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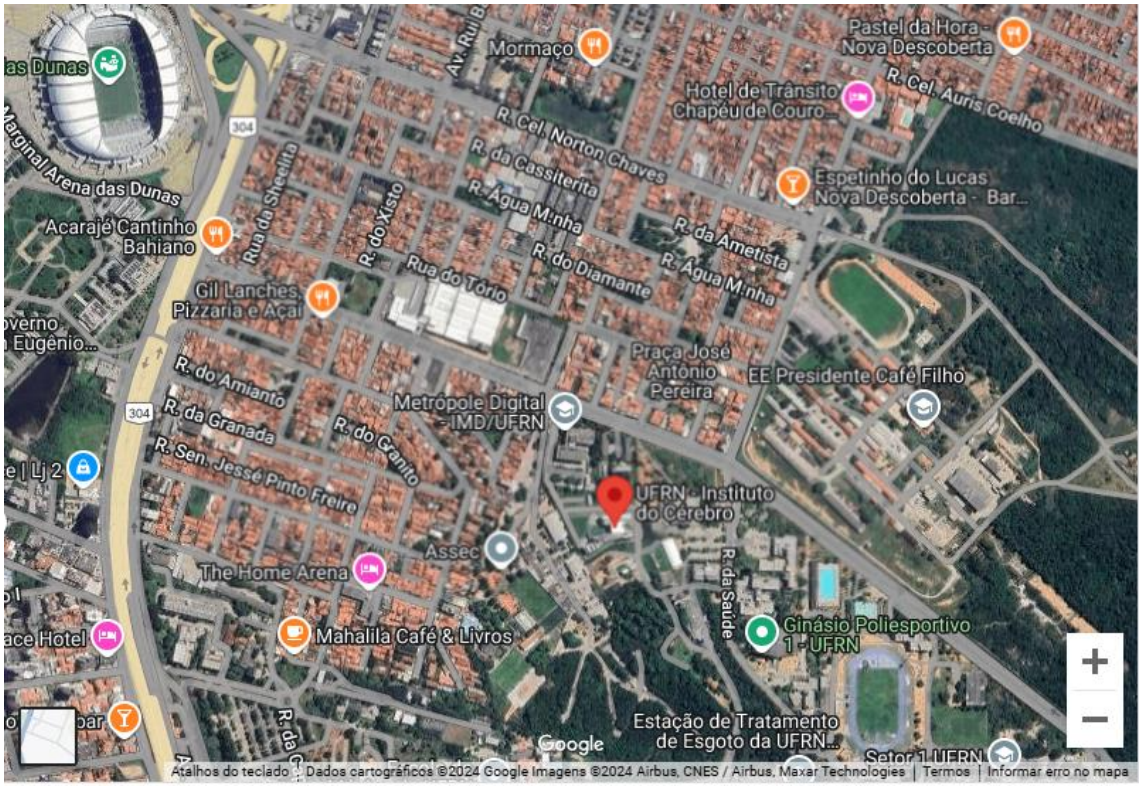
INSTITUTO DO CÉREBRO



UFRN CAMPUS

NATAL
December 07-08, 2023

Venue: Brain Institute/UFRN, Auditorium, Natal – RN
https://neuro.ufrn.br/



Program at a glance*

DECEMBER 7nd

08:00	Registration
09:00	Opening words **Organizing Committee**
09:15	Greetings **Kerstin Schmidt/Maria Bernardete** (Directors of the Brain Institute)

Lectures and Micro-courses

09:30	Vision and Illusion at the crossroads- perceptual grouping mediated by callosal connections **Kerstin Schmidt**
10:00	Don't panic, just breathe: exploring respirationcoupled brain oscillations during anxiety **Ana Luiza Alves Dias** (Tort Lab)
10:30 – 11:00	**Coffee Break & Poster Session**
11:00	**Students flash talks 1**
11:30	Auditory event-related potentials in tinnitus and models of psychosis **Katarina Leão**
12:00 – 14:00	***Lunch break***
14:00	Micro-courses 1 **Dráulio Araújo** (Professsor, Brain Institute) and **Daniel Brandão** (Bioinformatician and IT Analyst, Brain Institute)
14:00	Micro-courses 2 **Rodrigo Santiago** (Ph.D., Computational Neurophysiology of Brain Institute) and **Lucas Caiã** (Ph.D. Student, Computational Neurophysiology of Brain Institute)
15:30 – 16:00	**Coffee Break & Poster Session**
16:00	Postnatal mice zika virus infection as a model for the infection during the human third trimester **Jhulimar Doerl** (Sequerra Lab)
16:30	Skin conductance changes after participation in a Capoeira initiation program based on a global approach to teach motor skills **Patrick Coquerel** (Ribeiro Lab)

17:00	***Cultural activity***

DECEMBER 8rd

Lectures

09:00	On the network responsible for paradoxical (REM) sleep generation **Pierre-Hervé Luppi, PhD**
10:00	**Students flash talks 2**
10:30–11:00	**Coffee Break & Poster Session**
11:00	Visual entrainment in the LGN reveals perceptual binding **Lucas Lira** (Neuenschwander Lab)
11:30	Emotional contagion in an animal model of autism **Debora Hashiguchi** (Pereira Lab)
12:00 – 14:00	***Lunch break***

Panel Discussion and Lecture

14:00	Depression: what it is and current psychiatric treatments **Professor Emerson Arcoverde**
14:00	Caveats of modeling depression in animals **Rafael Lima, PhD**
14:00	Depression biomarkers and their modulation by ayahuasca **Professor Nicole Galvão-Coelho**
15:30 – 16:00	**Coffee Break & Prize Draw**
16:00	Evolution and physiology of the supramammilarydentate gyrus projection” **Monique Esclapez, PhD**
16:30	**Closing**

POSTER SESSION

P01 - INFLUENCE OF ZIKA VIRUS INFECTION ON THE MATURATION OF THE GABAERGIC SYSTEM

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In rodents, the birth period triggers the inversion of intracellular Cl- concentration in cortical and hippocampal neurons. Developmental high chloride concentrations cause an excitatory effect of GABA signaling, mainly due to the exit of this ion upon GABAA receptor activation. However, this inversion in chloride potential is inhibited by the activation of the immune system during pregnancy. Since the congenital infection by Zika virus (ZIKV) causes epilepsy, not controllable with anticonvulsants, in a large number of patients we decided to test if this infection disturbs the development of the GABAergic system. This research aims to establish whether postnatal motor reflexes development and death caused by ZIKV brain infection can be reversed by the inhibition of the Cl- importer, NKCC1, with its antagonist, bumetanide. For this, we injected 1µl of 0.9% sodium chloride (Mock) or 1µl of ZIKV solution containing 10EXP3 PFUs of ZIKV into the lateral ventricle of postnatal day 1 (P1) mice. Our data show that animals in the ZIKV group begin to experience a behavioral decline starting on P11. Based on this information, we started daily treatment with bumetanide (2 mg/kg) in half of the animals infected with ZIKV or Mock on P10. This treatment occurs until P15. Our results indicate that P11 ZIKV animals decreased their behavioral response and their symptoms intensified as the days progressed. On the other hand, the proportion of ZIKV+bumetanide-treated animals that show a decline is smaller than in the ZIKV group. The survival of animals in the ZIKV group is 50% and in that ZIKV+bumetanide treated is 75%. Both groups with control animals had 100% survival. In conclusion, our data points to a positive response to bumetanide for the survival and motor behavior reflexes of animals infected with ZIKV.

Funding: CAPES; International Center for Genetic Engineering and Biotechnology

P02 - ACTIVATION OF THE BASAL GANGLIA DURING VOCAL COMMUNICATION IN A NON-HUMAN PRIMATE

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Flexible speech is one of the core aspects of human communication. Despite being considered uniquely human among primates, recent evidence shows that some non-human primates also have vocal plasticity. Marmosets (Callithrix jacchus), a New World monkey, exhibit exceptionally flexible vocalizations. Given the homologies between human and marmoset brains, investigating the neural correlates of vocal flexibility in marmosets leads to a deeper understanding of the origin of vocal flexibility in humans. Much of the literature on the neural basis of primate vocalization focuses on cortical areas, leaving fundamental gaps in our knowledge about the role of subcortical regions. Basal ganglia are related to the choice/initiation of actions, fine motor control, and learning of motor sequences; hence, it is likely to be relevant for vocal flexibility. Here, using histological data previously collected, we test the hypothesis that basal ganglia in marmosets activate during vocal communication. We use the expression of immediate-early gene egr-1 to map neural activation in basal ganglia in three marmoset groups (n = 2 per group). The first group did not vocalize during testing (C), the second group heard playback vocalizations but did not vocalize (H/O), and the third group

heard playback calls and vocalized (H/V). Using stereological methods, we quantified the number of cells expressing erg-1 in the caudate nucleus (Cd) and putamen (Pu). Our results show an increase in egr-1 expression in both areas in the H/O condition (Cd: μ±ep, 193.33±13.87cells/mm2; Pu: 167.5±14.67cells/mm2) compared to the C condition (Cd: 110.52±11.33cells/mm2; Pu: 77.5±9.35cells/mm2; $p<0.001$, t-test). We observed a further significant increase in egr-1 expression in the same areas in the H/V condition (Cd: 502.10±24.55cells/mm2; Pu: 715.55±34.85cells/mm2) compared to the H/O condition ($p<0.001$, t-test). These results indicate that basal ganglia activate during listening and vocal production, supporting our hypothesis.

P03 - ANALYSIS OF FETAL AND MATERNAL MICROCHIMERISM IN A MOUSE MODEL OF CONGENITAL ZIKA VIRUS SYNDROME

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During pregnancy, the maternal immune system adjusts to tolerate the cells from the embryo, carrying half of the paternal genetic material, while maternal antibodies provide passive immunity. However, congenital infections can disrupt the immune balance, potentially leading to or contributing to brain malformations. Here, our purpose is to develop a method for testing the hypothesis that zika virus (ZIKV) congenital infection increases the exchange of cells enabling the presentation of embryonic antigens to maternal immune cells and maternal immune responses against the embryonic CNS. We use in utero ZIKV injections and different combinations of transgenic mice to track the cells of one individual in the other one's body. There is an increase in the exchange of embryonic cells to the maternal blood 24h after the surgery, observed both in saline-injected (N=3, mean= 0,35, SD= ± 0,21) and animals injected with inactivated ZIKV (inZIKV; N=4, mean=0,245, SD=± 0,34). This increase ends at 48h (saline mean= 0,0066, ±0,008; inZIKV=0,0175, SD= ±0,01). Our preliminary data shows that the female immune cells reach the embryonic brain and liver in control and in ZIKV injected animals. We also detect an increase exchange of cells in the siblings reaching the embryonic brain between ZIKV injected embryos (ZIKV; N=4; Kruskal-Wallis test p=0,0041, Dunn's multiple comparison p=0,0121) compared to the saline control (N=8; Kruskal-Wallis test p=0,0041, Dunn's multiple comparison p=0,0121) and the embryonic liver between the Inactivated ZIKV (inZIKV; N=3; Kruskal-Wallis test p=0,0018, Dunn's multiple comparison p=0,0368) and saline control group (N=8; Kruskal-Wallis test p=0,0018, Dunn's multiple comparison p=0,0368). Our study establishes a method for studying microchimerism between the mother and the fetuses in mice. We show that the surgery for in utero injections produces a bridge in the placental barrier that lasts at least 24 and less than 48h. We were able to identify both female and sibling cells in the embryonic CNS and liver. Further experiments will be necessary to determine if the active ZIKV changes the microchimerism between the maternal blood and the embryonic brain and if this phenomenon possibly contributes to the phenotypes found in the congenital zika virus syndrome.

Funding: International Centre for Genetic Engineering and Biotechnology

P04 - ANALYSIS OF THE EFFECT OF POSTNATAL ZIKA VIRUS INFECTION ON THE DEVELOPMENT OF THE GLYMPHATIC SYSTEM

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Introduction. In 2015, Brazil experienced an outbreak of microcephaly. Soon after this outbreak, cases of the malformation were associated with the congenital infection by

zika virus. Some children in the syndrome display a continuous inflammation of the CNS, revealed by the continuous production of cytokines in the liquor, the development of postnatal microcephaly in normocephalic-born children and a progressive malformation of the brain in microcephalic patients. Here, we test the hypothesis that the development of the glymphatic system, which is essential for the proper dynamics of fluids and elimination of remnants of metabolism, is impaired by ZIKV. Aims. Mice are born during the end of corticogenesis and beginning of gliogenesis. Astrocytes are essential players in the regulation of the glymphatic system. Therefore, we aimed to test the effect of postnatal ZIKV brain infection on the development of functioning of the glymphatic system and its morphometric characteristics. Methods. Wild-type C57/Bl6 mice with one day of birth (P1) were separated into two groups: ZIKV (1µl of virus containing 103 PFUs) or Saline (1µl per animal) injected into the right lateral ventricle. In order to follow the progress of the disease, sensorimotor development was assessed from P1 to P14 through the analysis of the palmar grip, lying recovery, vibrissa placement, bar holding and negative geotaxis tests. The body weight and morphometric measurements of each pup were also recorded. To analyze the drainage of fluorescent tracers between the CSF and the brain parenchyma, 10 KDaltons Dextran conjugated to FITC was injected at a concentration of 2% into the cisterna magna. After 30 minutes of dye circulation, the animal was euthanized. Results. ZIKV infection acts on the CNS causing impairment in sensorimotor development, as well as a reduction in body weight from P9 onwards. Regarding morphometric measurements, there was no significant difference in the body proportions, but ZIKV-infected animals were smaller. Alizarine staining reveals the accumulation of calcium in the brains parenchyma, with no clear association to blood vessels. The detection of fluorescent tracers in different regions of the brain reveals that ZIKV impairs the drainage of the fluid in the meninges to the parenchyma. Conclusion. Our preliminary data suggests that ZIKV infection impairs the development of the glymphatic system in postnatal mice.

P05 - ARTIFICIAL NEURAL NETWORK FOR MARMOSET CALL CLASSIFICATION

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Marmosets (Callithrix jacchus) are, together with humans, one of the few primates known to exhibit vocal plasticity. Since most other primates do not have vocal plasticity, marmosets and human vocalization are examples of convergent evolution. We can infer evolutionary robust connections by studying marmoset vocal communication and its commonality to human speech. However, current studies require manual call classification, expertise, and significant in-person time investment. One of the main difficulties lies in the relatively large number (~13) of different call types that marmosets have, sometimes differing by subtle details in the acoustics. In this work, we train an automated computation pipeline for marmoset call detection and classification. We used a hybrid convolutional-recurrent neural network for segmentation first developed for birdsong classification (Cohen et al., 2022, eLife). The model trained in a controlled environment achieved an accuracy of 95.84% in a controlled environment and 86.21% when applied to field data, demonstrating its robustness across adverse conditions. Furthermore, the accuracy of the models trained in one marmoset's call and tested in other marmoset vocalization was never below 90%, demonstrating that variations in vocalizations among individuals do not significantly affect accuracy. Finally, the model achieved peak performance with minimal training data, requiring approximately 35 minutes of training audio. Our result shows that the obtained model is accurate and can generalize the classification across individuals, social contexts, and environments, allowing for use in large-scale experimental data.

Funding: CNPq

P06 - CHANGES IN CORTICAL ACTIVITY INDUCED BY INTRACRANIAL DIRECT CURRENT STIMULATION IN NON-HUMAN PRIMATES

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In the past years, the use of electric currents has been widely studied in humans as a non-invasive brain stimulation. As an example, the transcranial direct current stimulation (tDCS) technique has been used to treat psychiatric and cognitive disorders with electrodes placed on the scalp, modulating brain activity. In animal studies, however, there is the possibility of applying direct currents (DCs) directly on the cortical surface and recording activity for a better understanding of changes in neurons' membrane resting potential. With that, it has been shown that a surface anode elicits neuronal excitation and enhances neuronal firing rate, while cathodal stimulation causes inhibition, leading to a reduction in their firing rates. Our study aims to investigate the relationship between the strength of the electrical current and neuronal activity in the auditory cortex while applying DC, as well as to characterize the time course of this activity. Two cynomolgus monkeys (macaca fascicularis) were used for chamber implantation and electrophysiological recordings. Recordings were performed with a multitrode containing 8 contacts placed in the region of the auditory cortex (20 mm recording chamber) where multi-unit activity (MUA) and local field potentials (LFP) were recorded simultaneously. We performed a passive DC-stimulation paradigm, where an epidural macrode made of platinum, with dimensions of 7x8 mm2, was centered above the auditory cortex. Cathodal and anodal stimulation with intensities of -1mA, -0.5mA, +0.5mA, and +1mA were delivered in a randomized order divided into blocks, totaling six blocks per current. Each block had a duration of 15 seconds, and blocks were separated by another 15 seconds of no stimulation. For MUA analyses, we computed the firing rates during peri and post-stimulation. For LFP recordings, Delta (1-3Hz), Theta (4-7Hz), Alpha (8-12Hz), Beta (13-30Hz), Gamma (31-90Hz), and high-frequency Gamma (91-200Hz) band power were computed in the peri stimulation interval. Here we demonstrate the feasibility of the iDCS applied on the auditory cortex surface as well as changes in brain activity. In general, MUA activity was dependent on current polarity, with cathodal stimulation causing significant inhibition while anodal, excitation. Also, the highest current of both polarities (-1mA and +1mA) caused higher inhibition/excitation when compared to the weaker current (-0.5mA and +0.5mA). On low-frequency bands of LFP recordings were increased for all currents, while high-frequency Gamma activity was increased only for anodal stimulation.

Funding: Deutsche Forschungsgemeinschaft; Leibniz Institute for Neurobiology

P07 - COVID-19 PANDEMIC INCREASED LUCID DREAMING RECALL FREQUENCY

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Introduction: Anxiety and stress induced by the pandemic negatively affected sleep quality, but an increase in total sleep time was also observed. Dream recall frequency also increased, especially for nightmares. However, to date, there are no consistent

reports focusing on pandemic-related changes in lucid dreaming (LD), a physiological state of consciousness during which dreamers know they are in a dream. Materials and Methods: We used the International COVID Sleep Study Questionnaire (ICOSS), an online questionnaire that aimed to understand possible effects of COVID-19 on sleep and wakefulness parameters in 1,857 subjects. For the analysis of other factors influencing our results, we fitted a logistic regression model to predict LD frequency enhancement. Results: Firstly, we found that most participants (64.78%) maintained their LD recall frequency during the pandemic, but a considerable fraction (22.62%) informed that LD became more frequent, whereas a smaller subset (12.60%) reported a decrease in LD during the pandemic. Secondly, we observed that the number of participants reporting LD at least once per week increased during the pandemic. Using the mixed logistic regression model, we confirmed a significant increase in the recall frequency of LD during the pandemic ($p = 0.002$). This LD increase was associated with an enhancement in both dream and nightmare recall frequencies, as well as with sleep quality and symptoms of REM sleep behavior disorder. Conclusion: LD recall frequency significantly enhanced during the pandemic, probably due to anxiety, sleep fragmentation and extended duration, which enhance REM sleep awakening.

Funding: CAPES

P08 - DASEIN-AUTISTIC: THE PHILOSOPHY AS A NEW PERSPECTIVE FOR UNDERSTANDING THE AUTISTIC EXPERIENCE

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The term autism was introduced by Eugen Bleuler (1857-1939) in 1911, a Swiss psychiatrist who used the name to describe schizophrenic patients who seemed disconnected from the outside world. Since then, the term has been given new meanings and among them, the autistic psychopathy, described in 1944 by the Austrian physician Hans Asperger (1906-1980), having its name linked to the denomination of the mildest level of autism until 2015 with the publication of the Diagnostic and Statistical Manual of Mental Disorders – 5 (DSM-5). According to the medical literature, the DSM-5 considers the main criteria for designating the term autism, constant deficits in communication and social interaction. Therefore, the present work seeks to elucidate the autistic person beyond terms, prejudices, historical context and medical designations. Based on the study, through the exegetical method, the philosophy expressed in the book Philosophical Investigations (2014) by the Austrian Ludwig Wittgenstein (1889-1951) and the work Being and Time (1927) by the German philosopher Martin Heidegger (1889-1976), with their respective concepts of Rules, Following Rules, Lebensformen, Sprachspiel, Dasein, Historicity, Temporality, Being-in-the-World. It sought to demonstrate through language and hermeneutic phenomenology, the existing problem in the practice of reducing the human to terms and diagnoses, announcing, consequently, the urgency of breaking with capacitism and the search for validation of a human ideal or a human utility.

P09 - DEVELOPMENT OF A SYSTEM FOR ESTIMATION OF THE SKULL CURVATURE IN NON-HUMAN PRIMATES

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Behavioral studies of the visual system in non-human primates (NHP) require surgical implants to stabilize the head and open access to the cortex. Typically, these implants are made of titanium (GR5), aiming for osseointegration over extended periods (of several years). A precise fitting to the cranial vault is a prerequisite for the success of

these techniques. Generally, fitting is done through individual skull reconstructions from CT or MRI images. However, obtaining imaging for experimental purposes can pose challenges, both financially and logistically. Here, we propose a new, minimally invasive method to obtain accurate estimates of the skull curvature. Our approach is based on systematically placing a transcutaneous needle (0.6 mm in diameter) over the skull, covering a systematic grid of points (11 X 9 points). We developed a semi-elliptical arch in Blender (open-source 3D graphics software) that attaches to a stereotaxic apparatus's ear bars. This arch has 11 centrifugal holes distributed laterally at every 12° for insertion of the needle, and it can be rotated in the sagittal plane every 10º. Each hole and sagittal inclination combination enables us to define a straight line in three-dimensional space, thereby precisely estimating the needle's travel distance until it reaches the cranial surface. To validate our method, we will obtain cranial surface estimates using 3D-printed models of capuchin skulls generously provided by the American Museum of Natural History. We are confident that our approach provides a viable alternative to established methods in developing cranial prostheses—an essential step for accessing the brain in long-term behavioral studies in NHP.

P10 - DEVELOPMENT OF SOCIAL BEHAVIORS IN MARMOSET MONKEYS

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Only Callitrichidae and humans exhibit cooperative reproduction behavior and vocal turn-taking over long periods among the known primates. Both species are prosocial, in which social behaviors and bonds are key factors that modulate their behavioral development. Nevertheless, different from the comprehensive developmental studies of human social behaviors, there is a scarcity of studies on social and vocal development from infancy to adulthood in marmosets (Callithrix jacchus). In this work, we sought to answer three main questions by observing marmoset infants' development: Do social behaviors develop? Is the development of different behaviors co-modulated? Is there a relationship between development and the social hierarchy of the animals? We collected data from four marmoset infants (two families) during the second to fifth month of postnatal days. We used the focal method to collect the data. We longitudinally analyzed the presence of foraging, play, nursing, vocalizations, and piggy-back behaviors. We observed a significant increase in play behavior ($r = 0.52$, $p = 0.004$) and a decrease in breastfeeding ($r = -0.45$, $p = 0.013$) during development. We also observed a significant correlation between the number of piggy-back behavior and infant crying vocalizations ($r = 0.37$, $p = 0.038$), and between the duration of grooming and play behavior ($r = 0.39$, $p = 0.03$). We did not find a significant difference in the duration spent being groomed ($p > 0.05$) by breeders and non-breeders. Our results suggest that some marmoset social behaviors change during development and can be co-modulated. We did not observe a robust role of hierarchy during social development.

P11 - ECOLOGICAL IMPLICATIONS IN CYCLICAL ROCK-PAPER-SCISSORS MODELS WITH MULTIPLE WEAK SPECIES

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Understanding the dynamics of weak species in ecological systems is crucial for comprehending ecosystems' overall stability and biodiversity. This study focuses on the impact of multiple weak species within cyclic rock-paper-scissors models. We aim to describe how their reduced competitive abilities shape population dynamics in spatial environments. Our investigation focuses on systems with an odd number of species,

providing diverse ecological interactions. Specifically, we explore scenarios involving five, seven, and nine species, capturing different complexities inherent in these models. By incorporating vulnerable species into these systems, we gain insights into the mechanisms driving population dynamics and the resulting ecological outcomes. Through our analyses, intriguing patterns emerge regarding the behaviour of weak species and their interactions within the cyclic order. We observe that weak species, with their limited capacity to win in resource competition, significantly influence the overall balance of the spatial game. These interactions can lead to an imbalanced distribution of resources and territories among the species. Furthermore, our findings shed light on how the presence of weak species affects the competitive advantage of the more dominant species. We reveal that in the unbalanced game, certain species exploit the weaknesses of their counterparts, further enhancing their own population growth and survival. The disproportionate distribution of resources resulting from the limitations of weak species can disrupt the system's equilibrium, potentially causing species extinction over time. Considering competitive exclusion and spatial heterogeneity, we explore the underlying mechanisms driving this biodiversity loss. These insights can inform conservation strategies and aid in ecosystem management, particularly when addressing the challenges of vulnerable species and their effects on biodiversity.

P12 - EFFECTS OF CANNABINOL (CBN) AND CANNABIGEROL (CBG) ON PTZ-INDUCED BEHAVIORAL SEIZURES IN THE MICE

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Phytocannabinoids, such as cannabidiol (CBD), have been explored for treating numerous neurological disorders, including epilepsy. Our study examined the antiseizure effects of two other phytocannabinoids, cannabinol (CBN) and cannabigerol (CBG). CBN results from CBD degradation, while CBG is the precursor for CBD biosynthesis. Using pentylenetetrazol (PTZ)-induced seizures, we evaluated whether prior CBN and CBG administration (with doses of 3, 30, and 300 mg/kg, i.p., and administered 60 min before PTZ) modify the expression of ictal behaviors. Our preliminary results showed no differences between treatments. The high variability among animals in the same group may explain this lack of significant differences in statistical comparisons (N=1 - 7 / group). However, our experiments suggest that lower doses of CBN and CBG favor seizure expression (animals with seizure/total number of animals; Vehicle: 0/5, CBN 3 mg/kg: 2/4, CBN 30 mg/kg: 1/3, CBN 300 mg/kg: 1/6, CBG 3 mg/kg: 2/3, CBG 30 mg/kg: 2/4, and CBG 300 mg/kg: 3/7). Since a high CBN dose (300 mg/kg) strongly reduced locomotor activity, we confirmed that this phytocannabinoid does have (some) psychotropic effects. Notably, mice treated with diazepam (5 mg/kg, i.p.) showed reduced spasms and myoclonia. This study enhances our understanding of phytocannabinoid behavioral effects, emphasizing the need for further research into their applications in seizure management.

Funding: CNPq; CAPES; FAPERN; UFRN

P13 - ELECTROPHYSIOLOGICAL SIGNATURES OF APPARENT MOTION ASSOCIATED WITH ORIENTED CONTOURS IN V1

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Throughout the recent years, evidence of fundamental abnormalities that cerebral connectivity exhibits in neuropsychiatric conditions has been accumulating. The corpus

callosum is an important connective pathway of the brain, which presents possibilities for studies by means of psychophysical tasks of relatively simple execution, with reproducibility and objectivity. In the present study, we modified a classical visual stimulus challenging the visual callosal connection, the Motion Quartet (MQT), by replacing its elements with either Gabor gratings (contours) or isoluminant circles, and also presenting it in different visual field positions. The MQT consists of two visual stimuli alternating in sequence, which induce an illusory motion perception in either vertical or horizontal direction. The present study aimed to analyze the visually evoked potentials (VEP) of healthy individuals subjected to visualization of that stimulus during different subjective percepts of apparent motion. To this end, we compared the potentials evoked by the alternating stimulus, to those evoked by a control condition (Flicker) that utilizes identical stimuli, which, however, does not generate apparent motion due to the irregular sequence of stimulus presentation. Upon analysis of electrodes topographically associated with the V1 area, we found that the VEP p100 amplitude was suppressed in the MQT condition as compared to the control condition (N Flicker = 594 versus N MQT = 1170, Median Flicker = 0.069, Median MQT = -0.175, U = 280748.000, $p < 0.0001$), and that on a closer look this difference was restricted to when the stimuli were Gabor gratings (for the isoluminant control: N Flicker = 198 versus N MQT = 381, Median Flicker = -0.074, Median MQT = -0.108, U = 33996.000, $p = 0.0512$; for the horizontal Gabors: N Flicker = 198 versus N MQT = 393, Median Flicker = 0.081, Median MQT = -0.307, U = 28015.000, $p < 0.0001$; for the vertical Gabors: N Flicker = 198 versus N MQT = 396, Median Flicker = 0.237, Median MQT = -0.108 U = 30856,500, $p < 0.0001$). In addition, there was an increased p100 amplitude with apparent motion when Gabor gratings were vertical (N vertical Gabor = 594 versus N horizontal Gabor = 591, Median vertical Gabor = -0.023, Median horizontal Gabor = -0.173, U = 160311.000, $p = 0.0098$), which upon closer inspection was restricted to when the MQT stimulus was also being perceived as moving vertically (N horizontal Gabor = 195 versus N vertical Gabor = 198, Median horizontal Gabor = -0.382, Median vertical Gabor = -0.045, U = 16096.000, $p = 0,0044$) ($p > 0.05$ in both the horizontally-perceived MQT periods and the Flicker condition). On the other hand, the n75 amplitude was increased during MQT as compared to the Flicker condition (N Flicker = 594 versus N MQT = 1170, Median Flicker = 0.348, Median MQT = 0.446, U = 320607.500, $p = 0.0078$), especially with isoluminant stimuli (N Flicker = 198 versus N MQT = 381, Median Flicker = 0.142, Median MQT = 0.354, U = 30999.000, $p = 0.0004$) ($p > 0.05$ in both Gabor conditions). These results indicate a complex pattern of excitation and suppression in V1 in response to apparent motion of shapes, which could be associated with both horizontal computations and suppressive feedback input from higher areas belonging to both the contour processing ventral (V4) and the motion processing dorsal pathway (V5).

Funding: CNPq; UFRN

P14 - EXPLORING THE GENETICS OF DEPRESSION: REPRIORIZATION OF GENES USING MULTI-TRAIT ANALYSIS OF PSYCHIATRIC MANIFESTATIONS

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Single-trait genome-wide association studies (GWAS) have previously reported several overlapping genetic loci of depression (DEP) and other psychiatric manifestations. Leveraging this genetic correlation we conducted a multi-trait analysis, providing greater power compared to univariate GWAS. We aimed to uncover novel genetic variants associated with DEP. We used the multi-trait analysis of GWAS (MTAG), which improves effect estimates for a given trait using information from other highly correlated traits. The MTAG method was applied to GWAS summary statistics for broad depression (DEP) (N=322,580), neuroticism (N=170,911), bipolar disorder (41,917 cases and 371,549 controls), attention deficit hyperactivity disorder (38,691 cases and

186,843 controls), and subjective wellbeing (N=298,420). With the results for broad DEP, we carried out Functional Mapping and Annotation (FUMA) to identify genome-wide significant (P≤5x10-8) single nucleotide polymorphisms (SNPs) for this disease and lead variants within each region along with their corresponding genes. Additionally, we conducted an enrichment analysis to elucidate the biological processes associated with these genetic signatures. Our multi-trait analysis unveiled 143 independent genome-wide significant variants across 53 distinct loci. Among these variants, 61 were designated by FUMA as lead SNPs, with a majority residing in intronic or intergenic regions, and all of them showing stronger associations in MTAG compared to single-trait GWAS for broad DEP. The variants were looked up for associations with depression on GWAS Catalog database and six of them were not previously associated. Then, we assigned to the unreported variants the nearest gene and identified nine potentially novel genes for broad DEP: PTPRD-AS2, TYRP1, RERE, LINC01929, TCF4, HS6ST3, RPL10L, MDGA2, UBE4A. Seven of these genes have been previously associated with other psychiatric traits. Of particular interest is the role of MDGA2 in several nervous system functions; furthermore, the protective allele of the MDGA2 variant for depression was associated with decreased expression of the gene in brain, which suggests that molecules that inhibit MDGA2 could serve as therapeutics for depression.
In summary, our findings reinforce the use of genetic correlation between psychiatric diseases in MTAG to discover new predisposing loci for broad DEP and gain a deeper understanding of the biological mechanisms underpinning the disease offering promising avenues for future research and therapeutic development.

P15 - INHALED DMT INCREASED LUCID DREAMS AND NIGHTMARES: A PRELIMINARY REPORT

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Introduction: Studies indicate that there are several similarities between dreams and psychedelic states, such as mental imagery, emotion activation, fear memory extinction and sense of self and body. Psychedelic states are closer to lucid dreams, which are characterized by being a mixed state of dreaming and waking consciousness. Objective: Here, we aim to analyze how the use of inhaled DMT relates quantitatively to the dream recall frequency in healthy subjects. Methods: This is an open-label, single-ascending, fixed order, dose-response study to assess the feasibility of inhaled DMT in healthy volunteers in preparation for a phase II clinical trial with treatment-resistant depression patients. On D0, a smaller first dose was applied, followed by a second larger dose 2 hours later. From the day of the dosages to 28 days after dosing (D28), we applied different questionnaires (including about sleep and dreams), and provided psychological integration and medical follow-up. Preliminary results: Our sample comprised 25 volunteers, including 13 men and 12 women, being mainly young, white, single adults, with completed higher education, employed, without a defined religion, but with spirituality. We observed a decrease in the total number of dreams reported in the two weeks before the dosing day (173 dreams) compared to the two weeks after (162 dreams) and also in relation to the period between 15 and 28 days after dosing (165 dreams). On the other hand, comparing the two weeks before dosing and the period from 15 to 28 days later, we found an increase in both nightmares (29%) and lucid dreams (23%), comparing to the total number of dreams reported by participants within each time interval.

P16 - LABORATÓRIO ABERTO: TRAINING AND DISSEMINATION OF NEUROSCIENCE IN PUBLIC SCHOOLS OF RIO GRANDE DO NORTE STATE

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Neuroscience and scientific experimentation is still an area of knowledge very restricted to the university walls. Moreover, neuroscience centers are usually located in central cities and state capitals, leaving the access of those students who are in smaller cities and wish to follow a career in neurosciences very difficult. With the idea of taking neuroscience experimentation to underprivileged schools of Rio Grande do Norte, we created the Laboratório Aberto project. In this project, we propose to take neuroscience-related issues closer to the school community by improving the scientific literacy of public high school educators and coordinators. We aim to train state high school education professionals to replicate practical activities in neurophysiology and psychophysics in the classroom. Our interventions are organized in one school in each city visited, and teachers from multiple schools can participate. It usually includes a presentation lecture, two workshops where practices occur, and a closing moment where we exchange experiences and receive criticisms and requests from schools, totaling three days. At the same time, we also carry out activities with students with information about life at the university and what grants they can apply for. We have visited eight cities, including Petrolina (PE), Jardim do Seridó, Parelhas, Santa Cruz, Parnamirim, Caicó, Currais Novos, and Natal. During the three editions held, the Laboratório Aberto developed experiments on artificial intelligence, visual perception, smell and taste, memory, biological recordings with electroencephalogram, electrocardiogram, and action potentials in insects' legs. Along with the experiments that address psychophysical or physiological content presented to teachers, we show them how to analyze the data obtained. More than 600 people participated over the years, and we consolidated the extension project and created links with several schools. We hope to follow up with the groups that participated in providing tools for establishing neuroscientific practices in their schools. Moreover, we want to expand the cities in which the Laboratório Aberto operates.

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P17 - MARMOSET MONKEY'S ACOUSTIC NICHE

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Different species within an ecosystem occupy different niches that are adapted to their life. Acoustic niches allow animals to optimize communication in noisy environments. Several constraints shape the acoustic niche. For example, animals must maximize the chance to communicate with their group, especially when group coordination is relevant (e.g., foraging, playing), while avoiding sounds from other animals to increase communicative efficiency. Moreover, the production of the sound should avoid detection by predators. Since several animals share the same constraints and occupy the same ecosystem, each species must establish a flexible strategy to navigate the complex acoustic landscape. In this study, we ask what are the characteristics of the acoustic niche marmoset monkeys (Callithrix jacchus) occupy in the field. Marmosets have been increasingly relevant in the study of vocal communication, and characterizing their acoustic niche is a crucial step to better understanding their communicative capacity. We recorded two marmoset groups in their natural habitat for three months, employing five recorders strategically positioned at each group's sleeping tree and resting site. In our recordings, we found marmoset, birds, and insect sounds. We identified three avian species in our recordings: Abre-fecha (Coryphospingus pileatus), bico-chato-amarelo (Tolmomyias flaviventris), and Sabía-laranjeira (Turdus rufiventris). We observed two different patterns in the acoustic niche that were dependent on the temporal scale we were looking. At the scale of each call production (short temporal scale), we noticed that bird and insect vocalization never overlapped with marmoset vocalization in our data. This shows that marmosets avoid overlapping

sounds with other animals, optimizing the effectiveness of acoustic transmission. Nevertheless, at a scale of one-minute time intervals (long temporal scale), marmoset vocalization co-occurred with bird and insect sounds (Spearman correlation = 0.46, $p < 0.001$). This is consistent with the idea that environmental constraints, like the time of the day, might substantially affect the acoustic behavior of several animals. Our result shows that marmosets, birds, and insects compete for acoustic niches at short temporal scales while sharing the niches at larger temporal scales.

Funding: CAPES

P18 - MENTAL HEALTH, SLEEP AND PSYCHOSOCIAL SAFETY CLIMATE IN HIGHER EDUCATION

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Mental health issues among graduate students have sparked debate within the academic community. Previous studies identified anxiety and depression levels up to 6 times higher than the general population. Sleep disorders and substance abuse are also commonly reported. The phenomenon of academic suffering requires further research to identify etiological factors – whether they are intrinsic or extrinsic to the individual – for preventive actions and support. The present study aimed to investigate risk and protective factors for mental illness among a Brazilian sample. 476 graduate students (mean age 33.9, SD=8.62) from all Brazilian regions completed an online questionnaire, as approved by the local ethics committee (CAAE: 54127221.0.0000.5537). Questions covered sociodemographics aspects, lifestyle and health, COVID-19 impact, academic experiences, social context, and dream reports. Psychometric screening instruments for depression (PHQ-9: mean=13.8, SD=7.21), anxiety (GAD-7: mean=11.9, SD=6.23), sleep disorders (PSQI: mean=8.41, SD=3.85), and psychosocial safety climate (PSC-12: mean=35, SD=18) were also applied. Results were tested for assumptions of normality and homogeneity of variance, statistical analyses were adjusted accordingly. Non-parametric t-test was performed with the PSC-12 classification for mental illness risk as a grouping variable (risk X safety). Participants in the risk group had significantly higher scores than those in the safety group, indicating a higher presence of symptoms for depression (PHQ-9: risk group mean=14.4, SD=6.89; safety group mean=11, SD=7.92; $U=12337$, $p<.001$, $r=0.271$), anxiety (GAD-7: risk group mean=12.4, SD=6.13; safety group mean=9.62, SD=6.18; $U=12661$, $p<.001$, $r=0.252$), and sleep disorders (PSQI: risk group mean=8.68, SD=3.81; safety group mean=7.18, SD=3.85; $U=13197$, $p=.001$, $r=0.220$). Scores from different instruments were normalized with square root transformation for simple linear regression with the general PSC-12 score as a predictor variable. The overall regressions were statistically significant for depression (PSC-12xPHQ-9: $R^2=0.0570$, $F(1,474)=28.7$, $p<.001$), anxiety (PSC-12xGAD-7: $R^2=0.0443$, $F(1;474)=22$, $p<.001$), and sleep disorders (PSC-12xPSQI: $R^2=0.0389$, $F(1;465)=18.8$, $p<.001$) symptoms. Global mental health challenges have reached new proportions after the COVID-19 pandemic. Predictions about future pandemics and global warming-related crises are not optimistic, and the main hope for dealing with these issues should come from future scientific and technological advances. Taking into account that increasing diversity in science is a direct way to enhance the diversity of approaches and creativity in problem-solving, there's a responsibility to protect scientists in their formative years in order to minimize mental health issues, career abandonment and suicide rates.

Funding: CAPES

P19 - OBTAINING HIGH-PURITY N,N-DMT AND OPTIMIZATION OF EXTRACTION PARAMETERS, CHARACTERIZATION, AND ITS PURIFICATION FROM MIMOSA TENUIFLORA

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The use of alkaloids produced from natural sources has seen increased demand in recent years due to promising results in safety and therapeutic response in the treatment of mental disorders, such as N-N-dimethyl-tryptamine (DMT), the active ingredient in Ayahuasca, from which rapid and significant antidepressant effects are suggested in patients with treatment-resistant depression. Its production can occur through synthesis routes with reagents that are not readily available and are not environmentally friendly with subsequent purification or by extraction from plants that have it as a constituent. The extraction methods of DMT are not consolidated and time-consuming. In this context, the objective of this study is to optimize the extraction procedure for N,N-DMT obtained from Jurema-preta (Mimosa tenuiflora). The roots, stems and leaves of M. tenuiflora were collected in Quixadá-CE, Brazil. A few grams of the roots were subjected to factorial experiments with variations in parameters such as particle size (75 and 250 micrometers), mixing time with the raw material (1 and 8 hours), NaOH concentration (0.1 and 2.0 M), mixing methods (ultrasonic bath and orbital mixer), temperature (25 and 75 ºC) and eluent volume (1 and 5 mL). The results indicated that all the factors within the conditions studied were significant for the final yield, with the exception of the mixing methods. The best condition obtained (particle size 75 micrometers, NaOH 2.0 M, ultrasonic mixing at 55 ºC for 8 hours and 5 mL of eluent) gave a yield 3.82 times higher than that obtained by the non-optimized method. Previous extractions with the non-optimized protocol allowed for chemical characterization through FTIR and chromatographic analysis by GC-MS, LC-DAD and LC-MS. A purity of 99.0±0.4% (range: 98.4-99.5) was found for DMT obtained from Mimosa tenuiflora. The resulting data will be useful for a more efficient process of obtaining DMT, with subsequent use in in vitro and in vivo assays, mainly because its access and purchase are restricted in the vast majority of countries.

P20 - PARENTAL FEEDBACK SHAPES VOCAL DEVELOPMENT IN MARMOSET MONKEYS

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In contrast to human speech development, primate vocalizations are believed to undergo minimal developmental changes, with almost no role of parents in their vocal development. This apparent evolutionary discontinuity generated several theories on the origin of human communicative capacity. We recently revised this widely held assumption by showing that marmoset monkeys, a cooperative breeding New World primate, have vocal development guided by parental feedback, similar to what we observe in humans. However, the evidence of vocal plasticity was limited to a single behavioral context. Therefore, the extent to which the vocal development in marmosets is similar to that of humans is still unknown. Here, we tested whether marmosets learn to produce different vocalizations in different contexts through social interactions. We focused on two very distinct vocalizations that marmosets produce in distinct contexts: long-distance contact calls, produced when the animals are out-of-sight from each other, and short-distance contact calls, produced when the animals are in visible distance. We recorded the vocalizations of nine infant marmosets from postnatal day seven to postnatal day eighty. Each marmoset infant was exposed to playback of long-distance/short-distance contact calls for five/five minutes daily,

contingent on infant vocalization. When the marmoset infants were not receiving playbacks, they were with their families. Simulating the expected association between social context and vocal type, four marmosets received contingent short-distance contact call playback in the presence of a doll, mimicking an adult marmoset, and long-distance call playback in the absence of the doll (control group). Five other marmoset infants received contingent playback in switched social contexts (switched group). We hypothesize that the infants that received playback in switched social contexts would learn to produce shorter contact calls without a visible marmoset/doll. We observed that the proportion of short-distance contact calls in the absence of visual stimuli in the switched group (proportion ± standard error, 0.57 ± 0.02) was significantly larger than in control (0.24 ± 0.03, chi-squared test, $p < 0.001$). We also observed that the duration of short-distance calls produced by infants was shorter in the switched group (mean ± standard error, 363.4 ± 18.1ms) compared to the control (494.6 ± 46.4ms, rank-sum test, $p < 0.001$). Our results show that context-dependent contingent vocal feedback modulates infant marmoset vocalization, indicating that marmoset monkey vocalization exhibits larger flexibility than previously thought. Furthermore, our results support the hypothesis that marmosets and humans' vocal communications are examples of evolutionary convergent behaviors, possibly due to their unique cooperative breeding systems.

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P21 - RESPIRATION-COUPLED OSCILLATIONS AS MODULATORS OF FREEZING BEHAVIOR IN RATS

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We know that breathing is fundamental to life. However, breathing is responsible for much more than gas exchange, including being able to modulate our emotions. In 1942, Lord Adrian discovered an oscillatory rhythm that synchronizes with nasal respiration, in what nowadays became known as respiration-coupled oscillations (RCOs). Several lines of evidence suggest that these oscillations are initiated by the activation of neurons in the nasal epithelium. After reaching the olfactory bulb, RCOs are transmitted throughout the brain, in regions such as the amygdala, hippocampus, and prefrontal cortex, among others. Recent studies show that a strong 4-Hz oscillation appears during freezing, an expression of fear behavior in rodents. During freezing, rodents can emit ultrasonic vocalizations (USVs), which are coupled to the exhalation phase of the respiratory cycle. Here we propose to simultaneously record freezing behavior, USVs and electrophysiological signals from the medial prefrontal cortex and hippocampus in a cue-driven fear conditioning paradigm. Our main hypothesis is that RCOs occur during freezing and moreover are differentially expressed during the emission of USVs. Furthermore, we hypothesize that USV activity produces a natural disturbance in the sniffing cycle that is also observed in RCOs. Our experimental setup will include the synchronization of electrophysiology, sound, and video acquisition systems. To this end, a master clock will be programmed to emit binary pulses to the analog inputs of each component. Also, we will use the Kinect camera during the recording sessions as we plan to create an algorithm to extract freezing behavior through the depth data.

P22 - SPIKING ACTIVITY IN PRIMARY VISUAL CORTEX AFTER INTRACORTICAL INJECTION OF BETA-AMYLOID

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Alzheimer's disease (AD) is the most common cause of dementia, with more than half of those affected living in developing countries. Brain imaging studies have revealed gradual atrophy, and neuronal loss in the hippocampus and a majority of neocortical areas as the main correlates of AD being responsible for the mnemonic and cognitive deficits. According to the amyloid hypothesis, the low molecular weight oligomer of amyloid beta-peptide, particularly the toxic 42-residue (Ab1-42), accumulates and aggregates in the brain, forming senile plaques. Tau accumulation (tauopathy) and alterations in non-neuronal cell types like astrocytes are also linked to AD. Supposedly, Amyloid beta 1-42 initially also alters the balance of excitation/inhibition (E/I), resulting in both neuronal silencing and hyperactivity. Transgenic models commonly used to study AD, such as APP23 x PS45 mice, suggest that hyperactivity is responsible for altered sensory integration and the corresponding behavioral defects. Yet, response properties emerge from the intricate connectivity of neurons underscoring the importance of understanding how intracortical circuits get affected and disrupted. Questions remain about how Ab1-42 affects the electrical activity within cortical circuits in vivo, and rodent models suffer the disadvantage of exhibiting less topographic cortical circuits than primates and also not developing AD spontaneously. Domestic cats (Felis catus) offer a potent translational model for AD for possessing well-investigated selective circuits and columnar cortical maps homologous to primates. Moreover, akin to humans, they exhibit cognitive decline in their elderly years, the Feline Cognitive Dysfunction Syndrome, senile plaques, neurofibrillary tangles, and ensuing neurodegeneration, also in the visual cortex. Ongoing and sensory-evoked activity of the primary visual cortex can be examined by extracellular recordings in anesthesia using basic stimuli such as moving bars, and powerful tools for comparing cortical neuron and circuit functionality in healthy and diseased brains. In this pilot study, we aimed to explore the acute impact of Ab1-42 oligomers on neuronal activity and intracortical functional connectivity within the feline visual system. Using two microelectrode arrays (4x4, spacing 250 µm) implanted bilaterally in the primary visual cortex (Brodmann areas 17 and 18) of anesthetized cats (n=2), we assessed the spiking activity and classic receptive field characteristics. Each array, positioned in one hemisphere, allowed us to investigate the effects following an acute local intracortical injection of the Amyloid beta 1-42 oligomer via a glass micropipette. Preliminary results indicate an initial decline in both spontaneous and evoked spike rates as well as orientation selectivity close to the injection site (up to about 3 hours post-injection), followed by compared-to-baseline increased ongoing and evoked spike rates for (up to 13 hours), and only a partial recovery afterward (> 13 hours). Future analyses should aim to unveil the short- and long-term effects on intracortical dynamics.

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P23 - THETA-GAMMA HIPPOCAMPAL PHASE AMPLITUDE COUPLING AS A MARKER OF HIPPOCAMPUS-DEPENDENT OF AVERSIVE INSTRUMENTAL MEMORY EXTINCTION

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Fear is one of the most important survival responses for living beings. Therefore, forms of learning based on fear have been widely investigated in recent decades, enabling advances in the neurobiology of learning and memory. Extinction of a fear response involves exposing the individual to the same environmental conditions, without the aversive stimulus. The extinction process is important because it allows a learned behavioral response to change and adjust according to different environmental cues. Although extinction may seem to erase previous memories, it is, in fact, a form of new learning that overlaps and inhibits the previous response. The literature on extinction points out that the activity of the amygdala, the prefrontal cortex and hippocampus are

directly involved in extinction learning processing. However, it is not known whether there is an electrophysiological signature that characterizes aversive instrumental extinction learning. Recent studies have demonstrated that theta-gamma hippocampal phase amplitude coupling can be an important marker for decision-making and learning processes. Therefore, this work aims to identify electrophysiological marks for an inhibitory avoidance extinction memory. To do that we used adult male Wistar rats (n = 4) with arrays of 16 microelectrodes bilaterally implanted in the CA1 region of the dorsal hippocampus. After surgery, we submitted the animals to the behavioral apparatus. Training consisted of placing the animals above a platform (rear corner of the apparatus), and, when they stepped down and placed their four paws on the grid, received a 2-s-long 0.4 mA scrambled footshock. A day later animals were placed again on the training box platform and, latency to step-down to the grid was used to measure learning. Once animals come down to the grid, a 5-minute extinction session begins, in which animals freely explore the environment. The following day animals were placed again on the training box platform and, latency to step-down to the grid was used to measure extinction memory. Our results show an increase in theta-gamma hippocampal phase amplitude coupling during the first test session, just before animal's step-down the platform and, during the first 60 seconds of exploration after stepping-down to the grid. These results suggest that phase-amplitude coupling may serve as both a marker for decision-making and a signal indicating that the environment is no longer aversive. Future investigations will explore whether disruptions in theta-gamma coupling affect the acquisition and retrieval of extinction memory.

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P24 - VISUAL ENTRAINMENT IN THE LGN REVEALS PERCEPTUAL BINDING

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Gamma rhythms have long been linked to key processes in visual perceptual binding and attention. In the retina, this link has been made by numerous studies showing that gamma activity changes in response to stimulus size and continuity. However, recent investigations in our laboratory have uncovered a more complex relationship. We found that the levels of halothane concentration significantly influence retinal gamma responses, and notably, these responses are absent in awake cats (Neuenschwander et al., J Neurosci., 2023). Intriguingly, our findings also indicate that robust response entrainment to the monitor refresh was observed during awake states and under the influence of ketamine. This entrainment of the responses is similar to intrinsic gamma oscillations as it depends on the size and contrast of the stimulus. The observed peak frequencies for intrinsic rhythms (mean, 80 Hz; maximum, 118 Hz) and entrained rhythms (tested up to 120 Hz) can reach high values, well above the temporal resolution of both the X- and Y-cells in the cat LGN (12 and 20 cycles/s, respectively; Lehmkuhle et al., J. Neurophysiol.,1980). These results suggest that the entrainment of the retinal ganglion cell responses relies on an active synchronization mechanism in the retina. In the present study, we used tripartite, spatially-specific, flickering stimuli to test this hypothesis. Preliminary results show that, when activated in isolation, small, local neuronal populations in the retina (or the LGN) cannot follow fast-flickering stimuli (60 Hz), just as small spots do not trigger synchronous oscillatory responses under halothane. Importantly, flickering, discontinuously concentric stimuli around the receptive fields do not exhibit response entrainment. These findings indicate that the synchronization of responses to flickering stimuli may abide by the same principles as visual binding, highlighting that, at the retina level, it is not the oscillations per se but rather the synchronization that holds significance.

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P25 - WHAT IS COGNITION? EXPLORING ITS BIOLOGICAL ROOTS

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Cognition is among those concepts that are hard to define. Many different definitions exist, and there is an intense debate surrounding the most appropriate one. Its etymological roots trace back to the 15th century, and it means the ability to know or act of knowing. Although knowledge is fundamental to the word cognition, its usage in the cognitive sciences (which involves disciplines like neuroscience, psychology, computer science, anthropology, and linguistics) goes further than just saying cognition is knowledge. Among the traditional approaches, those that are based on the traditional cognitive sciences paradigm, the most prominent and widespread view takes cognition to be information processing (IP). (there are other views within the traditional approaches, but this is the most used). More precisely, it is viewed as a collection of informational processes like perception, memory, learning, attention, decision-making, communication, sociality, behavior, and more, that interact with each other, and together they form this bigger process called cognition. Shettleworth, in her 1998 book Cognition, Evolution, and Behavior, defines cognition as the mechanisms by which animals acquire, process, store, and act on information from the environment. These include perception, learning, memory, and decision-making. This is the most common definition. Most of the other ones that exist are related to it. Within this approach, cognition is the result of nervous systems that are able to implement and orchestrate these single processes. In this traditional view, cognition is a matter of information processing in neural systems, therefore it includes only animals (with nervous systems) inside the club of cognitive beings. Organisms like plants, fungi, protozoans, and bacteria are excluded from this list. The argument goes that they don't need these processes, nor do they have ways of implementing them, as they don't have a nervous system to do that. Perception, memory, learning, decision-making, problem-solving, attention, and action are something only animals need and do, more specifically, they are the only ones that have the mechanisms necessary to make these processes possible and therefore are the only cognitive beings that exist. But is it so? When we consider this definition more deeply, we find that this neural constraint on cognition is arbitrary. The idea behind this traditional definition is that these IP processes are made possible by the brain, this great information processor. But there is a problem: every living system is capable of processing information! If we take Shettleworth's definition and change animals for living beings, we get the mechanisms by which living organisms acquire, process, store, and act on information from the environment. The question is, does it make sense? Information processing is an essential component for the existence of every living being. One just needs to look if they perform the right set of information processing to implement the single cognitive processes (perception, memory, decision-making, and so on). When this search is done, we find ourselves drowned in evidence that this is indeed the case, that aneural organisms are cognitive, possessing the processes needed to perform these cognitive operations. Let's take the example of bacteria, and see if we can find hints of cognitive processes in their working. Escherichia coli (E. coli) has a set of flagella that allows it to swim around its world (behavior). However, this behavior is not random, it can be biased by the sensory inputs it gets from the world (perception). How does this happen? The name of the process is chemotaxis, which means movement directed by chemical stimuli. There is a set of receptors in its membrane that collectively are able to sense the surrounding concentrations of amino acids, peptides, carbohydrates, fatty acids, and toxic stimuli (e.g., alcohol, nickel), among others (and even temperature). These stimuli are not neutral, they mean something to the bacterium. More specifically, there are positive and negative stimuli that, respectively, attract or repel the organism. This is a case

where we see a valence process, where stimuli or states are judged and given a meaning for the living system, based on whether it affects it in a positive or negative way. The activity of these receptors will direct how the flagella are beating, and therefore the way the cell goes into the world. There are two ways the flagella can beat. First, in the run mode, all flagella are beating together, making the organism move forward. In the second mode, called a tumble, the flagella beat dispersedly, making the bacterium change its direction. This ensures the organism can guide itself in the world based on the relevance of its environmental state. Although bacteria are often considered 'simple' life forms, the processing of information that they use to bring forth this behavior is amazingly complex. The number of stimuli the bacteria can sense is immense, and at any one time, it will be receiving a combination of them. There are basically five different types of receptors that collectively are able to sense all of these varied stimuli. These receptors are not evenly distributed on the bacterium's membrane, but they form a cluster on the anterior pole of the cell. There, these receptors have the job of acquiring the information of the varied stimuli the organism is exposed to, processing it based on the relative concentration of every one of them, as well as their relevance to itself, and ultimately, they reach a conclusion of how to its flagella should beat. These receptors are performing an amazing feat of integration and effectively reaching a decision on the appropriate behavior for the bacterium (decision-making). For all of this to happen, to capture information from the environment and let it affect the organism's behavior, there must be a trace inside of the organism that represents the outside (representation). This trace, which in this case is a molecular one, is given by the proteins that can store in their structure the relevant information (memory). The concentration of every chemical the bacteria are exposed to varies a lot, spanning many orders of magnitudes. There are mechanisms that allow the receptor to adapt to the current concentration and keep track of what was the previous concentration of chemicals, giving the organism the capacity to retain, however brief, information from its past, and use it to influence its behavior (learning). Beyond this elegant behavior, E. coli is able to communicate with other bacteria, through a specialized system of communication where it both produces a signal and is able to receive signals from others, which allows them to coordinate their collective behavior (sociality). Indeed E. coli, and this is true for bacteria generally, is able, very cleverly, through some specialized cellular mechanism, to cognize in its world. What this example shows us is that even a simple organism like a bacterium, which is a prokaryote, is able to have cognitive processes. They are endowed with mechanisms that allow them to acquire, store, manipulate, deal and use information from the world, allowing them to guide their interactions with the world, fulfilling the core of Shettleworth's definition, and showing that its biological version is indeed valid. This is not the case only for bacteria, but for every living system there is. Similar processes are found in single-celled eukaryotes, fungi, plants, single-cells within multicellular organisms, and non-neural multicellular systems, like the immune system. Living systems need cognitive processes to guide themselves in the world. It is by perceiving their environment and changing its relation to it through action that they are able to maintain their living processes going on. This gives us a more expanded definition of cognition, one that includes all living beings, as well as its biological function. Cognition can be defined now as "the set of informational processes that allows an organism to know itself and its world, and to use this knowledge to achieve its biological goals of maintenance and replication". This definition is able not only to encompass the core of the traditional definitions while recognizing its biological roots but to include the etymological meaning of the word, which has to do with knowing, as well as the function cognition has to an organism. One common response to this conceptualization is that although the aneural organisms have these processes, as was shown in E. coli's example, they are not sufficient to be considered cognitive. Cognition, they would say, needs more complexity than that, and it is a mistake to say all of them are the same thing when clearly there are many differences among them. It is true that they vary a lot in their level of complexity, and as you go up in this scale you get much more complicated and nuanced processes. But when one takes the definitions of cognition

that exist and are used, it is clear that these processes are not exclusively of nervous systems. It is arbitrary to restrict them only to the neural level because the complexity of the process here is irrelevant to the concept. Indeed, the aneural processes are simpler but nonetheless, they still are something. Just because they are simple doesn't mean that they aren't. It just is a simpler version of cognition than that of animals, but all of them share the same core cognitive processes. It isn't a matter of not having (aneural) and having (neural) but of a gradation between these organisms in the level of their processes. Now, the goal should be to be able to make sense of these differences that exist between the many cognitive beings. Although this approach expands cognition based on the similarities they have, this may come at the price of specificity, where one is unable to spot the differences among them. In order to avoid losing this capacity for differentiation, a simple way to solve this problem is to use the labeling approach. The labeling approach consists of using a label to restrict the concept when needed to a particular instance of the phenomenon. If one wants to talk about cognition in neural systems, use neural cognition. As cognition is here understood as a living process present in all living organisms, it makes sense that it will differ based on the type of organization of the living system it is in. Living systems vary a lot in their organization, often with a variation in the level of their complexity. Single-cell eukaryotes are more complex than prokaryotes, and of course, a multicellular eukaryote is more complex than a single-celled one. Among the multicellular ones, some developed a truly amazing system with tremendous complexity. These are animals with nervous systems, and they represent a more complex level of biological organization than aneural multicellular organisms. This analysis could go further still within different types of nervous systems, going through neural nets, centralization in the form of brains, conscious animals, till we reach the arguably most complex level of cognition we know of, that of symbolic metacognitive species, us humans. The labeling approach allows the concept of cognition to remain broad, including all the instances of the phenomenon however simple, and at the same time to be able to differentiate and select a particular level of cognition one wants. There's no need to keep the concept constrained by some particular thing as a nervous system, brain, or symbolic use. But when needed, one can restrict the concept by applying one of these words as a label to select a particular instance of the phenomenon. In this way, the concept can be kept broad and specific at the same time, resolving both the problem of exclusion as well as differentiation. Now, what does this talk about bacteria cognition have to do with neuroscience? Although this discussion may seem dissociated from what neuroscientists do every day, it is in fact relevant. First, all these cognitive processes are in a way what neuroscientists are hoping to understand, they are trying to pin down how the brain makes all these processes possible. Now that it is recognized that these processes are not restricted to brains, one can take a more multidisciplinary approach in order to get at the core of every one of these phenomena. By considering how every organism can have these, one can reach a more fundamental conceptual understanding of these processes, their function, and goals for the living system, as well as draw parallels about the mechanisms that are involved in each. Although there's a lot of variation between these living systems, and as a consequence of how they implement these cognitive processes, most of the basic material is shared among them. This calls for an approach in the science of cognition that spans many different fields, from neuroscience, botany, microbiology, as well as the traditional cognitive sciences discipline. This multidisciplinary approach, which can be called Comparative Cognition, is an effort to join forces from many different perspectives toward the shared goal of understanding how living organisms can deal with information from their environment, have knowledge, and guide themselves in the world. Neuroscientists can and should draw inspiration from the humble aneural organisms when trying to understand what their intricate brain does for an animal. Therefore, we reach the conclusion that indeed cognition is not a neural thing, but a more fundamental process with roots deep down in the living organization. Every living organism needs and possesses such processes, they all need to continuously perceive and act on their surroundings, to adjust their internal states, based on what they perceive and get from the environment. They need

to know and put this knowledge to use to ensure their proper maintenance. While this is indeed the case, neural systems do possess a more advanced cognitive capacity, and this should not be denied. The field of cognitive science only has to gain by joining forces with biologists, botanists, and microbiologists, while neuroscientists should draw inspiration from these humble organisms that are the basis of what the nervous system evolved to do.

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