical contexts like post-stroke rehabilitation using motor imagery, benefit from improved classifiers for enhanced accuracy and noise resilience. The use of RG with the addition of temporal information aims to deepen our understanding of EEG signals and the synergy of RG with Deep Neural Networks.

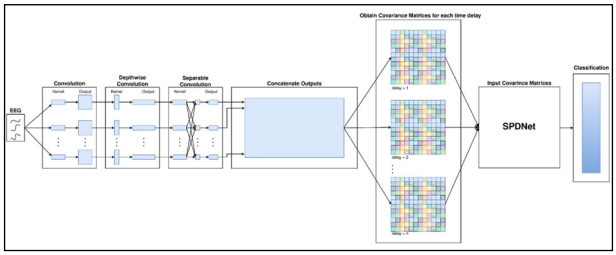

Figure 1.

MOTOR NEUROREHABILITATION THROUGH MANIPULATIONS OF THE RIEMANNIAN MANIFOLD

S. Y. Yamauti[1], G. O. S. Filho[1], E. Morya[1]

[1]Edmond and Lily Safra International Institute of Neuroscience, Santos Dumont Institute (ISD)

Introduction and Hypothesis: Neural signals in several brain cortices represent the overt activity of latent variables [1]. Invasive studies in non-human primates and rodents have shown that latent variables describe low-dimensional, embedded curves in the space of all possible neuronal activities known as manifolds. These manifolds appear preserved among species for the same behavior [2] and can be disrupted or changed due to learning and plasticity [3]. In non-invasive brain studies, manifolds are often represented as Electroencephalography (EEG) signals processed in the Riemannian geometry, in the form of covariance matrices [4]. Here, we hypothesize that a similar response to manifold manipulations observed in invasive processing can be elicited in non-invasive settings, with repercussions on behavior. Our study focuses on human motor learning in a rehabilitation context. **Objective:** To implement real-time signal processing to identify latent variables, provide subjects with meaningful feedback on these variables, extract and analyze motor behavior manifolds from EEG signals in rehabilitation, and use manifold manipulation to aid sensorimotor recovery. **Materials and Methods:** Eight chronic spinal cord subjects with upper and lower limb impairments will undergo motor imagery training in a system combining digital signal processing alongside feedback devices and traditional motor rehabilitation, with a paired control group without feedback, undergoing the same rehabilitation context. The regimen includes twenty training sessions over three months, with full clinical assessments at the start, midpoint, and end, aiming to enhance sensorimotor recovery through targeted feedback and manifold manipulation. We filter EEG signals from 16 channels positioned in the primary and secondary motor cortices in the alpha-beta range (8-35Hz), epoch the data (1-second epoch each 0.0625 second), convert these into covariance matrices, and project them onto a 2D Linear Discriminant Analysis (LDA)-reduced euclidean tangent space. The manifold is produced in the space of covariance matrices, and subjects are asked to reach motor behavior according to their respective regions of representation in the reduced-dimensionality space. The protocol involves initial supervised training of a classification model to label motor imagery trials, followed by sessions where EEG features are translated into visual or tactile feedback of upper and lower limbs' motor imagery. Data alignment via Riemannian Procrustes Analysis (RPA) [5] - to account for data distribution shifts - occurs at the beginning of each session, with model recalibration every two sessions - to account for neural activity changes due to plasticity. **Relevance:** This study aims to evidence the effectiveness of exposing the latent variables of motor control to a subject undergoing rehabilitation. This processing makes it possible to interpret and manipulate the same or similar representation of motor control in invasive settings, which has not yet been explored to its full potential in non-invasive settings, as far as we know.

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OLIGODENDROCYTE SECRETOME AND THE PECULIARITIES OF ATYPICAL ANTIPSYCHOTICS

C. H. S. F. Berdeville[1], Msc. D. Silva-Amaral[1], Prof. Dr. D. Martins-De-Souza[1,2,3,4]

[1]Laboratory of Neuroproteomics, Department of Biochemistry and Tissue Biology, University of Campinas, Campinas, SP, Brazil, [2]D'or Institute for Research and Education (IDOR), Rua Diniz Cordeiro, RJ, Brazil, [3]Experimental Medicine Research Cluster (EMRC), University of Campinas, Campinas, SP, Brazil, [4]National Institute of Biomarkers in Neuropsychiatry, National Council for Scientific and Technological Development (CNPq), SP, Brazil.

Introduction and Hypothesis: Schizophrenia is characterized by the presence of psychotic symptoms, with a lifetime prevalence of nearly 1% [1]. The treatment is mostly based on the use of atypical antipsychotics, which act by antagonizing D_2 receptors and blocking 5-HT_{2A} receptors [1]. Although quetiapine, olanzapine, and clozapine present similar efficacy and share a similar mechanism of action, each of these drugs presents important peculiarities, such as extreme sedation and mood-stabilizing properties, metabolic syndrome induction, and the ability to management refractory psychosis but also reducing seizure thresholds [1-5]. The secretome may be defined as the characterization of both the protein and metabolite content of a sample at a qualitative and quantitative level, with liquid-chromatography mass spectrometry (LC-MS)-based techniques being an important method due to their ability to perform proteomic and metabolomic assessments [6]. **Objective:** The aim of this project is to investigate if three second-generation antipsychotics, quetiapine, olanzapine, and clozapine, are able to modulate the MO3.13 oligodendrocyte cell line secretome, analyzing proteins and metabolites altered collectively and specifically by each treatment. **Materials and Methods:** The concentration of drugs will be determined by the MTT cell's viability assay, while the presence of D_2 and 5-HT_{2A} receptors will be assessed by immunocytochemistry. For the secretome obtainment, MO3.13 will grow to a 60–70% rage confluency, followed by a 24h treatment with olanzapine, quetiapine, clozapine, or control groups. After incubation, the culture medium will be characterized by LC-MS, comparing groups in an *in silico* analysis in *David Bioinformatics database*, *Reactome*, *Metascape*, and *Protein Reference Database*. Additionally, SH-SY5Y, a neuroblastoma cell line, will be exposed to MO3.13-conditioned medium by antipsychotic treatment, and its proteome will also be assessed by LC-MS and analyzed by the same platforms. Finally, validation assays for biological significance will be performed, with those defined after the realization of the omics-bioinformatic approach (see Figure below). **Relevance:** Due to their peculiarities, antipsychotic drugs present several utilities other than psychotic symptoms management [2,5], forcing the person in care to face several other effects, undesired on multiple occasions [2]. Thus, a deeper understanding of molecule pathways modulated by those drugs may favor future development of strategies for less promiscuous treatment, enhancing patient care and quality of life, and advances in precision medicine in the mental health field.

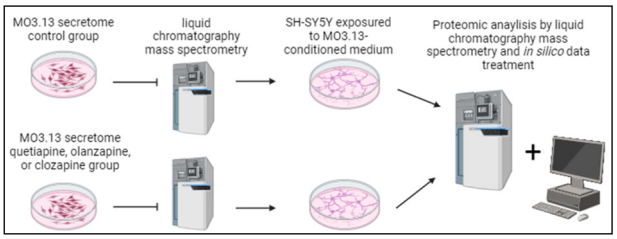

Figure 1. Representation of cell's treatment and data analysis workflow. Reference: Self-produced, utilizing biorender.

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PREVENTION OF THE CHRONICITY OF MUSCLE PAIN THROUGH PHYSICAL EXERCISE: INVOLVEMENT OF THE INFLAMMATORY CYTOKINE IL-1β

Oliveira, J. V. A,[1] Rodrigues, H. L,[1] Armelin, M. C. N, [1] Gomes, B. B, [1] Santos, T. S. [1] Dorta, E. O.[1] Oliveira, M. C. G[1]

[1]Laboratory of Pain and Inflammation Research - FCA/ UNICAMP, Limeira -SP

Introduction and Hypothesis: We recently demonstrated that, in the acute phase of muscle hyperalgesia, there is an increase in the IL-1β in muscle tissue, and regular physical exercise through swimming prevents the chronicity of muscle pain as well as the increase in IL-1β concentration [1]. Our hypothesis for the present study is that regular physical exercise prevents chronification of muscle pain through inhibition of IL-1β effects on muscle tissue, either by increasing the production of the endogenous IL-1β receptor antagonist (IL-1ra) and/or by decreasing the availability of IL1-R1, the receptors for IL-1β. **Objective:** We aimed to evaluate whether the prevention of chronic muscle pain by regular physical exercise involves the inflammatory cytokine IL-1β. We will analyze whether regular physical exercise through treadmill running modulates IL-1ra and/or the IL1-R1 receptor in the gastrocnemius muscle during the acute and chronic phases of muscle hyperalgesia. **Materials and Methods:** C57BL/6 mice, 6-7 weeks, from CEMIB-UNICAMP (6332-1/2023), will be used. Carrageenan (100μg) will be injected into the gastrocnemius muscle to induce inflammatory pain, and 10 days later, PGE_2 (1μg) will be injected at the same site to reveal the state of chronic hyperalgesia. Mechanical muscle hyperalgesia will be quantified by the Randall Selitto test at different time points (0-17 days). The treadmill running protocol consists of 50-minute sessions, a progressive increase in speed over the 3 weeks of exercise [2]. The gastrocnemius muscle will be collected for RTqPCR analysis to assess whether there was an increase in IL-1ra mRNA and/or a decrease in IL1-R1 receptor mRNA. Statistical analysis will be carried out using Two-Way ANOVA, with a significance level set at $p < 0.05$. **Relevance:** Our initial results demonstrated that the treadmill running protocol, similar to swimming in our previous study [3] prevented the acute muscle hyperalgesia and the development and maintenance of the chronic muscle hyperalgesia (Figure 1). Understanding the mechanisms involved in prevention of chronic muscle pain through exercise has social and economic impact. In addition, the findings of the present study may highlight physical exercise as an efficient strategy for preventing chronic muscle pain.

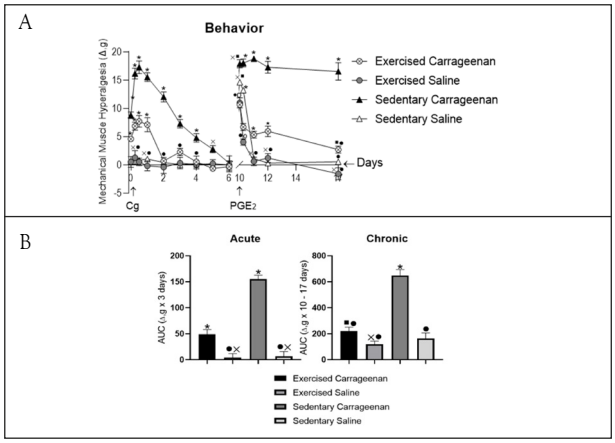

Figure 1. Treadmill running exercise prevented acute and chronic muscle hyperalgesia. (A) Timeline graph of behavioral nociceptive responses. (B) Area under the curve (AUC) data. The symbols "X" demonstrates difference to Exercise Cg groups, "▪" – difference to Exercise Sal groups, "●" - difference to Sedentary Cg group, "○" - difference to Sedentary Saline group, "*" – difference to other groups.

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ROLE OF IL-1β IN THE DORSAL HORN OF THE SPINAL CORD IN CHRONIC MUSCLE PAIN AND ITS PREVENTION BY PHYSICAL EXERCISE

Armelin, M.C.N,[1] Rodrigues, H. R,[1] Gomes, B. B[1], Oliveira, M.C.G[1]

[1]Laboratory of Pain and Inflammation Research - FCA/ UNICAMP, Limeira, SP.

Introduction and Hypothesis: Muscle pain affects a large proportion of the world's population. The negative impacts are not only limited to the patients but

also to socio-economic domains [1]. Recently, our research group demonstrated that acute and chronic muscle hyperalgesia is associated with an increase in pro-inflammatory macrophages in muscle tissue. An increase in interleukin-1 beta (IL-1β) release in muscle tissue was observed in the acute stages of muscle hyperalgesia, and the physical exercise prevented this increase by activating local PPARγ receptors [2]. The transmission and modulation of painful information from muscle tissue follows a path that passes through the dorsal root ganglion until it reaches the dorsal horn of the spinal cord, where synaptic communication occurs. In addition to sensory neurons, glial cells such as microglia and astrocytes play a crucial role in this process, especially in the dorsal horn of the spinal cord, contributing significantly to pain modulation. It is well known that glial cells may contribute to pain modulation through the release of cytokines. Therefore, we hypothesized that, similar to muscle tissue, IL-1β may be released in the dorsal horn of the spinal cord and contribute to development of chronic muscle pain. In addition, the exercise-induced hypoalgesia may be modulated by the inhibition of this process. **Objective:** To investigate whether IL-1β released in the dorsal horn of the spinal cord contributes to the chronicity of muscle pain and whether physical exercise can prevent this chronicity by modulating IL-1β. **Materials and Methods:** Male C57BL/6 mice, aged 6-7 weeks, will be used. The animals will be injected with carrageenan (100 μg) into the belly of the gastrocnemius muscle to induce acute muscle hyperalgesia and ten days later, in the same place, PGE_2 (1 μg) will be injected to show chronic muscle hyperalgesia. Mechanical muscle hyperalgesia will be quantified using the Randall Selito test at different time points (0-17 days).To intramuscular injections, the drugs or their vehicles will be injected directly into the belly of the gastrocnemius muscle using a 30-gauge needle, in a total volume of 20 μl. To intrathecal injection, the animals will be anesthetized with isoflurane (5% for induction and 3% for maintenance in O_2 flow) and then positioned in ventral decubitus for manual identification of the L5-L6 intervertebral space. The drug will be injected into the intradural space in a volume of 5 μL. The regular physical exercise will be performed by Treadmill Running, for 4 weeks. The collected tissues will be analyzed by immunofluorescence and *Western Blotting*. Data with homogeneity of variance will be analyzed using the One-Way ANOVA. Multiple comparisons will be made using the Tukey test. Where appropriate, Student's t-test will be applied. The significance level will be set at $p<0.05$ for all tests. **Relevance:** The findings of the present study will probably clarify another mechanism underlying chronic muscle pain and reinforce de relevance of both regular exercise and/or selective analgesics to control chronic muscle pain. These results may potentially improve patients' quality of life and reduce the costs associated with pain' treatments.

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STUDY AND APPLICATION OF TEXTURE ANALYSIS TO MAGNETIC RESONANCE IMAGES OF PATIENTS WITH SCHIZOPHRENIA

G. F. Ricardo[1], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, [2]BRAINN-FAPESP

Introduction and Hypothesis: In this project, we intend to study the texture analysis technique, and apply it to magnetic resonance images (MRI) of patients with schizophrenia who may or may not have auditory hallucinations, and to a control group of healthy individuals [1]. Schizophrenia is a psychiatric disorder that affects more than 20 million people worldwide, according to the World Health Organization, and generally appears between late adolescence and early adulthood [2]. Due to brain's heterogeneity and difficult differentiation of changes in brain structure resulting from mental disorders, determining a diagnosis or prognosis for schizophrenia from MRI analysis is very difficult, and it is one of the greatest challenges for individuals who are still healthy [3]. **Objective:** Our main objective in this project is to study and apply texture analysis techniques to brain MRI from a group of patients with schizophrenia with or without auditory hallucinations and a group of healthy patients. We also aim to learn more about physical methods applied to clinical data and contribute to a better understanding of schizophrenia. **Materials and Methods:** MR images of schizophrenia patients and healthy individuals obtained from the platform OpenNeuro, collected for the study "Brain correlates of speech perception in schizophrenia patients with and without auditory hallucinations" [4] will be used for this study. The Matlab programming platform and software programs MaZda [5], SPM12 [6] and AAL [7] will be used for MRI processing, texture analysis, image manipulation and segmentation, respectively. Texture analysis is a computing-mathematical method, which allows identification of subtle image alterations that cannot be perceived by visual inspection, and which may be possibly due to alterations of the underlying tissue. This, in turn, may help us to differentiate among schizophrenia patients with different types of symptoms (in this case, with or without auditory hallucinations), and discriminate those from healthy subjects. **Relevance:** As mentioned before, schizophrenia affects about 24 million people worldwide and the presence of auditory hallucinations affects 70% of the patients. The process of diagnosis follows the procedures mentioned in Diagnostic and Statistical Manual of Mental Disorder V (DSM - V) and, since schizophrenia is a multifactor disease, factors like genetics, phenotypes, psychological and social environment are relevant for an early diagnosis [8]. Our project intends to improve the understanding of schizophrenia, and the application of these results to improve the diagnosis, prevention and treatment of this disease.

Acknowledgement: FAPESP (2013/07559-3), CNPq (304008/2021-4)

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STUDY AND APPLICATION OF THE TEXTURE ANALYSIS TECHNIQUE TO MAGNETIC RESONANCE IMAGES FOR COMPARISON BETWEEN HEALTHY YOUNG AND ELDERLY PEOPLE

G. P. Lopes[1], G. Castellano[1,2]

[1]Neurophysics Group, IFGW, UNICAMP, [2]BRAINN

Introduction and Hypothesis: Magnetic resonance imaging (MRI) is a common and non-invasive technique for investigating the human body. Digital images produced by MRI can be analyzed using image processing techniques, such as texture analysis, which describes the image by a reduced set of specific parameters [1]. This project aims to apply texture analysis to MR images of healthy people, comparing young and elderly people to identify possible statistical differences. **Objective:** The main objective of this project is the study of the texture analysis technique, its application to MR images and the comparison of the results obtained between young and healthy elderly people. **Materials and Methods:** The data for this research will be obtained from the OpenNeuro database (https://openneuro.org/). This is an open database available online, which compiles neuroimage and clinical data obtained with several techniques in a variety of studies. In our project, data from healthy adults will be used, from the "Single Dose Intranasal Oxytocin Administration: Data from Healthy Younger and Older Adults" study [2], comprising two distinct groups: a younger group (44 individuals; age range 18-31 years; 48% female), and an older group (43 individuals; age range 63-81 years; 56% female). The software Mazda [3], SPM12 [4] and AAL [5] will be used to perform, respectively, texture analysis, image manipulation and segmentation. The Matlab platform will be used for the development and implementation of image processing and analysis algorithms. **Relevance:** The human brain intrinsically has asymmetries in its structures and functions and it is believed that they can change over the years and lead, in the future, to some type of pattern that may be linked to illnesses that appear with age. Thus, the relevance of this study lies in the possibility of understanding the changes that can occur over the years in brain tissue, so that we can have support to predict possible diseases.

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STUDY OF ANTIHYPERALGESIC AND ANTIDEPRESSANT EFFECTS OF TRANSCRANIAL PHOTOBIOMODULATION (830 NM) IN A MODEL OF SOCIAL DEFEAT STRESS IN MICE

A. van Leeuwen[1], W. F. Vieira[2], C. A. Parada[1], C. H. Tambeli[1]

[1]Centre for Pain Studies, IB, UNICAMP, [2]Department of Anatomy, ICB, USP

Introduction and Hypothesis: Although pain is not a symptom of depression, epidemiological studies have shown an association between these conditions, sharing several clinical and biological features and similar changes in neuroanatomical structures, neural circuits and neurotransmitter systems [1, 2]. The most

critical trigger of depressive disorders in humans is social stress, which is why an animal model of social defeat stress (SDS) – mice can become susceptible, exhibiting depression-like behaviour, or become resilient [3] – is appropriate for studying the association between social stress and chronic pain, since in humans only some individuals exposed to chronic stress develop psychopathology or chronic pain. Even though the neuronal mechanisms underlying chronic pain are not yet completely elucidated, it is plausible to raise the hypothesis that neuroplastic changes may be implicated, involving the mesolimbic dopaminergic system, a brain circuit particularly susceptible to neuroplastic changes induced by chronic stress, including mitochondrial metabolism dysfunctions that are involved in the development of psychopathologies [4]. It is well established that the biological effects of transcranial photobiomodulation (t-PBM) in brain disorders include neuroprotective responses such as increased mitochondrial metabolism and modulation of inflammation and oxidative stress. The use of photobiomodulation presents itself as an emerging therapeutic option for the treatment of depressive conditions, and its effectiveness in the treatment of pain of neuropathic origin has also been demonstrated [5, 6, 7, 8]. **Objective:** This project aims to advance the study of the interrelationship between social defeat stress (SDS), nociceptive sensitivity, depressive-like behaviour and mitochondrial dysfunction in mice. Furthermore, we intend to investigate the modulation exerted by t-PBM on these phenomena, targeting genes related to mitochondrial function in structures of the mesolimbic dopaminergic system, such as the ventral tegmental area (VTA) and the nucleus accumbens (NAc). **Materials and Methods:** Adult mice will initially undergo basal mechanical nociceptive threshold test (electronic von Frey) and, after 24 hours, they will (or will not) be subjected to SDS protocol daily for 10 days. Depressive-like social avoidance behaviours (social interaction test) and mechanical nociceptive threshold (von Frey test) will be assessed, then mice will be assigned into six experimental groups, once the presence of depressive-like behaviour is confirmed (or not): social stress (n=10); social stress + t-PBM (n=10); social stress + fluoxetine (n=10); not stressed (n=10); not stressed + t-PBM (n=10); non-stressed pre-SDS t-PBM (n=10). Mice will be subjected to t-PBM (830 nm, 100 mW, 1 point, 1x daily) for 10 consecutive days or similarly receive 10 mg/kg of fluoxetine diluted in water daily. Once the treatments (t-PBM or fluoxetine) have been completed, the mice will be subjected again to von Frey and social interaction tests. Additionally, in the two days following these tests, the mice will be subjected to the open field test (OF). Finally, the animals will be euthanized 24h after the last behavioural test and the brain tissues will be collected and sliced for microdissection to RNA extraction of the subfields (VTA and NAc) for RT-qPCR analysis. **Relevance:** This study may contribute to improving the effectiveness of clinical treatment of depression associated with chronic pain, also contributing to the production of basic scientific knowledge with the potential to support the future development of alternative clinical approaches to prevention and treatment of pain and its chronification.

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STUDY OF THE MODULATION OF PPARγ RECEPTORS THROUGH THE ALTERATION OF PGC-1α EXPRESSION IN MUSCLE CELL CULTURE

Almeida, M.F.,[1] Gomes, B.B.,[1] Simabuco, F.M.,[1] Oliveira, M.C.G[1]
[1]Laboratory of Pain and Inflammation Research - FCA/ UNICAMP

Introduction and Hypothesis: Chronic pain is a complex disease and has a great socioeconomic impact; it is generally not adequately treated, with success in only 30% of cases [1]. Recently, we showed that regular physical exercise prevents muscle pain from becoming chronic, by modulating the profile of macrophages and inflammatory cytokines via PPAR-γ receptors [2]. However, we showed that there is no expression of these receptors in macrophages, suggesting that there is a paracrine communication between PPARγ receptors expressed in muscle cells and macrophages. Therefore, knowing that physical exercise modulates PGC-1α, one of the coactivators of PPAR-γ receptors, in muscle cells, our hypothesis is that, with increased expression of PGC-1α via physical exercise there is communication between PGC-1α and PPAR-γ within the skeletal muscle cell that predisposes the release of cytokines capable of modulating the macrophage phenotype towards an anti-inflammatory profile. **Objective:** The aim is to evaluate whether changes in PGC-1α expression in cultured skeletal muscle cells modulate the expression of PPARγ receptors and whether only the alteration of PGC-1α expression in muscle cells is sufficient to induce modulations in the expression of the PPARγ receptor. **Materials and Methods:** The PGC-1α protein will be overexpressed in mammalian cells using the pcDNA3 plasmid. For the transfection of plasmids and other nucleic acids, such as RNAi, the reagents lipofectamine and polyethylenamine (PEI) will be used. The C2C12 strain, cells derived from mouse skeletal muscle, will be cultured in DMEM medium containing 10% SFB at 37ºC, under an atmosphere of 5% CO_2. Proteins will be extracted from the cells using a *Western Blotting* lysis buffer (Cell Signaling, USA). Protein concentration will be determined using the bicinchoninic acid (BCA) protein assay (Cell Signaling, USA). Band intensities will be quantified using the following program: Quantity One software (Bio-Rad, Hercules, CA, USA). The expression of β-tubulin will be used as a positive control. Data with homogeneity of variance will be analyzed using the One-Way analysis of variance (ANOVA) statistical test. **Relevance:** Chronic muscle pain is a very difficult challenge for society, specifically for individuals who suffer from this condition. Therefore, it is necessary to explore new strategies to complement the classic treatment with drugs, so that the pain can be relieved as quickly and forcefully as possible. Therefore, this study seeks to understand how physical exercise, considered a complementary treatment for chronic muscle pain, acts in an anti-inflammatory way, benefiting the therapeutic approach for individuals with this condition.

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TRUSTWORTHY MACHINE LEARNING FOR ALZHEIMER'S DISEASE AND HEALTHY AGING

Farzaneh Dehghani[1], Sayeh Bayat[1, 2], Mariana Bento[1,3]
[1]Biomedical Engineering Dept., University of Calgary, [2]Geomatics Engineering Dept., University of Calgary, [3]Electrical and Software Engineering Dept., University of Calgary

Introduction and Hypothesis: Alzheimer's Disease (AD) is an irreversible and progressive brain disorder that causes brain cells degeneration, cognitive abilities deterioration, and memory loss [1]. Two main biomarkers for AD detection are brain amyloid biomarkers, such as positron emission tomography (PET), and neuronal injury biomarkers, such as magnetic resonance imaging (MRI) [2]. Accurate and timely diagnosis of AD can promote the best prognosis and impede its progression [3]. Due to the recent development and deployment of AI-empowered systems in clinical settings, patients and medical professionals have benefited from early and accurate diagnosis and superior decision-making [4]. However, ethical challenges due to the black box nature of these systems hinder their advanced development for clinical practice. When deploying human data, ethical issues such as bias, fairness, privacy, and safety, present challenges. This necessitates the development of AI systems that are Trustworthy. Trustworthy AI refer to compliance with laws and adhering ethical guidelines when developing AI-driven systems, promoting trust among its end users and affected communities [5]. Machine/Deep learning (ML/DL) models are data-intensive in nature, requiring large-scale training data with a wide range of input variations. However, having access to large-labeled datasets in medical imaging is restricted due to patient privacy and lack of manually annotated images by experts. While building a large dataset by combining data from various acquisition/research sites can increase the amount of annotated data, this approach can increase heterogeneity due to varying hospital procedures (scanners or scanning protocols) and various subject populations (ethnicity, gender, and age) [6]. Models can be trained on datasets containing all of these instances without any modification. However, domain shift can impact model generalization. Domain Shift is indicated as differences in the probability distribution of datasets across sites (source domain and target domain). Domain Adaptation (DA) has been developed in medical image analyses to improve model generalizability and secure consistent accuracy in different distributions. In DA, knowledge is transferred across domains to adapt a model trained in one or more source domains to different target domains [7]. **Objective:** The proposed research aims develop a Trustworthy decision-making system to detect brain abnormalities and distinguish brain imaging data diagnosed with AD from healthy controls. By developing DA algorithms, we intend to improve the generalizability of

ML/DL-based algorithms for AD identification. Domain adaptation techniques would allow our model to be more robust as it is unable to distinguish acrross different domains, thus, improving its generalizability. **Materials and Methods:** Here, we will consider large heterogeneous brain imaging datasets acquired from multiple sites, such as "Alzheimer's Disease Neuroimaging Initiative" and "Australian Imaging, Biomarkers and Lifestyle", to develop multi-modal (using different modalities such as PET and MRI) and multi-domain (multi-source/multi-target DA) models. We will propose techniques to identify and mitigate data bias by considering the aggregation of different datasets to an appropriate representative and large dataset, and evaluating models to ensure that results do not reflect bias in different populations. We will thoroughly scrutinize various shallow and deep learning DA methods to develop a baseline model. We intend to use DA strategies in a federated learning (FL) setting to analyze heterogeneous data. FL is a paradigm to tackle data governance, making it possible to develop algorithms collaboratively from different research institutes without exchanging the data itself [8]. We will also use data augmentation strategies to include more diversity in our datasets. **Relevance:** We expect to develop a Trustworthy, robust, and generalizable model to refine the existing ML/DL methods for brain aging and AD diagnosis, which will provide trustworthy results and facilitate translation to clinical practice.

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USE OF EEG IN THE INVESTIGATION OF CEREBRAL CONNECTIVITY IN MEDITATION PRACTITIONERS

Amanda R. V. Nunes[1], Gabriela Castellano[1,2]
[1]Neurophysics Group, IFGW, UNICAMP, [2]BRAINN-FAPESP

Introduction and Hypothesis: Electroencephalography (EEG) is one of the most important techniques to study the brain nowadays. The EEG consists in the use of electrodes to gain information on the brain's electrical activity. One of the ways to interpret the data obtained is through methods that analyze the cerebral functional connectivity (FC), which means that instead of simply interpreting the data from a specific electrode individually, the idea is to look at the similarity between electrodes' signals over time [1]. Given its characteristics (such as being silent and portable), EEG has been applied to study the brain of meditation practitioners [2]. Indeed, there has been a growing interest in these practices given the incorporation of mindfulness, which is one of the main psychological components of meditation, into psychotherapeutic and clinical interventions [3]. Therefore, the present study aims to use measures based on FC, obtained from EEG data, to try to evaluate possible differences between the brain activity of meditation practitioners and participants who do not perform meditation, and also investigate whether different types of meditation practices can be distinguished from EEG-FC. **Objective:** The main objective of this project is to verify whether it is possible to distinguish individuals who practice meditation from those who do not, based on EEG-FC, using the motif synchronization (MS) method [1] to compute FC. We also intend to verify the feasibility of using these measures to distinguish between groups that practice different types of meditation. **Materials and Methods:** We will use the dataset "Meditation vs thinking task" [4], from the OpenNeuro platform (https://openneuro.org/). This consists of EEG data from 98 individuals, 31 from a control group (without meditation practice), 19 participants from the Vipassana tradition, 24 participants from the Himalayan Yoga tradition and 20 participants of the Isha Shoonya Yoga tradition. In this experiment the subjects performed two mind-wandering and two meditation tasks (the controls only did the mind-wandering task). For this study we are going to use data from only 10 subjects from each group. The data will be processed using the software HAPPE (https://github.com/PINE-Lab/HAPPE). EEGLab (https://sccn.ucsd.edu/eeglab/index.php) will be also used to visualize the EEG signals. Then the necessary codes (MS method) will be written in Matlab. **Relevance:** In the present days there is a great interest in meditation practices from a clinical and psychotherapeutic stand point. Recent evidence has shown that, when practiced regularly, meditation might lead to a decrease in levels of perceived anxiety [5]. In a context where, in Brazil alone, 18,2 million people have an anxiety diagnosis [6], having a better understanding of the biological mechanisms of a practice that was found to be useful as a therapeutic tool is extremely important. Also, the study of forms of automatizing the analysis of EEG signals is also relevant.

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USE OF TEXTURE ANALYSIS FOR STRUCTURAL BRAIN ASSESSMENT IN YOUNG ADULTS UNDERGOING A MODERATE-INTENSITY RUNNING TRAINING PROGRAM

Mateus Santos Bonadia[1], Gabriela Castellano[1,2]
[1]Neurophysics Group, IFGW, UNICAMP; [2]BRAINN-FAPESP

Introduction and Hypothesis: Magnetic Resonance Imaging (MRI) is widely used due to the large amount of information those images can provide. Posterior processing of MRI data can provide even more information. In particular, methods jointly known as "texture analysis" are able to distinguish subtle alterations in the images, possibly due to underlying tissue changes, not perceptible through a simple visual inspection [1]. On the other hand, several studies have shown structural brain changes resulting from physical exercise, using methods such as volumetry [2,3] and voxel-based morphometry [4,5]. This project aims to analyze possible changes in structural brain data (using texture analysis) of young male adults resulting from a moderate intensity running program. **Objective:** The main purpose of this project is to use and test different image processing methods to extract texture data from structural MRI images of the brain of young adults before and after they undergo a moderate intensity running program, as well as compare these results to verify possible textural changes due to the program. **Materials and Methods:** All the data that will be used is available on OpenNeuro (https://openneuro.org), a data hosting website. The data was obtained for the study "Effects of a seven-week running intervention with moderate intensity on the volume of the hippocampus and depressive symptoms in young men from the general population" [6]. The dataset comprises T1 weighted MRI and demographic data (among others), of 22 young male participants. The images will be processed using the following software programs/platforms: MatLab for image processing algorithms implementation; MaZda [7] for texture and statistical analysis; SPM12 [8] and AAL plugin [9] for image manipulation and segmentation. **Relevance:** This project can help the comprehension of possible origins of the effects observed in physically active people, as well as further explore image processing methods to extract brain structural data.

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