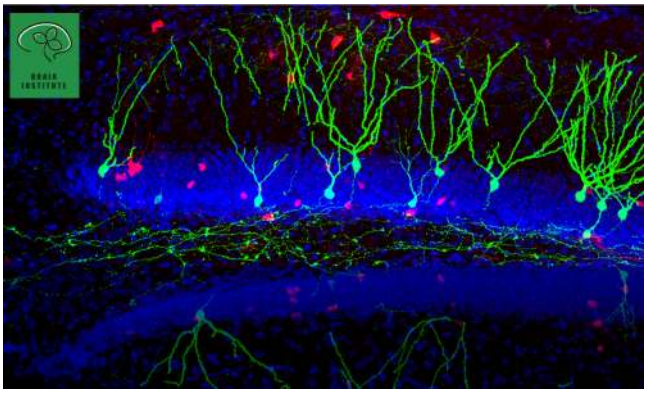
UNIVERSIDADE FEDERAL DO RIO GRANDE DO NORTE

INSTITUTO DO CÉREBRO

4th HOUSE SYMPOSIUM OF THE BRAIN INSTITUTE



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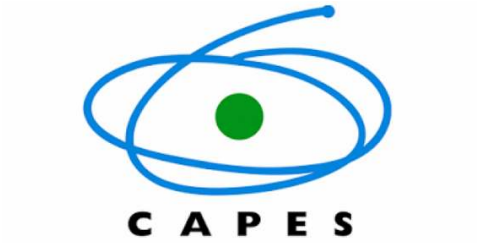


GREETINGS

Welcome to the 4th House Symposium of the Brain Institute (Instituto do Cérebro - ICe) of the Federal University of Rio Grande do Norte (UFRN)! In spite of the political turmoil, the lack of consistent funding for science and, delays in the construction of our "new house" within the Campus of the University, we are still here. And producing good science! In 2018, the ICe's team put a great effort in pursuing top research on how the brain works in both health and disease. And not only that, recent findings obtained at ICe questioned neuroscientific textbook knowledge carved in stone regarding concepts about the neuronal fate, about how brain oscillations encode perception, about support learning and about pharmacological alternatives for the treatment of neurological and psychiatric disorders.

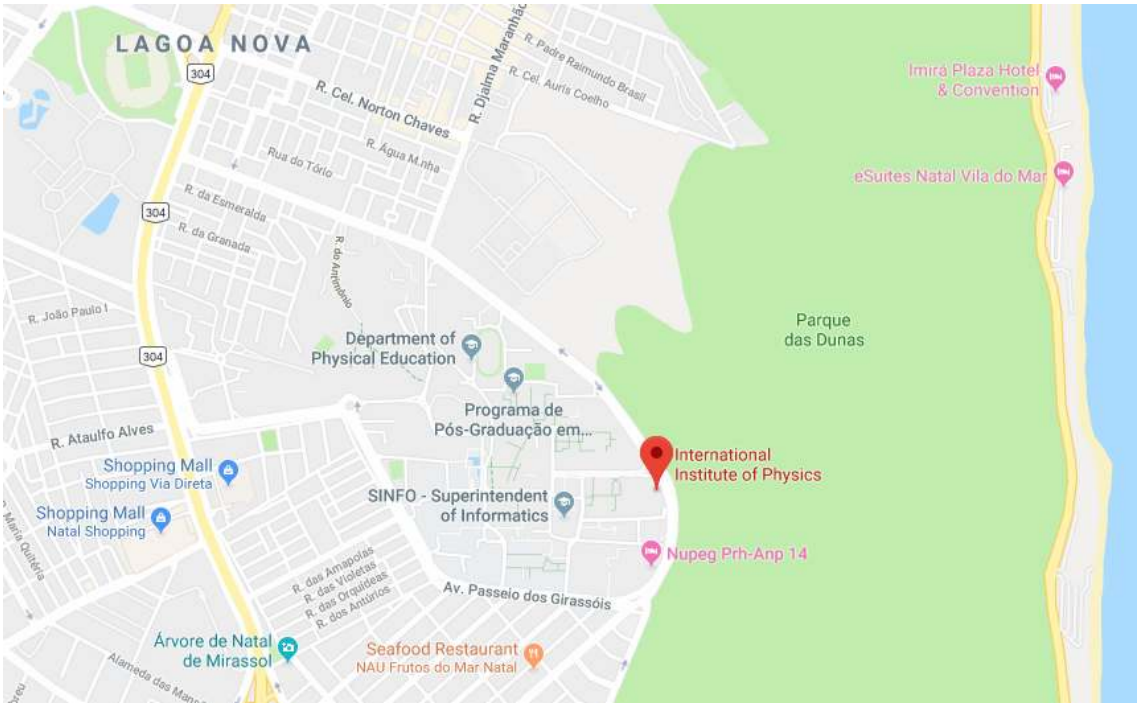
One of the goals of our annual symposia is to discuss how far we can go with bending classic concepts before breaching them. In this respect, Dr Enzo Tagliazucchi from Universidad de Buenos Aires, our invited keynote speaker, will enlighten us with his new ideas on how psychedelics can assist in understanding the link between molecular events and cognition. Dr Gustavo Rohenkohl from Ernst Strüngmann Institute (ESI - Max Planck Society) and Biosciences Institute (USP), another invited speaker, will discuss how synchronization among cortical visual areas improves the transmission of visual information. The participation of both speakers is only possible thanks to generous funding provided by the Graduate Program Office of UFRN and the International Brain Research Organization (IBRO). The 4th House Symposium program further includes 20 talks, 2 datablitz sessions (in which graduate students will promote their posters in only 2 minutes) and 39 posters, including the latest findings of ICe's research groups.

Finally, we would like to cordially thank the International Institutes of Physics for hosting our meeting again, and to our invited speakers from UFRN (Selma Jeronimo), FACISA (Hindiael Belchior) and the FioCruz/UFRJ (Cecília Hedin-Pereira) for sharing their knowledge with us. Also, we appreciate the university's unconditional administrative and financial support and thank all ICe's students, staff and principal investigators for making this neuroscience meeting possible.

We hope you will enjoy these two exciting days of science, discovery and friendship!

The Organizing Committee

Venue: International Institute of Physics/UFRN, Auditorium, Natal – RN
https://www.iip.ufrn.br/



PROGRAM AT A GLANCE *

THURSDAY, NOVEMBER 29th		FRIDAY, NOVEMBER 30th	
8:00 – 8:30	Registration and Welcome		
8:30 – 9:00	Introductory remarks (Kerstin Schmidt)	**Topic 3 - The building blocks of the nervous system** **Chair: Anna Karynna Rocha**	
Topic 1 - Manipulation of brain function in health and disease **Chair: Ignácio Gendriz**		8:30 – 9:00	Eduardo Sequerra
09:00 – 09:30	Fernanda Palhano (Dráulio Araújo group)	09:00 – 09:30	Bruna Landeira (Marcos Costa group)
09:30 – 10:00	Igor Sales (Claudio Queiroz group)	09:30 – 10:00	Selma Jerônimo (CB-UFRN)
10:00 – 11:00	**Coffee & Poster Session 1**	10:00 – 11:00	**Coffee & Poster Session 2**
11:00 – 11:30	Katarina Leão	11:00 – 11:30	Viviane Nogueira (Bernardete de Sousa group)
11:30 – 12:00	Richardson Leão	11:30 – 12:00	Sandro de Sousa
12.00 - 13.30	***Lunch break***	12.00 - 13.30	***Lunch break***
13:30 - 14:00	Datablitz: session 1	13:30 - 14:00	Datablitz: session 2
Topic 2 - Perception and memory **Chair: Dardo Ferreiro**		**Topic 4 –Oscillations and behavior** **Chair: Renato Maciel**	
14.00 – 14:30	Hindiael Belchior (UFRN-Santa Cruz)	14.00 – 14:30	Cecília Hedin-Pereira (Fiocruz/UFRJ)
14:30 – 15:00	Kerstin Schmidt	14:30 – 15:00	Rodrigo Romcy-Pereira
15.00 - 15.30	Carolina Gonzalez (Martin Cammarota group)	15.00 - 15.30	Adriano Tort
15:30 – 16:30	**Coffee & Poster Session 1**	15:30 – 16:30	**Coffee & Poster Session 2**
16: 30 – 17:00	Ana Raquel Torres (Sidarta Ribeiro group)	16: 30 – 17:00	Diego Laplagne
17:00 – 17:30	Natália Branco (Sergio Neuenschwander group)	17:00 – 17:30	Tarciso Velho
17.30 - 18.30	Gustavo Rohenkohl (USP-MPI)	17.30 - 18.30	Enzo Tagliazucchi (UBA)

* The Program at a Glance is subject to change.

THURSDAY, NOVEMBER 29th, 2018

08:00 Registration and Welcome (IIP hall)

08:30 WELCOME AND INTRODUCTORY REMARKS
Kerstin Schmidt (Director of the Brain Institute)

Topic 1 – Manipulation of brain function in health and disease
Chair: Ignácio Gendriz

09:00 NEW FINDINGS FROM A RANDOMIZED PLACEBO-CONTROLLED TRIAL WITH AYAHUASCA FOR TREATMENT-RESISTANT DEPRESSION
Fernanda Palhano

09:30 CANNABINOIDS AND EPILEPSY: IS CBD THE ONLY ANTICONVULSANT IN CANNABIS THAT MATTERS?
Igor Sales

10:00 – 11:00 Coffee & Poster Session 1 (P01 - P19)

11:00 EXAMINATION OF CORTICAL CIRCUITS TO SUPRESS TINNITUS SENSATION
Katarina Leão

11:30 ILLUMINATING THE EFFECT OF TINNITUS IN THE LIMBIC SYSTEM
Richardson Leão

12:00 – 13:30 Lunch break

13:30 - 14:00 Datablitz (Session 1)

Topic 2 – Perception and memory
Chair: Dardo Ferreiro

14:00 RUNNING SPEED MODULATES DELTA OSCILLATIONS IN THE RAT HIPPOCAMPUS
Hindiael Belchior

14:30 DO LOCAL FIELD POTENTIAL FLUCTUATIONS IN V1 DEPEND ON THE CORTICAL LAYOUT?
Kerstin Schmidt

15:00 PKMζ INHIBITION DISRUPTS RECONSOLIDATION AND ERASES OBJECT RECOGNITION MEMORY
Carolina Gonzalez

15:30 – 16:30 Coffee & Poster Session 1 (P01 - P19)

16:30 MULTISENSORY TRAINING BREAKS MIRROR LETTER INVARIANCE DURING LITERACY ACQUISITION, AND POST-TRAINING SLEEP MAKES THE LEARNING ENDURE
Ana Raquel Torres

17:00 THE ENTRAINED EYE: UNTYING EXTERNALLY- FROM INTERNALLY-DRIVEN GAMMA OSCILLATIONS IN THE RETINA
Natália Castelo Branco Matos

17:30 INTERAREAL SYNCHRONIZATION IMPROVES THE TRANSMISSION OF VISUAL INFORMATION
Gustavo Rohenkohl (Active Vision Lab, ESI - MPI & USP)

FRIDAY, NOVEMBER 30th, 2018

Topic 3 - The building blocks of the nervous system
Chair: Anna Karynna Rocha

08:30 ELECTRIC ACTIVITY INFLUENCE OVER NEURONAL TYPE SPECIFICATION DURING OLFACTORY BULB ADULT NEUROGENESIS
Eduardo Sequerra

09:00 EVIDENCE FOR PROGENITOR CELL REPROGRAMMING IN THE DEVELOPING NEOCORTEX FOLLOWING SELECTIVE NEURONAL ABLATION
Bruna Landeira

09:30 GENE EXPRESSION IN EMERGING AND REEMERGING INFECTIOUS DISEASES: HOST AND PATHOGEN INTERACTION
Selma Jerônimo (CB-UFRN)

10:00 – 11:00 Coffee & Poster Session 2 (P20 - P42)

11:00 DIFFERENCES IN GENE EXPRESSION OF COMMON MARMOSETS (CALLITHRIX JACCHUS) AND CAJADB - A FRAMEWORK OF MOLECULAR ANALYSIS
Viviane Nogueira

11:30 GENOMICS AND THE PEOPLING OF SOUTH AMERICA
Sandro J. de Souza (BioME, Brain Institute)

12:00 – 13:30 Lunch break

13:30 - 14:00 Datablitz (Session 2)

Topic 4 – Oscillations and behavior
Chair: Renato Maciel

14:00 THERAPEUTIC POTENCIAL OF PEPTIDE CANNABINOIDS FOR OLIGODENDROGENESIS AND MYELIN REGENERATION
Cecília Hedin-Pereira (Fiocruz/UFRJ)

14:30 STUDYING NEURAL CIRCUITS GOVERNING SOCIAL BEHAVIOR: CAN RODENTS BE AUTISTIC?
Rodrigo Romcy-Pereira

15:00 RESPIRATION-COUPLED BRAIN RHYTHMS
Adriano Tort

15:30 – 16:30 Coffee & Poster Session 2 (P20 - P42)

16:30 REREADING THE MIND: UNBIASED DISCOVERY OF NEURAL CORRELATES OF BEHAVIOR
Diego Laplagne

17:00 DISSECTING MICROCIRCUITS CONTROLLING VOCAL DEVELOPMENT AND PRODUCTION
Tarciso Velho

17:30 FROM MOLECULES TO CONSCIOUSNESS: TOWARDS AN INTEGRATIVE NEUROSCIENCE OF PSYCHEDELICS
Enzo Tagliazucchi (UBA)

18:30 Closing remarks (Image Prize)
Organizing Committee

19:00 Social

ORAL PRESENTATIONS

OR01 - NEW FINDINGS FROM A RANDOMIZED PLACEBO-CONTROLLED TRIAL WITH AYAHUASCA FOR TREATMENT-RESISTANT DEPRESSION

Fernanda Palhano-Fontes (Brain Institute, UFRN; Onofre Lopes University Hospital, UFRN; fernandapalhano@neuro.ufrn.br)

The use of ayahuasca, an indigenous brew from the Amazonian basin with psychedelic properties, has increased worldwide and its therapeutic value have begun to be investigated. Recently, we conducted a randomized placebo-controlled trial with ayahuasca in 35 patients with treatment-resistant depression. The results suggest a significant antidepressant effect of ayahuasca with rapid onset, already one day after a single session with ayahuasca. Compared to placebo, between-groups differences increased from one day (Cohen's d = 0.8) to seven days (Cohen's d = 1.4) after dosing. In addition to the antidepressant effects, in this trial we also explored the sub-acute effects of ayahuasca on a number of markers such as psychiatric scales, neuropsychological tests, functional magnetic resonance imaging (fMRI), electroencephalography (EEG) at sleep, and, saliva and blood tests. All assessments occurred one day before and one day after the treatment session with ayahuasca or placebo, in all patients with depression as well as in a group of 50 healthy individuals. This presentation will focus on showing some of the new findings from these measurements, which should help inform on safety and on the mechanisms behind the observed antidepressant effect of ayahuasca.

OR02 - CANNABINOIDS AND EPILEPSY: IS CBD THE ONLY ANTICONVULSANT IN CANNABIS THAT MATTERS?

Igor Sales (Neural Networks and Epilepsy Lab, Brain Institute, UFRN; igorrps@neuro.ufrn.br)

Despite substantial improvement in our understanding of the underlying mechanisms of epilepsies, seizures are unsatisfactorily controlled in 25% of the patients. Also, the development of better treatments is imperative for the management of catastrophic seizures and difficult-to-treat epileptic conditions, as status epilepticus. New drugs must convey clinical improvement with reduced adverse effects. Recent clinical trials have demonstrated a reduction in seizure frequency in two types of refractory epilepsies (Dravet and Lennox-Gastaut syndromes) by chronic administration of one isolated cannabinoid, the cannabidiol (CBD). Also, anecdotal reports suggest whole cannabis extracts can also reduce seizure frequency and improve patient's quality of life. Early pharmacological studies on cannabis-based therapeutics indicated the biological activity of some endocannabinoids could be enhanced by related substances, a synergistic pharmacological response named 'entourage effect'. In the present talk, we will review the evidence behind this proposition and discuss how this hypothesis could be tested in animal models of temporal lobe epilepsies. Preliminary results from our lab show that THC-rich cannabis extract (THC:CBD ratio = 11) attenuate pilocarpine-induced status epilepticus in mice. This dose-response suppression of behavioral seizures by THC-rich extract was similar to the one observed after diazepam administration (5 mg/kg). Also, preliminary results showed that pure THC is capable of reducing interictal spikes of chronic epileptic animals. Together, these results demonstrate that antiepileptic effects are not restricted to only one phytocannabinoid, but instead might be shared by some others types of cannabinoids. Ongoing experiments in chronic epileptic animals will confirm whether whole-plant extracts with different cannabinoid ratios can better suppress epileptiform discharges (interictal spikes, pathological high-frequency oscillations, and spontaneous seizures) in chronic epileptic animals in comparison to purified, dose-controlled, cannabinoids.

OR03 - EXAMINATION OF CORTICAL CIRCUITS TO SUPRESS TINNITUS SENSATION

Katarina Leão (Brain Institute, UFRN; katarina.leao@neuro.ufrn.br)

Tinnitus is a neurological phenomenon of maladaptive plasticity in the auditory system, creating an often stressful sensation of a constant sound in our head. So far, there are few successful treatment options for tinnitus, reflecting the lack of studies investigating how auditory cortical circuits are affected by tinnitus. Here, we use a mouse model of tinnitus perception, induced by noise-overexposure that does not cause hearing loss. Initially, we examine membrane properties of layer 5 pyramidal cells, and subdivide them into type A and type B cells based on electrophysiological responses, of control and tinnitus mice. To directly identify individual neurons showing increased calcium influx following tinnitus induction, we are implementing novel optogenetic tools of Ca2+-sensitive photo-conversion of fluorescent proteins (CaMPARIs). As tinnitus is a multifactorial condition in humans, we are also investigating if tinnitus alters sensory filtering, for instance if we pay more attention to sound when having tinnitus. By measuring auditory event-related potentials (ERPs) using intrahippocampal electrodes in control and tinnitus mice, we can quantify sensory filtering and investigate if direct and indirect manipulation of the auditory cortex alters auditory ERPs. In a parallel line of research, we target brainstem auditory populations to see if we can inhibit the sensation of tinnitus on a lower level of the auditory system. We find that decreasing the activity Ca2+/Calmoduline kinase II alpha (CaMKIIα) positive neurons of the dorsal cochlear nucleus can alleviate tinnitus perceptions, and that this population is crucial for the induction of tinnitus. Whether manipulations of cortical activity can impact neuronal activity of the dorsal cochlear nucleus remains to be investigated.

OR04 - ILLUMINATING THE EFFECT OF TINNITUS IN THE LIMBIC SYSTEM

Richardson Leão (Brain Institute, UFRN; richardson.leao@neuro.ufrn.br)

Tinnitus is often related to anxiety and my lab has previously demonstrated that anxiety-like symptoms related to tinnitus may arise in the hippocampus. In my talk will show results using calcium imaging that demonstrate the involvement of specific hippocampal neuronal types in controlling mood and generating synchrony and oscillations. in tinnitus-generated anxiety. I will also show how tinnitus can cause anxiety-like behaviors by affecting the limbic system. Finally, I will discuss new experiments that relates hippocampal circuits with abnormal risk taking behavior in different tinnitus models.

OR05 - RUNNING SPEED MODULATES DELTA OSCILLATIONS IN THE RAT HIPPOCAMPUS

Hindiael Belchior (FACISA, UFRN; hindiael@gmail.com)

Neuronal networks in the rodent hippocampus oscillate in many different and sometimes coexisting frequency rhythms according to behavioral states. While theta (5-12 Hz) oscillations are prevalent during active behaviors, like attention, exploration, and also during REM sleep, hippocampal delta (1-4 Hz) oscillations occurs mostly in quiet and drowsy behaviors, non-REM sleep and anesthesia. These two rhythms are traditionally viewed as mutually exclusive, and often used to characterize "online" and "offline" hippocampal states. Here we report the emergence of hippocampal delta oscillations while rats increase their locomotion speed in a computer-controlled treadmill. The amplitude and frequency of delta oscillations were strongly associated to speed of running, and become remarkably periodic above speeds of 30 cm/s. Our results demonstrate that running speed strongly modulates delta oscillations in the rat hippocampus, and that this rhythm can coexist with theta oscillations.

OR06 - DO LOCAL FIELD POTENTIAL FLUCTUATIONS IN V1 DEPEND ON THE CORTICAL LAYOUT ?

João Patriota & Kerstin Schimdt (Brain Institute,UFRN; joaoh_patriota@hotmail.com)

Even though several mammalian orders have orientation-selective neurons, these neurons can be organized in different functional cortical layouts. A prominent example is the columnar orientation preference map found in carnivores (cats, ferrets, tree shrews) and all primates (human, macaque, mouse lemur, etc.) studied so far, as opposed to the seemingly random arrangements commonly referred to as salt-and-pepper configurations, observed in rodents. Orientation selectivity is generally deduced from stimulus-driven spiking activity. However, it has also been observed in oscillations of the local field potential (LFP), especially in the Gamma-band. In several of the species expressing a columnar map, preference orientation of spiking activity and Gamma power is similar compatible with the interpretation that the LFP samples activity from contiguous cortical patches responding to the same orientation. Because spikes can be also strongly locked to certain phases of LFP oscillations, the latter are thought to not only establish temporal windows coordinating spiking activity of local neuronal populations but to also enable communication between distant neuronal populations. We thus hypothesized that a columnar/non-columnar functional layout might also be reflected in long-range field-field interactions. In the present ongoing study, we examined spikes and LFP oscillations in the low Gamma band of +/-30-50Hz obtained from multiple parallel recordings in visual cortex during grating stimulation in two representatives of different mammalian order and similar V1 size but different functional layouts – the domestic cat for carnivores, and the Amazonian agouti for rodents. Previously, we observed that although Agoutis possess orientation selective neurons, they do not express columns as cats do. We correlated the orientation tuning of spikes with that of the Gamma power of the same electrode. This analysis revealed that units exhibiting both orientation selectivity in spikes and Gamma power (OSI > 0.1) exhibit similar preference in cats (n = 210, circular correlation = 0.56, p = 1.44e-12), but much less in Agouti (n = 47, circular correlation = 0.40, p = 0.0067). In order to examine short- and long range interactions, we quantified coupling strength between iso- and distant recording sites (250-1200 µm) by quantifying the phase-locking value of either spike-LFP (same electrode) or LFP-LFP (distant electrode pairs). Preliminary results indicate that the distribution of these values does not reveal any clear relation to orientation or cortical distance in both species. Our observations support the interpretation that the lower similarity of spike and Gamma tuning in Agouti reflects a lesser or absent organization of orientation preference in a contiguous columnar layout. However, we cannot confirm that phase coupling to low Gamma oscillations mirrors an orientation specific long-range communication when orientation preference changes periodically across cortical surface such as cats.

OR07 - PKM ζ INHIBITION DISRUPTS RECONSOLIDATION AND ERASES OBJECT RECOGNITION MEMORY

Maria Carolina Gonzalez (Memory Research Laboratory , Brain Institute, UFRN; mariacarolinagonzalez@gmail.com)

Object recognition memory (ORM) confers the ability to discriminate the familiarity of previously encountered items. Reconsolidation is the process by which reactivated memories become labile and susceptible to modifications. The hippocampus is specifically engaged in reconsolidation to integrate new information into the original ORM through a mechanism involving activation of brain-derived neurotrophic factor (BDNF) signaling and induction of long-term potentiation (LTP). It is known that BDNF can control LTP maintenance through protein kinase Mζ (PKMζ), an atypical protein kinase C isoform that is thought to sustain memory storage by modulating glutamatergic neurotransmission. However, the potential involvement of PKMζ in ORM reconsolidation has never been studied. Using a novel object recognition memory task combined with pharmacological, biochemical and electrophysiological tools, we found that

hippocampal PKMζ is essential to update ORM through reconsolidation, but not to maintain inactive recognition memory engrams stored over time. Our results also indicate that hippocampal PKMζ acts downstream BDNF and controls AMPAR insertion into synaptic plasma membranes to elicit reconsolidation, and suggest that blocking PKMζ activity during this process deletes active ORM.

OR08 - MULTISENSORY TRAINING BREAKS MIRROR LETTER INVARIANCE DURING LITERACY ACQUISITION, AND POST-TRAINING SLEEP MAKES THE LEARNING ENDURE

Ana Raquel Torres (Brain Institute, UFRN; torres.ar@neuro.ufrn.br)

Human brain plasticity is tremendous, but how fast can the human brain inhibit the expression of a phylogenetically-old neural mechanism? Here we tested whether a neuroscience-inspired training program could break mirror invariance for letters, a putatively old neural mechanism also present in primates, cats and other animals. Mirror invariance, also called mirror generalization, enables an effortless recognition of left or right image profiles, and thus represents an ecological advantage (e.g. to recognize both the left and right profiles of a predator). However, this mechanism creates a specific difficulty at the early stages of literacy acquisition: Children struggle with mirror letters such as 'b' and 'd', which leads to a high prevalence of 'mirror errors' in the initial school years. Our experimental design was based on laboratory evidence that multisensory training helps the breaking of mirror invariance and that sleep consolidates memories in a long-lasting way. We used a 3-week protocol for daily multisensory training during 30 min, followed by 2h nap sessions. The children were pre-evaluated for performance in writing mirror letters and were then randomly sorted into 4 groups: training followed by sleep (TS); training not followed by sleep (T); neutral training not followed by sleep (NT) and control without training nor sleep (C). Subjects were tested at 30 days and 120 days. The results show that multisensory training in children learning to read was sufficient to inhibit mirror generalization specifically for letters. However, the learning faded by half after 4 months, except when post-training naps were employed to crystalize it near 100% of performance. The specific training protocol used improved reading fluency, and therefore the results have implications for formal education..

OR09 - THE ENTRAINED EYE: UNTYING EXTERNALLY- FROM INTERNALLY-DRIVEN GAMMA OSCILLATIONS IN THE RETINA

Natália Castelo Branco Matos (Vislab, Brain Institute, UFRN; nataliacbmatos@gmail.com)

Fast gamma oscillations in the retina are transmitted to the cortex via the lateral geniculate nucleus (LGN) and may carry information about stimulus size and continuity. Still, whether the retina actually uses temporal coding for processing remains an open question. In this talk, I will discuss this hypothesis based on multi-site spiking data obtained from the retina and the LGN of anesthetized and awake cats. Under halothane anesthesia, gamma oscillations were found to be highly dependent on the spatial extent of homogeneous surfaces, even when embedded within a natural-scene context. Gamma, however, was drastically reduced as halothane levels were lowered, and were absent under ketamine. Notably, in the awake cat, entrainment to the monitor refresh was commonly observed up to 120 Hz. Under halothane, these externally driven rhythms were superseded by gamma. These latter findings indicate that endogenously generated oscillations in the early visual system may curtail the representation of fast-changing stimuli. On the contrary, in natural conditions, the retinal circuits may actively hinder the generation of internal oscillations, so that they can encode fast spatial relationships already in the first volley of spikes.

OR10 - INTERAREAL SYNCHRONIZATION IMPROVES THE TRANSMISSION OF VISUAL INFORMATION

Gustavo Rohenkohl (Active Vision Lab, Ernst Strüngmann Institute for Neuroscience in Cooperation with Max Planck Society; Biosciences Institute, University of São Paulo; gustavo.rohenkohl@esi-frankfurt.de)

Our behaviour is often driven by visual cues. The transformation of sensory inputs to motor responses requires the effective transmission of visual information from lower to higher visual areas, then further to motor regions. One of the major current theories of neural communication, i.e. Communication-Through-Coherence, proposes that effective communication between distinct brain areas is mechanistically implemented by synchronizing their neural activity. However, it remains unclear whether this synchronization occurs at an optimal phase relation that facilitates stimulus transmission. In this talk, I will present recent data showing that V1-V4 synchronization predicts reaction times in awake macaque monkeys, and that this synchronization occurs at the optimal phase for behaviour. Additionally, I will show preliminary data suggesting that firing rate variance, measured in a higher visual area (area 21a) of anesthetised cats, is also modulated by its synchronization to a lower primary visual area (area 17). Together, these findings support the idea that communication between brain areas rely on the synchronization of their neural activity.

OR11 - ELECTRIC ACTIVITY INFLUENCE OVER NEURONAL TYPE SPECIFICATION DURING OLFACTORY BULB ADULT NEUROGENESIS

Eduardo Bouth Sequerra (Brain Institute, UFRN; ebsequerra@neuro.ufrn.br)

Neurons are born from a continuous epithelium of proliferating cells that lies close to the center of the neural tube. This epithelium receives gradients of signaling molecules that codes for their location in the body axes. Different combinations of signaling molecules then trigger the expression of transcription factors that guide neuronal type differentiation. Therefore, the process of neuronal specification is achieved by informing a group of tabula rasa neural cells which type of neuron they are going to differentiate into according to their position in the body. Along with this early position-dependent differentiation, newly generated neurons sense the environment in order to define the neurotransmitter to express, before making synapses. In a process called homeostatic specification, neurons express inhibitory neurotransmitters in an environment with already high excitation, and vice versa. The combination of these two processes leads to the differentiation of neuronal type expressing the proper neurotransmitter. In adult neurogenesis, with the morphogenetic body axis already defined, it is suggested that the adult neural stem cells, generating different neurons at this age, are pre programmed by signals in the embryo. In this talk, I am going to show data produced in my lab and others that argue that the adult neural stem cells are also plastic and can be oriented to differentiate into different neuronal types. Along with that, we are testing for the first time the role of sensing the electrical/neurotransmitter environment by neuroblasts in guiding final neuronal type specification.

OR12 - EVIDENCE FOR PROGENITOR CELL REPROGRAMMING IN THE DEVELOPING NEOCORTEX FOLLOWING SELECTIVE NEURONAL ABLATION

Bruna Landeira (Brain Institute, UFRN; brunalandeira@neuro.ufrn.br)

The complex neuronal cytoarchiteture of the mammalian neocortex is established in a temporal sequence, where deep-layer neurons are generated prior to upper-layer neurons. Notably, there is a good correlation among the generation time, laminar position and hodological features of neurons: i) Deep-layer neurons connecting to distant targets corticothalamic layer VI neurons - CTN; corticofugal, layer V neurons - CFN); ii) Layer IV, stellate neurons; and iii) upper-layer neurons connecting to other cortical areas (cortico-cortical layer II/III neurons - CCN). In this study, we report the

influence from early-generated deep-layer neurons to the generation of subsequent neuronal cohorts. Using genetic strategies, we induced the selective cell death of early-generated CTN and CFN and fate-mapped the neuronal population generated after ablation. We observed that 24h after ablation, progenitor cells that are usually committed to generate upper-layer stellate neurons and CCN, resumed the generation of neurons expressing molecular hallmarks of CTNs. Interestingly, some of these neurons settled ectopically within layers II-III, as expected for CCN neurons generated at the same stage, suggesting that migration of post-mitotic neurons is independent of cell-type specification. Using in vitro assays to further interrogate the mechanisms of progenitor cell re-specification following neuronal ablation, we found that only neuronal ablation in situ was capable of inducing de novo generation of CTN., indicating that intracellular communication plays an important role in the acquisition of neuronal phenotypes. Together, our data indicate the existence of feedback signals from early-generated neurons to progenitor cells and/or immature neurons controlling the generation of CCN.

OR13 - GENE EXPRESSION IN EMERGING AND REEMERGING INFECTIOUS DISEASES: HOST AND PATHOGEN INTERACTION

Selma Jerônimo (Bioscience Center, UFRN; smbj@cb.ufrn.br)

TBA.

OR14 - DIFFERENCES IN GENE EXPRESSION OF COMMON MARMOSETS (CALLITHRIX JACCHUS) AND CAJADB - A FRAMEWORK OF MOLECULAR ANALYSIS

Viviane Nogueira (Brain Institute, UFRN; vivianebritonogueiraa@gmail.com)

Common marmoset (Callithrix jacchus), a small New World monkey, has been widely used as a biological model not only to elucidate brain dysfunction in neuropsychiatric disorders, but also for deciphering neural circuits involved in human social behaviors. In this regard, the availability of gene expression data derived from next-generation sequencing (NGS) technologies represents an opportunity for deeper studies on the genetic and epigenetic architecture of this species. One of the frontiers in neuroscience field requires handling omics large-scale data sets for connecting molecular pathways to nervous system behavior. To make these omics datasets more accessible for the scientific community without a solid bioinformatics background, we developed and made available an application—the CajaDB—to provide a friendly interface for genomic, expression, and alternative splicing data of marmosets together with a series of functionalities that allow the exploration of these data. CajaDB is available at cajadb.neuro.ufrn.br. Additionally, we analyzed sex – biased gene expression (RNA – Seq technology) across tissues (cerebellum, frontal cortex, liver, heart, and kidney) and focused on the frontal cortex of common marmosets. The data point to differences in gene expression of male and female common marmosets in all tissues analyzed. To emphasize the translational value of this species we compared marmosets' data to humans' expression data in the frontal cortex. It was found that genes whose expression is male-biased are conserved between marmosets and humans and enriched with "housekeeping" functions. On the other hand, female – biased expression in the frontal cortex of marmosets is more related to neural plasticity functions involved in remodeling of synaptic circuits, stress cascades, and visual behavior. These female differences might be involved with a more resourceful stress cascade to lead with social competition present in this sex as well as a higher sustained attentional control on their visual goal – directed behavior, and might be linked to biological and behavioral mechanisms of this sex. Knowledge of the brain circuitry that drives social interactions is limited, in part due to the technical limitations of measuring brain activity in humans. Animal models have been and will continue to be useful to study many aspects of behavior, particularly to decipher the molecular basis of human social behavior. In

this sense, the findings of our study emphasize the translational value of common marmosets.

OR15 - GENOMICS AND THE PEOPLING OF SOUTH AMERICA

Sandro J. de Souza (BioME, Brain Institute, UFRN; sandro@neuro.ufrn.br)

The peopling of America remains a fascinating, still controversial, topic. In my talk I will present results from the exome sequencing of 58 Native Americans from the east part of the Amazonian region. By comparing our data with other published genomic data covering both extant and fossils samples, we were able to model the demographic movements in the early occupation of South America.

OR16 - THERAPEUTIC POTENCIAL OF PEPTIDE CANNABINOIDS FOR OLIGODENDROGENESIS AND MYELIN REGENERATION

Cecília Hedin-Pereira (Fiocruz/UFRJ; cecilia.hedin@gmail.com)

TBA.

OR17 - STUDYING NEURAL CIRCUITS GOVERNING SOCIAL BEHAVIOR: CAN RODENTS BE AUTISTIC?

Rodrigo Romcy-Pereira (Laboratory of Neural Circuit Plasticity, Brain Institute, UFRN; rnrpereira@neuro.ufrn.br)

Social behaviors evolved in invertebrates and vertebrates as key elements for increasing fitness of individuals in a struggling environment. Cuddling, grooming, play behavior, threatening displays and courtship are examples of behaviors directed to conspecifics that reduce anxiety, increase bonding, convey dominance and propose procreation. Multiple neural circuits regulate such repertoire of interactions by monitoring the body's inner state, the cues from the environment and the behavior of other individuals in order to define a behavior plan appropriate to the circumstance. Combining the inputs, the organism controls internal drive and a motor plan. In my talk, I will present some directions our lab is taking towards the understanding of dysfunctional neural circuits in a model of autism.

OR18 - RESPIRATION-COUPLED BRAIN RHYTHMS

Adriano Tort (Brain Institute, UFRN; tort@neuro.ufrn.br)

Oscillations are ubiquitous in the electrical activity produced by the brain. They can be observed at multiple scales, from spike times of single neurons, through the mesoscopic scale of local field potentials (LFPs), up to more macroscopic EEG and fMRI recordings. In this talk, I will show results obtained through a joint Brazil-Germany collaboration, which were obtained by examining the relationship between brain oscillations and the respiratory rhythm in rodents. Our findings reveal that nasal respiration entrains oscillations at the same frequency as breathing in several regions of the rodent brain, though most prominently in frontal regions. Moreover, we found that rhythmic respiration modulates the amplitude of faster brain waves known as gamma oscillations through a cross-frequency coupling mechanism previously associated with information transfer. Our results thus suggest that respiration-coupled oscillations aid long-range communication in the brain.

OR19 - REREADING THE MIND: UNBIASED DISCOVERY OF NEURAL CORRELATES OF BEHAVIOR

Diego Laplagne (Brain Institute, UFRN; diego@neuro.ufrn.br)

About a century ago, we began measuring how brain activity correlates with behavior. Conceptually, little has changed since the work of Lord Adrian: we record brain activity during simple behaviors, generate intuitions on their correlations and verify them

through quantification. This has limited us to studying phenomena clear enough for us to grasp. Today, artificial intelligence is undergoing a revolution, to the point of 'beating' the human mind in highly complex tasks. I will describe an ongoing project in the La Rata Lab. We aim at giving neurobiology of behavior a fresh start, by momentarily forgetting what we have learned through intuition, and programming learning machines to freely search for the brain signals that explain what animals—in this case, rats—are doing. Our project can be summarized in 4 steps: 1) Obtain massive datasets from individual rats freely behaving in a large and enriched environment; simultaneously recording depth video, ultrasonic vocalizations, respiration, head accelerometry and distributed brain electrophysiology. 2) Develop unsupervised learning machines to construct the rat ethogram and automatically classify behavior. 3) Follow a similar strategy to discover the 'neurogram', a dynamic state map of brain activity. 4) Establish causalities between behavioral and neural states and explore the neural correlates of behavior. We expect this ambitious project to result in novel insights in the never-ending quest to understand how the brain contributes in making us who we are.

OR20 - DISSECTING MICROCIRCUITS CONTROLLING VOCAL DEVELOPMENT AND PRODUCTION

Tarciso Velho (Brain Institute, UFRN; velhot@neuro.ufrn.br)

In neurobiology, form and function are highly interconnected. Small changes in our genes can lead to changes in their products, e.g. proteins. Altered proteins, in turn, can lead to perturbations in brain assembly and dramatic changes in brain function and behavior, i.e. a neurological disorder. To understand how genes influence the form and function of brain circuits is necessary to manipulate them in the physiological context of an intact animal with a robust and relevant behavior that can be carefully measured. For vocal learning, an inherent component of speech development, zebra finches are the leading neurobiological model. Nonetheless, the zebra finch has yet to be fully exploited as a genetic model due to our inability to easily manipulate its endogenous genes. To overcome this barrier and to take the first steps towards unraveling how mutations linked to speech and language disorders affect related brain circuits, we are currently working towards: (i) generating a modular, flexible, system of transgenic finch lines based on the Cas9 enzyme and their accessory guide RNAs (gRNAs); (ii) developing enhanced viral vectors that can efficiently infect the zebra finch brain; (iii) and towards developing and testing efficient molecular tools to investigate the contribution of activity-dependent, plasticity-related genes for vocal learning in the vertebrate brain. These transgenic lines and molecular tools will allow us (and others) to target specific endogenous genes to investigate the genetic basis of vocal learning. In this lecture, I will present the current status of these and other scientific endeavors of my laboratory.

KEYNOTE LECTURE

OR21 - FROM MOLECULES TO CONSCIOUSNESS: TOWARDS AN INTEGRATIVE NEUROSCIENCE OF PSYCHEDELICS

Enzo Tagliazucchi (Universidade de Buenos Aires; nztglzcch@gmail.com)

Suppose someone consumes a typical dose of lysergic acid diethylamide (LSD). The molecules are absorbed by her body and cross the blood-brain barrier, finally interacting with proteins located at the cell membrane (receptors). Depending on the receptor and the type of interaction with the LSD molecule, different intracellular second messengers are recruited, which in turn modify the biophysical properties of the cell and influence its activity. The next two facts we know about are that the contents of her consciousness are deeply modified, and that such modifications are related to changes in brain activity, as measured with tools such as fMRI, EEG and MEG. But what happened in between? Currently, we have knowledge about the two ends of the process, but how can we connect both ends? In my talk I will move between theory and experiment to propose a way to link scales based on the following assumptions: 1) That it is possible to map the state of the brain (at different scales) into a space with a distance function or metric (i.e. there is a notion of the proximity between two states), 2) That it is possible to map the contents of consciousness into a similar space, and 3) That it is possible to investigate how the distance functions from both spaces relate to each other, e.g. does “being close“ in one space imply “being close“ in the other?

POSTER SESSION 1 (THURSDAY)

P01 - ON THE BOUNDARY CONDITIONS OF AVOIDANCE MEMORY RECONSOLIDATION: AN ATTRACTOR NETWORK PERSPECTIVE

DB

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The reconsolidation and extinction of aversive memories and their boundary conditions have been extensively studied. Knowing their network mechanisms may lead to the development of better strategies for the treatment of fear and anxiety related disorders. In 2011, Osan et al. developed a computational model for exploring such phenomena based on attractor dynamics, Hebbian plasticity and synaptic degradation induced by prediction error. This model was able to explain, in a single formalism, experimental findings regarding the freezing behavior of rodents submitted to contextual fear conditioning. In 2017, Radiske et al. showed in rats subjected to inhibitory avoidance (IA) that the previous knowledge of the current aversive context as non-aversive is a boundary condition for the reconsolidation of the shock memory experienced in that context. In the present work, by adapting the Osan et al. (2011) model to simulate the experimental protocols of Radiske et al. (2017), we show that such boundary condition is compatible with the dynamics of an attractor network that supports a synaptic labilization common to reconsolidation and extinction. Additionally, by varying parameters such as the levels of protein synthesis and degradation, we estimate boundary conditions and predict behavioral outcomes in the IA paradigm that can be tested experimentally.

Funding: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES)

P02 - SEMANTIC MEASURES OF MEMORY REVERBERATION DIVERGE AT DREAM ONSET

DB

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The ‘day residue’ - presence of waking memories into dreams - is a century-old concept that remains controversial in neuroscience. Even at the psychological level, it remains unclear how waking imagery cedes into dreams. Are visual and affective residues enhanced, modified or erased at sleep onset? What are the neural correlates of these transformations? To answer these questions we combined quantitative semantics, sleep EEG markers and multiple awakenings after reference stimuli. Healthy adults were repeatedly stimulated with an affective image, allowed to sleep and awoken seconds to minutes later, during waking, N1 or N2 sleep stages. We established an objective definition of ‘Image Residue’, as the formal semantic similarity between verbal reports describing the last image visualized before closing the eyes (‘reference’), and subsequent visual imagery (‘dream’). Similarly, ‘Affect Residue’ measured the proximity of affective valences between ‘reference’ and ‘dream’. Our grounded and objective measure of ‘day residue’ showed that closed-eyes imagery diverges early on from the reference stimulus, drifting towards random contents and neutral affects already at N1 sleep. The most-recently seen images did not fade for lack of recall, but rather merged into a spontaneous torrent of competing memories, proportional to bilateral EEG power in the theta band (4.5-6.5 Hz), and counter-acted by right-hemisphere EEG power in the beta band (14.5-24.5 Hz). The randomization of imagery at sleep onset suggests that the ‘day residue’ detected in overnight dream reports reflects de novo activation of memory traces during later sleep states.

Funding: Work supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) PVE grant 401518/2014-0, Universal grants 480053/2013-8 and 408145/2016-1, and Research Productivity grants 308775/2015-5 and 310712/2014-9; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Projects OBEDUC-ACERTA 0898/2013 and STIC AmSud 062/2015; Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE); Center for Neuromathematics of the São Paulo Research Foundation FAPESP (grant 2013/07699-0); and the Austrian Science Fund Project (FWF) Y00777

P03 - MELATONIN SPECIFICALLY INHIBITS AGONISTIC BEHAVIOUR IN WINNER CICHLID FISH

DB

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The establishment of social hierarchy influences aggressive behaviour. Social context may mediate androgens, cortisol and melatonin levels in fish. Studies suggest that injections of melatonin reduce agonistic behaviour in a cichlid teleost, Aequidens pulcher. Therefore the aim of this study was to evaluate in Acarichthys heckelii (Cichlidae) the effect of melatonin (MT) in aggressive behaviour, through analysis of agonist behaviour before and after melatonin manipulation, and also its effect in levels of cortisol and 11-ketotestosterone (11-KT) using ELISA and EIA tests, only after melatonin manipulation. The ethogram for aggressive behaviour in A. heckelii shows eight behavioural units: lateral, frontal and perpendicular displays, threat, attack, frontal confrontation, pursuit and escape.. According to the frequency of behavioural units displayed, each subject was identified as loser and winner. Winners exhibited more units related to dominance, while losers displayed a higher frequency of escape and were considered to be more submissive. There were significant differences in winner fishes, showing a decrease of frequency in frontal confrontation ($Z=2,02$; $p= 0,04$), threat ($Z= 1,99$; $p= 0,04$), attack ($Z= 1,99$; $p= 0,04$) and also in the total interactions ($Z=2,20$; $p= 0,02$) after melatonin manipulation, thus agreeing with a study where units of exhibition and bites decreased after melatonin injections in Aequidens pulcher. Melatonin decrease levels of androgens, therefore it may reduce the frequency of agonist behaviour in cichlids. Comparing subjects with and without melatonin, loser fishes showed an increase in confrontation and in the total of interactions when there were no MT ($Z>2,02$; $p<0,04$), which suggests that the animal´s previous experiences interferes in aggressive behaviour decreasing its motivation. Relating to physiological body levels, 11-KT was higher in winners that did not received exogenous melatonin (LSD, $p=0,01$), showing that melatonin reduces 11-ketotestosterone releases, corroborating with studies done for other species of cichlids, where it was noted a reduction of the aggressiveness after melatonin manipulation. Winning animals also showed higher concentrations of 11-KT (ANOVA, $F=4,63$; $p=0,01$) and lower cortisol concentrations (ANOVA, $F = 3,34$; $p = 0,03$) than losers in pairs that were not submitted to MT. This result was expected since high levels of 11-KT are usually presented in fishes that show higher behaviour frequency in pair disputes and cortisol levels are usually higher in submissive animals. There were no significant differences in body concentrations of 11-ketotestosterone (LSD, $p=0,41$) and cortisol (LSD, $p=0,54$) between losers that were and were not submitted to exogenous melatonin. These data may be a result of the increased levels of cortisol, especially for loser animals, triggered by social stress due aggressive interactions. Consequently, it can be concluded that melatonin affects the agonistic behaviour and body levels of 11-ketotestosterone in winning fishes but it does not affect aggressive interactions, cortisol and 11-KT body levels in losers of Acarichthys heckelii.

Funding: Fundação de Amparo à Pesquisa do Estado do Amazonas (FAPEAM)

P04 - ALTERATIONS OF SENSORY GATING IN SLC10A4 MICE

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Event Related potentials (ERPs) have been widely used to investigate neurophysiological correlates of sensory information processing. In patients with schizophrenia, auditory ERPs indicate impaired sensory filtering and this measure have been used as a biological marker of schizophrenia. Auditory ERP are routinely recorded as response to paired-clicks and different temporal peaks can be evaluated in humans using electroencephalography or magnetoencephalography. Still, there is a lack of adequate mouse models for schizophrenia and new transgenic and knock out (ko) mice lines are being tested for capability to mimic schizophrenia pathology. One novel candidate gene is the solute carrier family member 10A4 (SLC10A4) protein, which co-express with monoaminergic and cholinergic vesicular transporters. Previously, SLC10A4-ko animals were shown to demonstrate an increased sensitivity to psycomimetic drugs and increased vulnerability to epileptic conditions. Here, we compared the auditory event-related potentials in freely moving SLC10A4 knockout and littermate control mice, implanted with 16 channel chronic intrahippocampal electrodes. In this study, two different doses of ketamine, 5mg/kg and 20mg/kg were additionally used to provoke psychotic correlates. Preliminary tracking analysis shows an increased locomotor activity for 20mg/kg ketamine, for both littermate control and SLC10A4-ko animals compared to saline. Analysis of auditory ERPs shows that SLC10A4-ko mice displayed a more complex waveform with extra peaks compared to control littermates. Low dose ketamine (5mg/kg) weakly affect ERPs in control animals but strongly alter the waveform in ko animals. Also, spectral analysis of oscillatory activity during sessions without clicks indicates that 5 and 20mg/kg ketamine decreased theta oscillations. We found alterations in auditory ERP temporal components that may be potential markers for psychiatric disorders.
Funding: Coordenação de Aperfeicoamento de Pessoal de Nível Superior (CAPES)

P05 - THE PROBLEM OF CONSCIOUSNESS IN VISUAL PERCEPTION: A REVIEW OF THE DF CASE

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The processing of visual information is often explained through the two-stream hypothesis, according to which information is processed through two pathways: 1) the ventral stream, which is responsible for the discrimination and recognition of sense-data, and 2) the dorsal stream, that provides the spatial orientation for this same data. Yet, in spite of its relevance to visual guidance, many authors claims that the dorsal stream do not play a role in conscious experience due to its mere spatial orientation function. This dichotomic view on how the ventral and dorsal streams relates to conscious experience was cast into doubt through the theories of Christopher Mole (2009) and Wayne Wu (2013), according to which the functional division of visual information occurs in combination of both pathways. According to Mole there is no division between the ventral and dorsal systems, i.e. both plays a role in conscious experience. The difference between them is that, whereas the ventral system uses language in order to represent conscious states, the dorsal system uses body gestures. In contrast, Wu claims that there is not a unique system as Mole says, but there is a distance between conscious vision and action guiding vision. This Division opens room to what was dubbed as “zombie agency”, the idea that many brain systems are able to perform complex routine tasks without direct conscious input. The purpose of the present work is to discuss the problem of how conscious states relates to visual

perception. We shall illustrate the Wu-Mole's debate with the case of DF, a patient who experienced a form of agnosia due to a lesion in the lateral occipital complex. According to many experiments, DF was able to control her movements in relation to objects, but denied to be able to see them. The DF case then provides good information on to what extent the ventral and the dorsal streams are dependent upon each other. We shall expose the methodological and philosophical implications of Wu and Mole's theories by reviewing the DF case.
Funding: None

P06 - CHARACTERIZATION OF CELL TYPES AFFECTED BY NOISE-INDUCED TINNITUS IN THE AUDITORY CORTEX OF MICE

DB

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Tinnitus is an abnormal state of nerve cell activity of the auditory system, leading to perception of 'phantom' sounds. It can be acute, lasting hours or days, or chronically perceived. Although this continuous perception of sound is not harmful per se, it can lead to severe psychological stress, insomnia and depression. Several studies indicate the auditory cortex as a potential target for transmagnetical stimulation to alleviate tinnitus perception yet little is known of how tinnitus alters cortical circuits. Here we are investigating cellular populations of the auditory cortex in a mouse model of noise-induced tinnitus that does not generate hearing loss (preliminary data, T Malfatti). Our goal is to identify the tonotopic frequency region of the auditory cortex that is affected by a noise-trauma (8-12kHz, 90dB, 2 hrs) using an activity-activated calcium integrator (CaMPARI) and the whole cell patch clamp. We are recording the electrophysiological activity of pyramidal neurons in brain sections from health animals and tinnitus-induced animals. The CaMPARI is a fluorescent protein that photoconverts from green to red when stimulated by violet light (~400nm) during influx of calcium. Adeno-associated virus (AAV5/9-hSyn-CaMPARI) will be injected into the primary auditory cortex (A1) at several depths, to identify regions acutely activated by the noise-trauma, of 3-4 week old wild type mice. Approximately 2-3 weeks after the injection, mice will be subjected to the noise trauma while optically stimulated with violet light into the auditory cortex. Thereafter animals will be immediately sacrificed, the brains dissected and sliced (300µm) and 1) mounted for fluorescent microscopy, or 2) used for whole cell patch clamp recordings to characterize cell types affected and potential hyper excitability in activated (red) cells. These results will be a first step to identify neurons affected by acoustic trauma and will allow us to map regions of the A1 affected by tinnitus generating noise. To understand the cellular mechanisms of tinnitus is crucial for better treatments of tinnitus using cortical stimulation.
Funding: Coordenação de Aperfeiçoamento de Nível Superior (CAPES)

P07 - A BRIEF MINDFULNESS-BASED INTERVENTION ENHANCES PSYCHOLOGICAL MEASURES OF WELLBEING

DB

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Over the past decades, a growing body of research has targeted how interoception, the felt sense of the body, informs appraisals of subjective well-being. Mindfulness training (MT) describes a collection of attention practices aimed at cultivating such awareness, in an effort to renegotiate maladaptive self-referential tendencies. Here we report on a brief MT intervention relative to a randomized control condition, investigating the mechanisms by which MT mitigates the response to a well-validated stress reactivity paradigm. The MT group performed a 30 minute breath-focused mindfulness practice at

3 consecutive days in a laboratory environment. The control group performed a coloring activity for 30 minutes, also for 3 consecutive days in the laboratory. Based on Wilcoxon signed-rank tests, our results show consistent within-group improvements in the MT but not control groups in measures of interoception (Mindfulness: V= 23, p=0.001; Control: V= 99, p= 0.88); State Mindfulness (Mindfulness: V=32, p=0.006, Control: V= 135.5, p = 0.262); and Anxiety (Mindfulness: V=148, p=0.03; Control: V=115, p=0.72). There is a difference in both groups after the training in Perceived Stress (Mindfulness: V= 201.5, p= 0.0003; Control: V= 150, p = 0.027) suggesting an effect of the control group in this measure. Our data also shows a difference between groups regarding to interoception (W= 114, p=0.01) and state of mindfulness (W=92, p=0.003). Both measures present higher scores after MT. According to these results, even a brief MT intervention can significantly lower scores related to anxiety and can enhance interoception and mindfulness, corroborating similar results obtained from studies that use traditional interventions such as the 8-week Mindfulness-Based Stress Reduction Program.
Funding: CAPES

Po8 - DISRUPTION OF THE SLEEP WAKE-CYCLE DYNAMICS IN THE RAPID AMYGDALA KINDLING MODEL OF TEMPORAL LOBE EPILEPSY

DB

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Mapping electrographic brain oscillations in epileptic patients can contribute to unravel the underlying mechanisms associated with seizure generation, spread and termination and how these paroxysms can affect brain physiology. Gamma and theta oscillations are a remarkable feature displayed, respectively, during wake and REM sleep of healthy animals. However, epileptiform activity can disrupt physiological oscillations. Nevertheless, little is known about the temporal profile of the sleep-wake cycle during epileptogenesis. Descriptive feature retrieval from raw EEG has shown to be a complex task. In order to approach it, signal analysis by a state space map built out of spectral ratios was able to predict global forebrain dynamics and detect wake, slow-wave and REM sleep as three clusters in a state space map. Our main goal was evaluate with this technique how global brain dynamics evolves during sleep-wake cycle after rapid amygdala kindling. To evaluate how spectral state maps change by the recurrence of afterdischarges and seizures induced by electrical stimulation of the amygdala. Methods: Wistar male rats (250-350 g) were randomly assigned to control (n=24) and experimental groups (n=6) (UFSJ/CEUA protocol #17/2013). All animals underwent surgical implantation of recording electrodes in the right dorsal hippocampus, the right anterior nucleus of the thalamus, and bilateral prefrontal cortices. Stimulation electrodes were stereotaxically placed into the right basolateral amygdala. The experimental group was submitted to one protocol of rapid kindling. Stimulation consisted of 10 s-duration trains of biphasic square-wave pulses delivered at 60 Hz (I=500 μA). The kindling protocol comprised 2 days of stimulation, with 10 sessions per day and 30-min interval between sessions. Control animals underwent the same procedures, but no stimulation was applied. Electrographical and video recordings started at the 3rd day at 10 am extending for 6 hours. Electrophysiological signals were offline bandpass-filtered (0.5 to 55 Hz) and state space maps were built integrating power spectrum ratios in gamma and (30-55 Hz) and theta oscillations (4-9Hz). We quantified the size of clusters, the displacement of clusters through gamma and delta oscillations, the distances between clusters and the number of cortical spindles during slow-wave and intermediate sleep. Results and Conclusions: The size of slow-wave sleep clusters decreased in epileptic animals ($p < 0.0001$, unpaired t test). The state space maps were displaced upwards in the experimental group ($p < 0.001$, unpaired t test). The distances between wake and slow-wave sleep and between slow-wave and REM sleep clusters decreased in the experimental group ($p < 0.0001$, unpaired t test). Epileptic animals showed a reduced number of cortical spindles in the slow-wave sleep stage ($p = 0.0238$, unpaired t test) with any modification of the number of cortical

spindles on intermediate sleep. Our results shows that (1) although disturbed the structure of sleep-wake cycle stages was preserved on the state space maps of epileptic animals, (2) novel attractors in brain decreased the distances between clusters in epileptic animals moving sleep-wake cycle stages to the upper region on map, and (3) memory processing and storage can be impaired in epileptic animals due to reduced number of cortical spindles.
Funding: CAPES, UFSJ, CNPq, FAPEMIG

P09 - COMPUTATIONAL MODELS OF MEMORY CONSOLIDATION AND LONG-TERM SYNAPTIC PLASTICITY DURING SLEEP

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The brain stores memories by persistently changing the connectivity between neurons. Sleep is known to be critical for these changes to endure. Research on the neurobiology of sleep and the mechanisms of long-term synaptic plasticity has provided data in support of various theories of how brain activity during sleep affects long-term synaptic plasticity. The experimental findings - and therefore the theories – are apparently quite contradictory, with some evidence pointing to a role of sleep in the forgetting of irrelevant memories, whereas other results indicate that sleep supports the reinforcement of the most valuable recollections. A unified theoretical framework is in need. Computational modeling and simulation provide grounds for the quantitative testing and comparison of theoretical predictions and observed data, and might serve as a strategy to organize the rather complicated and diverse pool of data and methodologies used in sleep research. This review outlines the emerging progress in the computational modeling and simulation of the main theories on the role of sleep in memory consolidation. Besides we will also work on the application of the concepts from recent biological experiments to apply in the existing computational models, in order to reduce the catastrophic forgetting (when the learning of a new memory negatively interferes with the encoding of a memory learned in a previous occasion) in artificial neural networks.
Funding: Support obtained from the Federal University of Rio Grande do Norte, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) grants 308775/2015-5 and 408145/2016-1 to SR and 427575/2016-8 to CRC; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES-MINCyT) to SR; Fundação de Amparo à Pesquisa do Rio Grande do Norte grant Pronem 003/2011 to SR; Fundação de Amparo à Pesquisa do Estado de São Paulo grant #2013/07699-0 Center for Neuromathematics to SR, Pew Latin American Fellows Program to SR, Google Latin America Research Award 2017 to CRC, ACCS and SR.

P10 - UNRAVELING THE PHYSIOLOGICAL BASIS OF SPATIAL ATTENTION: RATS AS MODEL

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The ability to focus cognitive resources on relevant stimuli frequently defines how successful we and other animals are in our daily tasks, from simply searching for food to performing complex social behaviors. Orienting of attention is such ability. In humans, it is often investigated using the covert orienting of attention task (COVAT) described by Posner. It allows measuring the time required to move attention in space without confounding attentional control and perceptual aspects of stimuli detection. An

important contribution of this task was the identification of brain circuits involved in two partially segregated orienting systems: a goal-oriented and a stimulus-driven. While the former would involve preparation for stimuli selection based on the subjects' (top-down) expectations about the environment, the latter would act like a "circuit breaker", interrupting goal-oriented control to shift attention towards unexpected salient events, in a bottom-up fashion. Such advancements, made mainly through human and monkey studies, could be accelerated by using rat models analogous to the COVAT. Even though rats do show orienting of attention analogous to primates in this task, only a dozen studies have employed this potentially useful model to study the neural physiology of attention shifts. This may be partially due to the difficulty of training rats in such task and the lack of demonstrations of goal-oriented attention shifts in these animals when using symbolic cues. Recently, we have demonstrated that rats do orient attention in a top-down fashion, opening new possibilities to the study of attentional shifts using rats. Neurophysiological studies on orienting of attention in humans rely heavily on fMRI, a technique with suboptimal temporal resolution to capture attentional shifts. Even though cellular brain recordings in behaving monkeys compensated for this restriction, its use is not widespread because of practical restrictions. Since laboratory rats are more accessible and, as demonstrated recently in our laboratory, also capable of stimulus-driven and goal-oriented attentional shifts, we propose that studies on the neurophysiology of attentional control is strengthened and get benefits of using rats as model, bringing substantial practical advantages. Our studies aim at investigating physiological modulations in brain regions of rats in response to stimuli that might induce either goal-oriented or stimulus-driven attentional shifts. In addition, we aim at evaluating if these modulations are analogous to those observed in humans and monkeys. Rats will receive bilateral chronic implants of electrode matrices in the Frontal Orienting Fields (FOF) and Ventromedial Prefrontal Cortex (vmPFC). There is evidence in the literature that indicates homology between these structures and primate's Frontal Eye Fields (FEF) and Ventral Frontal Cortex (VFC) respectively, the former being involved in goal-oriented and the latter with stimulus-driven shifts. Subjects will be trained to perform the COVAT with either peripheral or symbolic predictive visual cues and visual targets. For each trial, we will register signals from cue presentation to target appearance. Admitting that rodents' FEF and VFC homologous exert an equivalent function as in humans, we expect an increase in spike rate of FOF just after cue presentation, indicating a top-down modulation preparing stimuli detection in the cued side. After target onset, if the cue corresponds to the target (valid trial), we expect observing a decrease in FOF activation, indicating the end of top-down control. However, if the cue does not correspond to the target (invalid trial), an increase in vmPFC activity is expected, indicating the occurrence of an unexpected stimulus. Ultimately, this would allow us to evaluate to what extent this promising animal model might be used in the future as a more accessible model for investigating the physiology of attention shifts.

Funding: Conselho Nacional de Desenvolvimento Científico e Tecnológico and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior.

P11 - EFFECTS OF THE SYSTEMIC ADMINISTRATION OF PILOCARPINE ON GENE EXPRESSION IN THE ADULT MICE HIPPOCAMPUS

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Affecting about 50 million people worldwide, epilepsy is one of the most common neuropathologies in the modern world. It can be defined as recurrent seizures that affect the brain as a whole, or only part of it; these convulsions come from an uncontrolled excitation of neurons, leading to cell death. About 70% of epileptic patients respond to anticonvulsant medication while 30% of patients do not respond to it. Because it is a pathology that reaches a large number of people, studying the molecular mechanisms involved in it becomes a fundamental task for understanding it.

Animal models help us to mimic a number of diseases, including epilepsy. Systemic administration of pilocarpine is one of this models. Pilocarpine is a muscarinic agonist, acting on metabotropic receptors, which leads to an increase of calcium in the cells and, consequently, the release of neurotransmitters; among them, glutamate, the main excitatory neurotransmitter of the central nervous system, which is toxic in large quantities. In order to better understand this model, and epilepsy itself, we analyzed in this work a dataset of an experimental systemic pilocarpine administration, focusing on the hippocampus of adult mice, a key region in the pathology of epilepsy. With tools from bioinformatics, differences in the gene expression of hippocampal cells were studied in three moments after intraperitoneal injection of pilocarpine: 12 hours; 10 days; and 6 weeks. Each of these time-points was analyzed separately for gene expression: which genes are the most expressed, the least expressed, besides a gene ontology. From these data, it can be concluded that there is a great change in gene expression, especially in relation to neurogenesis, apoptosis and microglial activation, and that there is mechanism against the activation of the immune response and neurogenesis, besides genes involving other cellular entities, such as oligodendrocytes, demonstrating the need for further studies to understand the gene expression of epilepsy.

Funding: No

P12 - NATURAL LANGUAGE PROCESSING IN HISTORICAL CIVILIZATIONS

DB

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In the beginning was the word, but what kind of word? Understanding language and context is a powerful tool when one is in a technological world, and machines are talking. Natural Language Processing (NLP) draws a line between human languages and computers, by developing computer systems that interpret speech and text as humans naturally do, but are able to process large amounts of data at a time. What are the most relevant parts of speech in the written record since the first texts appeared during the Bronze Age? Which word classes were responsible for disseminating information more effectively? We aim to answer these questions using NLP and word graphs to assess literary texts spanning ~4500 years. In word graphs, centrality measures are responsible for determining the most relevant nodes, putatively the ones that are more effective in spreading information. Here we first present an automated model to build word graphs and detect their central nodes, and we perform a semantic analysis by implementing a Part-of-Speech (PoS) tagging. Our preliminary analysis shows that verbs are crucial when transmitting information in contemporary texts, while nouns and pronouns are prevalent in ancient texts.

Funding: CAPES

P13 - DUAL-GAMMA OSCILLATIONS IN V1 CAN BE EXPLAINED BY VOLUME CONDUCTION WITHIN THE VISUOTOPIC MAP

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Several studies in awake monkeys and humans show that gamma oscillations are key to cognitive functions, such as perceptual binding, attention, and memory. Here, we recorded spiking activity and local field potential (LFP) simultaneously from different locations in V1 of (operculum and calcarine), corresponding to distinct eccentricity points in the visuotopic map (central and periphery locations respectively) (n = 150 pairs of recording sites). Data were collected from capuchin (n = 3) and macaque

monkeys (n = 4). Tuning curves were obtained for moving gratings for different orientations, sizes, and speeds. Our results show that the gamma oscillation frequency is higher at the central as compared to the peripheral representation of the visual field. Interestingly, frequency decreased systematically, following an exponential function that asymptoted a few hundreds milliseconds after stimulus onset. Overall, these results offer an alternative interpretation to the findings by Murty et al. (J. Neurosci, 2018) showing that two distinct gamma rhythms appear in V1 when large stimuli (full-screen gratings) are presented. The authors report a second slow-gamma component in the LFP and propose a new mechanism by which the two rhythms may boost stimulus encoding. A simpler explanation, however, that the low-frequency component results from responses originating in the periphery of V1 (calcarine, slow gamma), which spread to the central representation region (operculum, fast gamma) by volume conduction. Our data suggest the two gamma rhythms should be conceived, not as playing a complementary role in visual processing, but as an epiphenomenon from the topological arrangement of the underlying cortical circuitry.
Funding: CAPES, CNPQ

P14 - EFFECT OF FEMALE SEX HORMONES ON SENSORIMOTOR CORTEX EEG PATTERNS DURING OBSERVATION OF MOTOR ACTION AND MOTOR IMAGERY

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There is evidence that female sex hormones (FSHs) influence performance in tasks of fine manual dexterity and motor coordination. However, there is little information about effects on brain regions responsible for motor control. Receptors for FSHs are widely distributed in the brain, playing a crucial role in the development and modulation of cerebellum, nigrostriatal system, and sensorimotor cortex circuits. Investigations on the excitability of the primary motor cortex throughout the menstrual cycle have indicated that menstrual (low estrogen and progesterone levels) and luteal (high estrogen and progesterone levels) phases are associated with fewer evoked motor potential compared to the late follicular phase (high estrogen level). These findings suggest the facilitative effect of estrogen and the inhibitory effect of progesterone on the primary motor cortex. This study aims to investigate whether the activity induced on the sensorimotor cortex during the execution of tasks such as observation of motor action and mental simulation of movement (motor imagery) is higher in the follicular phase and lower in the luteal phase. Preliminary data of electroencephalography (EEG) records were performed in 8 right-handed women aged between 18 and 30 years and showing a regular menstrual cycle during the practice of a protocol of motor activities including the observation of the action and the associated motor imagery. The experiments were performed in three phases of the menstrual cycle (menstrual, late follicular and luteal) of each participant. Data sampling occurred in the menstrual phase (2nd to 4th days after bleeding); late follicular phase (9th to 12th days) and luteal phase (17th to 19th days). The participants were submitted to a habituation session before data collection. For signal processing, EEG channels containing noises were interpolated, the signal was re-referenced to mean of all channels, ocular artifacts were excluded using the Independent Components Analysis and the signal was divided into segments containing 7.5s, the first second corresponds to the pre-stimulus baseline. The event-related spectral perturbations were computed in power in each frequency by normalizing the power spectral estimate in each frequency bin by the mean power level during the pre-stimulus baseline. We found decreases in spectral power from baseline that were understood as an increase in event-related desynchronization (ERD) in cortical activity or arousal, while an increase in spectral power from baseline indicates a resting state of cortical neural activity (i.e., event-related synchronization - ERS). The mean spectral power for both, the mu- (8–12 Hz) and beta-bands (15–30 Hz), across the 4s period of interest for sensorimotor regions (C3, C4, CP3, CP4, P3 e P4) and T test was used to compare these variables in the

follicular phase (high estrogen level) with the menstrual phase (low estrogen level) and in the luteal phase (high progesterone levels) with follicular phase (low progesterone level). It was possible to observe a significant increase ($p<0.05$) of the alpha-band ERD in the follicular phase when compared the menstrual and luteal phases over the contralateral hemisphere during motor imagery of the right arm. A significant increase in beta-band ERD over the ipsilateral hemisphere during motor imagery of the right arm was also observed for follicular phase when compared to the menstrual phase. No statistical difference was found for observation of the action protocol. These preliminary results suggest that FSHs influence motor planning throughout the menstrual cycle. This effect can be observed during the self-imagination of motor action, but not during the simple observation of the action, suggesting that HSFs (especially estrogen) have a facilitator effect on the voluntary component of motor control.

Funding: CAPES

P15 - ADAM10 ENZYME INHIBITION INTERFERS IN THE PLASTICITY OF RETINOTECTABLE PROJECTIONS OF RODENTS

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Amyloid Precursor Protein (APP) is essential for biological processes such as synaptogenesis, cell survival and growth, and synaptic plasticity. Its proteolytic cleavage via the amyloidogenic pathway leads to the formation of Aβ, a constituent of the senile plaques, one of the markers of Alzheimer's disease. The non-amyloidogenic pathway leads to the formation of the soluble APP (sAPPα), peptide with neurotrophic properties. Our group has sought to understand the role of APP in central nervous system plasticity using the rodent retinocollicular pathway as a study model. Our mainly objective is to investigate the effects of inhibition of the main α-secretase, ADAM10, on the plasticity of ipsilateral retinocollicular fibers induced by monocular enucleation (ME). The experimental procedures of this work are in accordance with the Ethical Principles on Animal Experimentation of SBCAL and with the approval of the Committee of Ethics in Animal Research under No. 0020510. Lister hooded rats were used. Pharmacological inhibition of the ADAM10 enzyme was made through the intracanial implant of elvax, containing the selective inhibitor GI254023X in PND7. In the PND10 animals were submitted to ME. Experimental groups: ME with no elvax implant; ME and elvax implant containing DMSO (vehicle); ME and elvax implant containing the inhibitor at the concentration of 10 mM. After ME the survival time was 24h (PND11) or 18 days (PND28). The distribution of the ipsilateral terminals was examined in coronal cerebral sections after the intraocular injection of HRP and the expression of the proteins studied in the superior colliculus (SC) was evaluated by Western Blot technique. For the quantitative analysis, the ipsilateral total visual area of the SC was delimited, as well as the optical density of the bands obtained from the images of the Chemidoc apparatus. Our morphological data showed that animals submitted to ME only, showed, at PND11, an expansion of the retinal terminals to the dorsal regions of SC (n= 4). This effect was abolished in the presence of the inhibitor at the concentration of 10 mM (n= 3; p= 0.0126). Western blot analysis confirmed a significant reduction in ADAM10 (n= 3, $p<0.01$) and sAPPα (n= 4) levels in SC in the same survival. Our previous data at DPN28 suggest a return of sAPPα levels (n= 1) seen after ME, possibly indicating a loss of the inhibitory effect caused by GI. In conclusion, our data demonstrate that inhibition of ADAM10 causes a transient inhibition of ME-induced plasticity, confirming an essential role of sAPPα in the reorganization of ipsilateral retinocolicullar fibers.

Funding: CNPq, FAPERJ, CAPES, PROPPI-UFF

P16 - NUTRITIONAL RESTRICTION OF ÔMEGA-3 FATTY ACID ALTERS MICROGLIA AND INFLAMMATORY PROFILE IN THE VISUAL SYSTEM OF RATS DURING DEVELOPMENT

DB

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The relevance of lipids such as fatty acids (FA) is widely recognized in the literature, especially regarding the development of the central nervous system (CNS). The lipid composition of the FA n-3 and n-6 present in the diet directly affects the production and tissue addition of its derivatives, docosahexaenoic acid (DHA) and arachidonic acid (AA), respectively. These AGs are substrates for eicosanoids, which have several biological functions, such as synaptic plasticity and memory processes, pathological conditions and processes related to inflammation. Microglia is extremely dynamic and responsive to homeostatic changes that can lead to alteration of its motility, morphology and function, thus compromising the performance of crucial physiological tasks. In this work, using the visual system as a study model, we investigated the impact of dietary restriction of DHA on microglia and the possible effects of an early (P7 to P28) or late (P28 to P49) supplementation with fish oil (3g/Kg/day). The experiments were conducted according to the norms of use of laboratory animals in compliance with the protocol submitted to the ethical animal experimentation (CEPA-UFF) nº 0015009. Females of Lister Hooded rats received diet with soybean oil (n-3+) or coconut oil (n-3-) in the 5 weeks prior to mating and litters were used. In this work the techniques of gas chromatography, western blotting, immunofluorescence and RT-PCR were used. The weight gain of the animals remained unchanged in all experimental groups. Analysis of the FA profile indicated that the n-3- diet promoted a selective reduction in DHA content in the superior colliculus (CS) and in the retina and both supplementation windows were able to reverse these effects. During development, the n-3- group showed alterations in microglial morphology and increased levels of Iba-1 in the retina and CS. Preliminary data suggest that the n-3- group has elevated levels of the enzyme inducible nitric oxide synthase (iNOS) in the retina and CS, and early but not late supplementation seems to reverse this effect. Initial RT-PCR analyzes showed that the n-3- diet increased the levels of IL-6 in the retina at P14 and IL-1ß in CS at P7, P14 and P28, where early supplementation appears to reverse this effect. This study indicates that chronic dietary restriction of DHA may alter the correct course of CNS development since it interferes with the inflammatory pattern and the microglial population.
Funding: CAPES, CNPq, INCT-NIM

P17 - DEVELOPMENT OF RETINOCOLLICULAR PROJECTIONS AND DIFFERENTIATION OF POSTSYNAPTIC MARKERS IN A MODEL OF POSTNATAL HYPOTHYROIDISM.

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Thyroid hormones (TH) thyroxine (T4) and 3,5,3 '-triiodothyronine (T3) are essential for the normal development of the central nervous system (CNS). Congenital hypothyroidism represents the deficiency of TH in humans during the gestational and/or neonatal period and is related to severe forms of mental retardation in children. In this work, we have studied how TH deficiency interferes with neural circuits development using the visual system as a biological model. To induce hypothyroidism, developing rats were exposed postnatally to methimazole, a TH synthesis inhibitor, administered in the drinking water of dams just after offspring birth, so methimazole was continuously delivered through lactation until postnatal day (P) 14. Control animals received just

water. T3 and T4 hormones were measured by automated chemiluminescent assay. Anterograde neuroanatomical tracer mapped retinal projections to the superior colliculus. Western blot evaluated the content of NMDAR subunits (GluN1, GluN2B and GluN2A), AMPAR subunit GluR1 and postsynaptic density protein 95 (PSD95). GluN1 subunit expression was also observed by immunofluorescence. At P7, was observed an increase of subunit GluN1 in animals exposed to methimazole and a moderate decrease in T3 and T4 levels in serum. At P14, methimazole treatment promoted a robust reduction on T3 and T4 levels in serum which resulted in marked reduction in the density of retinal axons in the superior colliculus and a decrease in the content of GluR1. At P21, after treatment withdrawal at P14, was observed a decrease of GluN2A and PSD95. At P28, T3 and T4 levels are already restored and some of these results were reversed. The data suggest that the hypothyroidism during early development causes a malformation of retinocollicular projections. At P21, the animals exposed to methimazole until P14 presented diminished levels of proteins necessary for maturation of this topography, showing, therefore, a delay in the development. Only at P28, with the recovery of the T3 and T4 levels, the retinocollicular projections were similar to the control animals.

Funding: CAPES CNPq FAPERJ

P18 - METHODOLOGICAL ISSUES FOR SPEECHGRAPH ANALYSIS: IMPROVING A COMPUTATIONAL PSYCHIATRY TOOL FOR RESEARCH AND CLINICAL PURPOSES

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SpeechGraphs is a computational tool successfully applied to the differential diagnosis of psychosis based on the non-semantic structural analysis of speech graphs. This approach provides quantitative, fast, and low-cost measurements of clinical interest. To optimize it, some key methodological parameters need to be established. Here we aim to investigate specifically 1) the use of paragraphs, and 2) whether there is stability in speech connectivity measures from a longitudinal perspective. Speech samples from a previous study references (N=60 subjects, group Schizophrenia=20, Bipolar=20, Control=20) were analyzed with and without paragraphs to evaluate the impact of paragraphing on graph measures and diagnostic accuracy.. To assess the long-term stability of graph measures, we designed a longitudinal study with 12 sessions, each session with 3 time-limited verbal reports based on 3 recently seen affective pictures, (same content each session) during 3 weeks of follow up, repeating the same set of pictures 3 times, randomly. Paragraphing significantly changed graph connectivity measures such as the largest strongly connected component (LSC), with a clear impact on the difference between groups: with paragraphs, LSC Schizophrenia x Control: $p=0.0051$; without paragraphs, LSC Schizophrenia x Control: $p=0.7764$. The results show that the definition of paragraph breaks during an interview is crucial for the distinction between diagnostic groups. Our study points to the need of using time-limited reports with a standard methodology for paragraphing. We propose to use the standard we have so far adopted: Paragraphs correspond to moments of spontaneous speech interruption, followed by the interviewer's stimulation to maintain the conversation, thus generating additional speech samples produced by the patient.

Funding: Work supported by Boehringer-Ingelheim International GmbH (grant 270561), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), grants Universal 480053/2013-8 and 408145/2016-1 and Research Productivity 308775/2015-5 and 310712/2014-9; Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE); and Center for Neuromathematics of the São Paulo Research Foundation FAPESP (grant 2013/07699-0).

P19 - SLEEP AND LEARNING IN *OCTOPUS CF. VULGARIS* AND *OCTOPUS INSULARIS*

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Sleep is a behavior that occurs in several taxa of the animal kingdom, which suggests an early origin in the evolutionary chain of the metazoa. Although sleep is a well studied behavior in vertebrates, mainly in mammals, birds and reptiles, it is known that some invertebrates also show a comparable state of quiescence. The octopus is one of the invertebrates in which this behavior is expressed in a complex way, with behavioral and electrophysiological features that suggest the existence of at least two sleep stages. In addition, octopuses have the most complex nervous system among invertebrates, including a brain with a specific lobe for learning. In mammals, post-learning slow wave sleep (SWS) and rapid-eye-movement sleep (REM) have been shown to benefit memory consolidation. We set out to investigate the relationship between sleep and learning in the octopus. In this project we aim to investigate, classify and describe in detail the sleep states of Octopus cf. vulgaris and Octopus insularis through comprehensive behavioral quantification using video recordings. The O. insularis will also be exposed to both visual and vibratory stimuli during each identified sleep-wake state, to assess potential differences in the arousal threshold of each state. In addition, we also aim to evaluate whether young adults of these species are able to learn a novel task named "Russian dolls", which requires animals to sequentially open up to 3 different jars, one inside the other, one smaller than the other, with a reward (fish, mussel, crab or shrimp) inside the smallest jar. Preliminary results with O. cf. Vulgaris (n=5) and O. insularis (n=2) showed conspicuous behavioral variations during quiescence. Some of these variations have already been cited in the literature, such as the "half and half" body pattern, or "pale body color with narrow or completely closed eye pupils", but other changes have not been described yet, such as "body pattern alteration to dark color", "movement of one eye" and, in O. insularis, also a "REM-like" state that includes movement of both eyes, as well as rapid changes in the color and texture of the tegument. The sleep states "half and half", "pale body color with narrow eye pupils" and "REM-like" showed a significantly higher arousal threshold in comparison to the alert state. Interestingly, "half and half" had the lowest arousal threshold while the "REM-like" state had the highest. These results suggest the existence of at least 3 sleep stages in both octopus species. With regard to learning, we observed preliminarily that the octopuses were able to open the three jar types, as well as open the same jar in different manners, which emphasizes the behavioral and cognitive versatility of these animals. As a future perspective to this research, we are going to assess the expression of the immediate-early gene erk in the "half and half" sleep behavior. Besides, the sleep/wake cycles is also being investigated in the paralarvae of O. insularis with hatching time of 5, 6, 8, 9 and 14 days. We are describing the typical behaviors of these larvae and we want to see if there are differences in reaction to a light stimuli when they are in alert or in rest state.

Funding: CAPES

POSTER SESSION 2 (FRIDAY)

P20 - ANTICIPATED ITD STATISTICS ARE BUILT INTO HUMAN SOUND LOCALIZATION

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The variability of natural scenes places perceptual processes in the realm of statistical inference. Perceptual tasks may be optimized if the invariant statistical structure of sensory cues is built into the neural processing. We investigated this question in human sound localization. Localizing sounds in the horizontal plane relies on interaural time differences (ITD). We estimated components of ITD statistics from human head-related transfer functions (HRTFs), which can be assumed invariant across contexts. ITD varied with azimuth following a sigmoid relationship, whose slope was steepest at the center in most frequencies. In addition, ITD was more variable over time for sounds located in the periphery compared to the center, in a frequency-dependent manner. We tested the hypothesis that these statistics are anticipated by the human brain, influencing spatial discriminability and novelty detection. Previously reported thresholds for discriminating ITD changes were better predicted by a model relying on both ITD slope and variability than on ITD slope alone. Furthermore, mismatch negativity (MMN) brain signals, a pre-attentive index of deviance detection recorded in subjects undergoing a spatial oddball paradigm, were weighted by ITD slope and variability of the standard location. These results show that spatial discriminability thresholds and novelty detection are consistent with a representation of anticipated ITD statistics in the brain, supporting the hypothesis that high-order statistics are built into human perceptual processes biasing behavior.
Funding: personal.

P21 - HIPPOCAMPAL-PREFRONTAL INTERACTIONS DURING DECISION MAKING

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DB

The hippocampus has been linked to memory encoding and spatial navigation, while the prefrontal cortex has been associated with cognitive functions such as decision making. These two areas are hypothesized to communicate in tasks that demand both spatial navigation and decision-making processes, such as continuous alternation tasks. To test this hypothesis, we have analyzed LFP recordings collected from rats performing a spatial alternation task in an 8-shaped maze in which odor cues indicated the rewarded arm. To assess cross-regional interactions, we looked at power spectral decompositions and phase coherence between the regions. Although hippocampal spectral power analyses showed theta-frequency peaks (6-10 Hz) at specific spatial locations, such effect disappeared after controlling for speed. Coherence analyses were made using two approaches. In the first approach, we used concatenated time windows of 0.5 seconds centered at four different task events: trial start, choice point, turn and trial end. The second approach was more spatial-oriented, as we divided the locomotion trajectory into 20 spatial bins. In both methods, we found an increase in theta coherence between the two brain regions near the choice point, which could not be explained by changes in theta power. These results corroborate that the hippocampal-prefrontal network phase couples at theta frequency during decision making.
Funding: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES)

P22 - IDENTIFYING THE MECHANISMS FOR ZIKA VIRUS ENTRANCE AND SPREAD IN THE EMBRYONIC MOUSE BRAIN

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Background: Central nervous system (CNS) malformations related to Zika Virus (ZIKV) infection more often affect anterior structures, such as the cortex and the basal ganglia, whereas more caudal structures such as the cerebellum and brainstem are only affected in the most severe cases. There are some possible phenomena that can explain this effect, like viral tropism for anterior brain or anterior source for brain entrance in the brain. It is known that the amniotic liquid gets infected in pregnancies of ZIKV-derived microcephalies. Therefore, we hypothesized that the antero-posterior pattern found in human malformations derived from ZIKV is due to the entry of the virus through the embryonic olfactory system, which is in direct contact with the amniotic liquid. Objective: The aim of this project is to verify whether the ablation of the olfactory epithelium (OE), damaged by injection of zinc sulfate in the nostrils of post-natal mice, would prevent the virus entrance into the brain. In addition, we want to investigate the pattern of infection of the virus along the antero-posterior (A-P) axis of the CNS by identifying the cell types most affected by ZIKV. Methods: Animal experimentation use is approved by the Ethics Committee in Animal Experimentation of Universidade Federal do Rio Grande do Norte (UFRN), project number 004/2016. Mice colony is maintained at the Brain Institute, UFRN. We are using an isolated ZIKV lineage in Pernambuco in the year 2015. The pattern of ZIKV infection along the A-P axis is being characterized after injection in the amniotic liquid of E12 mice. We are using postnatal day 3 (P3) mice for the OE ablation assay. For ablating the OE, zinc sulfate solution (0.17M) is injected into the right nostril (approximately 5¤l). At P4, we are injecting ZIKV into the nasal route. Control animals receive saline instead of ZnSO4. Immunohistochemistry is performed with 4G2 antibody, which recognizes the envelope protein of flaviviruses. We are co-localizing this antibody with cell type-specific markers in coronal or sagittal whole head slices to preserve the olfactory pathway to the olfactory bulb. The infection of other brain regions, like the cerebral cortex, cerebellum and brainstem will be tested. Partial results and Conclusions: Our preliminary data demonstrates that ZIKV infects the OE and the fetal brain after injection in the amniotic liquid in at least three days post infection (dpi) but not earlier than 24 hours. The percentage of these cells that are postmitotic young neurons (Dcx+) in the OE is under 20 while in the olfactory bulb and cortical plate is about 50. At 3 dpi, brain parenchyma is infected while the proliferative zones have almost no ZIKV, suggesting that neurons are first infected and progenitors after. In the retina, 4G2 antibody labels the optic nerve and the ganglionic cell layer, suggesting that the virus infects first the diencephalon and gets to the retina through the nerve. These results suggest that the OE is a possible pathway for ZIKV embryonic brain infection and that the virus spread through the brain by using axons. For testing that, we are developing a model of postnatal ZIKV infection through nose injections. Six and ten days after injection in the P3 nostril, ZIKV is expressed in the olfactory epithelium of 50% and not in the brain (with the exception of few cells in the olfactory bulb of one animal). We observed ZIKV infected cells in the cerebral cortex and hippocampus of one animal 8 dpi. Although preliminary, these data suggests that the postnatal olfactory system is also susceptible for ZIKV and can be used in OE ablation experiments. In conclusion, our data shows that ZIKV infects the olfactory epithelium and this is a possible route of entrance of the virus into the brain. The temporal evolution of ZIKV expression through the brain suggests that the developing axons are used for transport.
Funding: CAPES; CNPq

P23 - INVESTIGATING HIPPOCAMPAL OSCILLATIONS OF RATS DURING AN ODOR DISCRIMINATION TASK

DB

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Some hippocampal oscillations are believed to play roles in cognitive tasks. The modulation of low-gamma (LG) and high-gamma (HG) amplitude by the theta phase has been suggested as a mechanism for switching from entorhinal cortex (EC) and CA3 inputs into CA1. Theta modulation of EC-driven HG would then favor memory encoding, while theta modulation of CA3-driven LG would favor memory retrieval. In this work, we further investigate this hypothesis by analyzing LFP oscillations recorded from CA3 and CA1 of rats performing an odor discrimination task. We found that theta oscillations in both regions gradually increase as the rat approaches the scented pot. On the other hand, the LG band presented an opposite trend, with a decrease in power near sniffing which was more evident in CA3. Interestingly, these differences were not apparent in the phase coherence between CA1 and CA3. Additional analysis separating the behavior response elicited after each sniff (i.e., digging the reward in the current pot or wandering to the other scented pot) showed no clear differences in LFP power. The previously described correlation between theta-LG phase-amplitude modulation and learning in this task, together with these preliminary results could represent a network change from a memory retrieval state (i.e., remembering which odor contained the reward) to an encoding state (i.e., identifying the sniffed odor).

Funding: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001

P24 - EXPRESSION PATTERN DESCRIPTION OF CHRNA2 POSITIVE CELLS IN MAIN OLFACTORY BULB

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Adult neurogenesis is a phenomenon that occurs in specific niches of the brain. New neurons are generated in adult life and added to pre-existing circuitry. The subventricular zone (SVZ) is the region around the lateral ventricles that serves as a niche for neural stem cells in adults. SVZ is where most of the adult-generated main olfactory bulb (MOB) neurons are generated. Different neuronal types are generated at segregated sites of the SVZ and can be classified by their calcium-binding proteins. The search for specific markers for each cell type is a constant within the field of neuroscience and allows detailed study of various aspects of specific cell types. We performed a pilot study of cell distribution using a conditional knock in mouse that expresses the protein Tomato in cells that express Chrna2 (alpha 2 subunit of the nicotinic acetylcholine receptor) at some point of their life. By using this animal, we have a unique opportunity to describe the neurogenesis of the cholinergic circuitry in the MOB. Therefore, P24 genetically modified mice (n=2) were used to express the Cre recombinase in Chrna2+ cells in order to recombine the genome and irreversibly release the expression of the red fluorescent protein Tomato. The animals were sacrificed and the olfactory bulb was left with paraformaldehyde 4% for 2 hours, placed in 30% sucrose solution for 24 hours and cut with a thickness of 30µm in a cryostat. The sections were stained with nuclear marker (DAPI) and Chrna2+ cells were counted manually at each layer of the MOB. A total of 1137 Chrna2+ cells divided between the layers of the olfactory bulb were counted. The inner plexiform layer and the mitral layer had the highest percentage of cells, 39.4 ± 8.5 % and 23.8 ± 3.9 %, respectively. In the external plexiform, glomerular and granular layers were found 17.6 ± 5.4 %, 10.1 ± 4.5 % and 9.1 ± 5.5 % of the cells respectively. The presence of Chrna2+ cells in the region of the rostral migratory pathway was not observed in the sections analyzed, suggesting that

either these neurons are not generated in adults or Chrna2 promoter is activated late in differentiation. In addition to the number of cells, morphological characteristics were also observed. Two main cell phenotypes were observed: horizontal cells with long dendrites and vertical cells. It is not yet known at which period of development these cells are generated and neither when they begin to express Chrna2 or the region where they are originated. From these preliminary data, there are perspectives for the study of this cellular population within the field of adult neurogenesis, mainly related to the temporal space characterization of its emergence. To continue this study, we will verify at what stage of development these cells are generated, whether they originate in a specific region of the SVZ, if they participate in the process of adult neurogenesis and if their appearance is influenced by the environment. Thus, we may try to elucidate what is its function in the olfactory bulb.

Funding: CAPES

P25 - INVESTIGATION OF THE BEHAVIORAL AND NEUROPHYSIOLOGICAL EFFECTS OF SEROTONERGIC AGONISTS IN THE RAT

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Among the psychoactive substances, the serotonergic agonists stand out due to their capacity of producing a highly altered state of consciousness accompanied by low toxicity and low effective dose. Little is known about the mechanisms underlying the effect of these drugs, especially at the electrophysiological level. In this project we investigate the effects of two serotonergic agonists - 5-MeO-DMT and N,N-Diethyllysergamide - on the rat's behavior and electrophysiology. Animals were implanted with electrodes in the dorsal hippocampus (HP) and prefrontal cortex (PFC) and injected with the either 5-MeO-DMT or N,N-Diethyllysergamide (i.c.v. or i.p.). At 15 minutes post-5-MeO-DMT injection, both i.c.v. or i.p., animals presented clear stereotyped behaviors (e.g., repetitive rotation around the body axis, headshaking movements, locomotion with the body collapsed on the cage's floor, backward or uncoordinated locomotion, etc). During this same period, absolute theta power in the HP decreased significantly in comparison to baseline levels. Nevertheless, theta power increased in relation to other frequencies, indicating a higher signal-to-noise ratio (i.e., the 1/f curve decreased except in the theta band). This effect was more prominent during states of reduced locomotion speed. We also observed a decrease in the comodulation between theta phase and high-frequency oscillation (HFO) amplitude in the HP, which possibly can be explained by a decrease in HFO power. In the PFC, differently from in HP, both absolute and relative theta power were decreased. Interestingly, coherence between PFC and HP increased in the theta range during the first 15 minutes following 5-MeO-DMT injection. Preliminary analysis of data from animals injected with N,N-Diethyllysergamide indicates similar results, showing the same increase in relative theta power found in HP. In order to dissect which signaling pathway underlies the effects observed, we are now investigating the effects of specific serotonergic antagonists. A more precise electrophysiological profile will be achieved by analyzing spiking activity (action potentials), and by controlling specifics states of behavior. We expect to shed new light on the mechanisms underlying the action of serotonergic agonists.

Funding: Capes/Cnpq/UFRN - Brain Institute

P26 - REPROGRAMMING OF ASTROGLIAL CELLS INTO NEURONS USING A COCKTAIL OF SMALL MOLECULES

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The reprogramming of different specialized cell types in others has been a field widely studied in recent years. More specifically, the generation of induced neurons (iNs) is used with the objective of applying these cells in the study of pathological models and in cellular therapy, focusing on the treatment of patients with neurodegenerative diseases or acute lesions in the central nervous system. Several methodologies have been used for this approach, including the reprogramming of cells from other lineages into neurons, either directly or indirectly. However, most of the cellular reprogramming protocols depend on the overexpression of ectopic genes, which may lead to other transient changes not desired in reprogrammed cells. In order to overcome these possible side effects, we investigated the possibility of reprogramming astrocytes from postnatal mice into neurons through the transient exposure of the cells to a cocktail of small molecules added to the cell culture medium. This cocktail includes molecules that act in different cellular pathways, among which the regulation of gene expression, the modulation of neurogenesis and the control of the cell cycle, previously been used in the reprogramming of fibroblasts into neurons. To demonstrate the phenotype of the cells after treatment with the cocktail, aspects such as the expression of typically neuronal and astrocytic proteins, morphology, survival, proliferation and gene expression were evaluated through the techniques of immunocytochemistry, time-lapse video-microscopy and RT-qPCR. Based on the data obtained it was observed that the drug cocktail used induced in the treated astrocytes an increase in the expression of genes related to the neuronal profile and a significant change in its morphology, although this is not typical of neurons. Thus indicating that the combination of small molecules used is not sufficient to effectively reprogram astrocyte cells into induced neurons.

Funding: Capes

P27 - HERITABILITY OF SOCIAL BEHAVIOR AND CHANGES IN NEURONAL COMPOSITION OF THE PREFRONTAL CORTEX IN AN ANIMAL MODEL OF AUTISM

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Autism comprises a heterogeneous group of disorders characterized by sensory, motor, language and mainly social deficits perceived early in childhood. Genetic and epigenetic factors, as well as environmental factors, are strongly involved in the predisposition to autism. Studies in animal models of the disease suggest that these same factors can alter the development of the central nervous system, modifying patterns of differentiation and neuronal maturation and generating a dysfunctional brain circuitry. Therefore, identifying the neural changes in the developing brain can provide clues about the causes and possible treatments of autism. Our group previously characterized the animal model induced by administration of VPA in pregnant rats. We demonstrated that VPA-exposed animals during pregnancy (F1VPA) exhibit "autistic" behaviors in postnatal life, such as hyper locomotion, prolonged stereotypy, and reduced social interaction. Histologically, we detected a reduction in the number of parvalbumin (PV)+ interneurons in the medial prefrontal cortex (mPFC) of these animals compared to controls. Considering the effects of VPA on chromatin structure and DNA methylation, we hypothesized that behavioral and histological changes observed in F1VPA animals would be transmissible for the next generation, independent of new VPA exposures. In this work, we analyzed the behavior and histology of mPFC in F1VPA

progeny, hereafter referred to as F2. We observed that these animals present a significant reduction in social interaction and in the frequency of exploratory surveys when compared to control animals. This reduction in social preference, however, was intermediate between that presented by control animals and F1VPA animals, with the latter showing the most severe deficit in social behavior. On the other hand, we observe neither hyper locomotion, nor alterations in the exploratory ambulation or stereotyped behaviors in F2 animals when compared to the controls. Locomotion, exploration and stereotypies had their profiles normalized with respect to F1VPA animals. In order to test whether behavioral impairments in F2 stemmed from differences in parental care of VPA mothers and control mothers on their offspring, we performed cross-fostering experiments. We observed that F2 animals cared for by control mothers presented low rates of sociability when compared to control animals cared for by control mothers, which corroborates the interpretation that the observed changes in F2 animals are from parental inherance. Histological evaluation of cortical tissue reveals alterations in the proportion of PV + interneurons in the mPFC of F1VPA animals. We also observed a slight increase in the total number of neurons in the CPFm of both F1VPA and F2 animals, suggesting that altered neuronal circuitry may be a common feature in these animals. Therefore, our data suggest that behavioral and histological alterations induced in rats by VPA treatment during embryogenesis can be partially transmitted to their descendants. However, no direct correlation could be established between social deficits and cellular changes in the mPFC, which may indicate that different changes in neuronal circuits are capable of producing the same behavioral effects. This model may contribute in the future to the identification of genetic signatures associated with the behavioral and histological changes observed in autism.

Funding: CAPES, CNPq, FINEP

P28 - ACUTE TREATMENT WITH A SEROTONERGIC AGONIST CAN IMPROVE LEARNING IN ADULT RATS 6 DAYS LATER.

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Research has shown that serotonergic agonists can cause changes in brain function that persist much after the acute effects. Moreover, several serotonergic agonists induce gene expression related to synaptic plasticity. The aim of this project is to assess whether different protocols of administration of the serotonergic agonists N,N-Diethyllysergamide can modulate learning in young (2 months) and adult (8-10 months) Wistar rats. Animals treated with different doses for one or three consecutive days were submitted to the object recognition task; training and testing were performed six days after drug administration. Five conditions were tested in the adult animals: (A) 1 day of treatment with 0.13mg*kg-1 of N,N-Diethyllysergamide; (B) 1 day of treatment with a tripled dose (0.39 mg*kg-1, n = 4); (C) 3 days of treatment with 0.13mg*kg-1 N,N-Diethyllysergamide; (D) control groups with 10ml*kg-1 of saline for 1 day; or (E) 3 days. The two groups of young animals comprised (F) 3 days of treatment with 0.13mg*kg-1 of N,N-Diethyllysergamide, or (G) saline. The results show that for both the young and adult groups, animals treated with N,N-Diethyllysergamide spent proportionally more time in the new object than animals treated with saline. Young animals performed better than old animals in all conditions except for group (A), which performed even better than the group of young animals treated with saline. Adult animals treated with saline groups spent less than 50% of the time exploring the new object, while all the other groups spent more than 50%; animals in groups (A), (F) and (G) spent more than 60 % of the time exploring the new object. Our results suggest that N,N-Diethyllysergamide improves the learning capacity and/or the preference for novelty. The fact that adult animals treated with N,N-Diethyllysergamide performed

better than young animals treated with saline suggests that this serotonergic agonist has potential for promoting a cognitive rescue of age-related deficits.
Funding: CNPq, Capes, Brain Institute (UFRN)

P29 - LOW DIMENSIONAL REPRESENTATION OF EEG RECORDINGS FOR THE DISCRIMINATION OF SLEEP STATES

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The sleep phenomena can be characterized by the spectral content and dynamics of neural activity. Electroencephalographic (EEG) recordings have been extensively used to describe sleep process, but some constraints (volume conduction, source summation, high dimensional data) limits the performance of EEG imaging. The present work proposes a low dimensional representation of 3 major stages -waking, N1 sleep and N2 sleep – with a consistent stage discrimination for different subjects and segments of 64-channel EEG recordings. Kernel Principal Component Analysis performed on selected frequency bands was used for dimensional reduction. Results agree with previous work, indicating that a low dimensional representation can effectively discriminate different states of the brain.
Funding: PNPD/Capes

P30 - MESENCHYMAL STEM CELL AND RESISTANCE EXERCISE MODULATE INFLAMATORY RESPONSE IN A BENEFICIAL WAY AGAINST ALZHEIMER DISEASE PATHOLOGY

DB

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The objective of this study was Investigate whether MSC hippocampal transplantation associated with resistance exercise would interfere in the inflammatory, immunoregulation and behavior responses of transgenic mice for AD. Double transgenic 6-7 month-old male mice APP/PS1 were used as Alzheimer's disease model, and wild type mice (WT) as controls. The mice were divided into six groups (n=15 each one): AD group (AD); AD submitted to MSC transplantation (AD+MSC); AD submitted to exercise program (AD+EX); AD transplanted with MSC and submitted to exercise (AD+MSC+EX); Wild Type group (WT); and WT submitted to exercise (WT+EX). MSC groups were transplanted with MSC bone-marrow of C57eGFP mice into the hippocampus. EX groups were submitted to resistance exercise protocol a week after transplantation, with progressive load for 4 weeks, 5 days/week. After exercise protocol, all animals were tested in Open Field (OF) and Object Recognize (OR) tests and then euthanized. Hippocampi were freshly removed for MAGPX essay for IL-1α, IL-6, IL-4, IL-10 and ELISA to amyloid beta, or perfused to be immunohistochemically processed for microglial Iba-1 marker and quantified by stereology. One way ANOVA showed that WT+EX decreased microglia number compared to WT group and AD groups treated with MSC transplantation increased this level against WT and AD groups (*P<0.0001); AD treated groups decrease IL-1α cytokine (*P<0.0001) and AD treated with exercise groups decreased IL-6 cytokine (*P<0.0001) compared to AD, approaching to WT group; AD+MSC group increase IL-4 cytokine (*P=0.0164) compared to WT group; WT+EX group increased IL-10 cytokine (*P=0.0008) compared to WT and AD groups; no changes were found in Aß protein; AD group presented higher exploratory behavior in rearing (*P=0.0032) and total (*P<0.0001) and peripheral (*P<0.0001) locomotion compared to

WT group and AD treated with exercise decreased this behavior approaching to WT. Student`s t test showed that WT groups, AD+MSC and AD+EX groups exhibited more contact exploration with the novel object compared to the familiar one (*P<0.05) and WT groups and MSC groups exhibited more time exploration with the novel object compared to the familiar one (*P<0.05). Our results suggest that MSC transplantation and resistance exercise can modulate microglia recruitment and the inflammatory response of the cytokines but were not able to decrease the amyloid beta protein. Nevertheless, these alterations may have led to decrease of the cognitive deficit observed in MSC groups in the OF and OR test. Our results bring therapeutic implications of both MSCs and resistance exercise approaches for the AD, as well as help to understand the probable mechanisms involved in the neurodegenerative process of the disease.

Funding: CAPES, CNPQ and FAPESP

P31 - PHASIC REM SLEEP EVENTS OPEN A GATEWAY FOR THE MEMORY-RELATED DIALOGUE BETWEEN HIPPOCAMPUS AND RETROSPLENIAL CORTEX

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We have recently showed that the retrosplenial cortex (RSC) shows a prominent theta oscillation during rapid-eye movement (REM) sleep, phase-locked to and guided by the hippocampal (HPC) theta rhythm, which modulates neuronal and high frequency oscillatory activity within the RSC. Since the hippocampal theta rhythm during REM sleep subsequent to contextual training is related to memory consolidation, in the present study we investigated whether the correlated activity of local field potentials (LFP) within the theta range between the RSC and the HPC changes immediately after contextual fear conditioning. We recorded from the RSC and the HPC of rats 3 hours before and after a contextual fear conditioning protocol (Shock), and from a control group in which rats were placed in the conditioning apparatus but no shock was given (Sham). We show that the theta directionality in Granger Causality (GC) during REM sleep between the HPC and the RSC persists from Pre to Post conditioning sessions for the Sham group. Conversely, in the Shock group, rats with poor retrieval when tested 24 hours after training increased GC for HPC leading the RSC theta rhythm, while animals that exhibited high retrieval showed a significant shift towards RSC leading the HPC. Moreover, the frequency and amplitude of GC peaks across REM sleep episodes are related to the GC shift found in the Shock group, and also to transient theta acceleration. Phasic REM sleep events are defined as transient periods during REM sleep with accelerated, high power theta oscillations related to increased correlation in the theta and gamma ranges across the tri-synaptic pathway. We found that during phasic REM events, the GC between HPC and RSC peaks irrespective of the direction. To the best of our knowledge, our results are the first direct evidence to suggest a functional relevance of phasic REM events for memory consolidation.

Funding: This work was supported by CNRS, Fondation pour la Recherche Médicale, Societé Francaise de Recherche et Médecine du Sommeil, University Claude Bernard of Lyon, CAPES/COFECUB (783/13) and Conselho Nacional de Desenvolvimento Científico e Tecnológico Grants 480875/2012-0 and 308775/2015-5 and, Fundação de Amparo à Pesquisa do Estado de São Paulo Grant 2013/07699-0 Center for Neuromathematics. CAPES PhD Scholarship.

P32 - EXPERIENCE-DEPENDENT PROTEOMICS OF THE HIPPOCAMPUS AND PRIMARY SOMATOSENSORY CORTEX ACROSS THE SLEEP-WAKE CYCLE

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Sleep comprises two main phases slow-wave sleep (SWS) and rapid-eye-movement sleep (REM). Both SWS an REM have been shown to be important for the consolidation of newly acquired memories through sleep-induced changes in neuronal activity and molecular cascades. Here we investigate the experience-dependent proteomics of the hippocampus (HP) and primary somatosensory cortex (S1) across the sleep-wake cycle using quantitative proteomic analysis of bottom-up shotgun mass spectrometry in a two-dimensional liquid chromatography-tandem mass spectrometry setup (MSE mode with label-free quantification). The brains were collected from rats exposed to novel objects for 10 min (+ groups), or from control rats not exposed to novel objects (- groups). The animals were kept awake for 3 hours and were killed after a criterion period rich in SWS or REM. Our preliminary analysis indicates that the brain proteome of the rats exhibits differences in numbers of proteins and phosphoproteins identified by STY tags (modification with phosphoryl), where a total of 343 validated proteins were identified in S1 of SWS rats, 118 in S1 of REM rats, 201 in the Hp of SWS rats and 82 in the HP of REM rats. The initial approach has been conducted comparing the proteomic profile of the treatments and regions (SWS+ x SWS-, REM+ x REM-, REM+ x SWS+ and REM- x SWS-). A comparison of the treatments identified 48 phosphoproteins significantly modulated. They were related to synaptic function, actin-microtubule regulation, DNA-RNA binding, proteases-phosphatases-kinases, cell death, cell membrane and other regulatory function. Interestingly, in the HP of rats exposed to novelty (comparison between REM+ and SWS+), there was a specific down-regulation of a portion of a calcium voltage-gated channel (Cacn2a). This modulation is a possible mechanism for the progressive hippocampal disengagement and cortical engagement in mnemonic processing induced by REM sleep. The analysis continues, using a variety of bioinformatics approaches and manual annotation. The identification of experience-dependent proteomic changes induced by specific sleep phases has potential to reveal major regulatory mechanisms that underlie the reverberation, storage, and propagation of memory traces during sleep.
Funding: CAPES, CNPq

P33 - COMPARING TWO DIFFERENT METHODS TO RECORD RESPIRATION IN FREELY MOVING RODENTS

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The recording of rodent respiration in freely moving animals is relevant to different subjects of study. In our lab, we use the concomitant recording of neural oscillations, vocalizations, whisker movement and respiration cycles to build a framework of how different sensorimotor rhythms are related to neural activity. Recent research has been providing evidence that rodent brain oscillations, such as delta (~0.5 to 4Hz) and theta (~4 to 10Hz), couples to respiration in different behavioral situations. This respiration entrained rhythm arises across different and relatively distant brain areas; it is dependent on the air flow input to the main olfactory epithelium and has been the subject of more than 15 relevant published studies in the last 5 years. Based on this, we predict an increase in the use of methods to record respiration in subsequent years; therefore, we decided to compare two methods used to record respiration cycles in

freely moving animals. We surgically implanted a rat with thermocouple and pressure cannula to analyze characteristics of acquired signals. We intend to show the strengths and weaknesses of both methods and shortly review the situations that they may be of use (from the study of sensorimotor rhythms to respiration coupled brain oscillations). We hope that this work will help researchers decide between both methods when planning their experiments.
Funding: CAPES, CNPQ, SERRAPILHEIRA INSTITUTE, UFRN

P34 - SOCIAL BEHAVIOR IN A NEONATAL RAT MODEL OF AUTISM

DB

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Recent studies demonstrated that adult animals pretreated with VPA during gestation present diminishment of social interaction, increasement of repetitive behaviors, anxiety and locomotor hyperactivity when adults. However, little is known about the dynamics of establishment of the behavioral repertoire in these animals during the postnatal period. The present study, thus, aimed to evaluate patterns of social and nonsocial behavior in rats pretreated with VPA over the postnatal ages PND7 - PND21. In addition, we sought to identify a simple phenotype indicator of the severity of the behavioral deficits by correlating these indices with a morphological marker, the tail curvature. For this, Wistar adult males and adult females were used to compose the parent couples of VPA and control rats. VPA rats and controls rats were generated from damns which received a single injection of valproic acid (500mg/kg, i.p.) or saline (0.15M NaCl) on gestational day G12.5, respectively. All animals from PND7 – PND21 were submitted to a free social interaction test, performed in a linear platform with transparent walls. Rat pairs (Control, n=44, control x control; VPA, n=46, VPA x VPA) were individually placed on each end of the apparatus (60cm x 10cm) and allowed to interact for 3 minutes. Each pair of rat performed only one trial and each trail was filmed by a high resolution camera and analyzed later in Kinovea software. The following behaviors were analyzed: crawling, walking, apparatus exploration, social interaction, self-grooming, allo-grooming, undercrossing and mounting. These behaviors were evaluated the occurrence, number of events, latency for onset and duration of behavior, and the experimenter had no knowledge of the experimental groups. Our results show that the emergence and expression of several social behaviors is gradual and follows a progressive time course in both controls and VPA. Although, we observed that many of them are altered in VPA animals in relative to age-matched controls. (1) VPA animals have greater locomotor activity than controls from PND 19; (2) VPA animals interact less socially from PND19; (3) VPA animals perform less allo-grooming than controls; (4) VPA and control animals present similar rates of self-grooming over the ages analyzed; and (5) subtle differences were observed in the number of mounts of one animal over the other and in the number of times an animal forced passage underneath each other. Therefore, this behavioral study over the postnatal period of breastfeeding suggests behavioral deficits that can be identified early, associated with treatment with valproic acid during gestation.
Funding: CNPq, CAPES

P35 - SPONTANEOUS OSCILLATORY ACTIVITY AND EVOKED RESPONSES IN THE SOMATOSENSORY CORTEX OF NEONATAL RATS EXPOSED TO VALPROIC ACID IN UTERO

DB

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During embryogenesis, immature neurons start developing membrane currents that populationally sum up into oscillatory patterns. The development of brain oscillations are influenced by a couple of key events, such as the functional maturation of excitatory and inhibitory circuitries, change in electrochemical potential of Cl-, and axon myelination. Although recently described in normal rats, the development of oscillatory patterns in animal models of autism is still poorly understood, and an opend field for searching for early pathophysiological biomarker. In the primary somatosensory cortex (S1) of neonatal mice (PND3), the occurrence of gamma oscillations is observed every 10-30 seconds on average. These oscillations are called early gamma oscillations (EGOs) and are functionally distinct from those found around P10, the so-called adult gamma oscillations. The occurrence of unusual oscillatory patterns in autism may imply the existence of neural circuitry impariments. In order to investigate oscillatory patterns in an animal model of autism induced by prenatal exposure to valproic acid (VPA) we set off to compare oscillatory patterns in S1 of experimental and control animals along along postnatal development. Wistar rats provided by the Brain Institute vivarium will be used to generate VPA rats, which will be implanted with a 4x4 array of micro-electrodes in S1 under urethane anesthesia. Spontaneous brain oscillations (LFPs; local field portentials) as well as stimulus (vibrissae stimulation)-evoked responses will be carried out at distinct postnatal ages. For data acquisition, we will used a digital pre-amplifier (RHA2000 system; Intan Technologies; A/D 16 bits; 0.1-7.5KHz filter; gain=200X) with sampling rate of 25 kHz. Data analysis will be performed through routines developed in our laboratory in the MATLAB program environment (MathWorks). Our goal is to quantify (1) gamma bursts and spindle bursts (frequency of events, power distribution, correlation between events), in the spontaneous recordings: and (2) evoked extracellular responses (amplitude and initial slope of the curve) and multiunitary activity (latency, firing rate distribution) following contralateral whisker stimulation with air puffs. Following the experiments, brains will be collected, washed in saline and fixated in formaldehyde for later histological analysis of the implant site.
Funding: CAPES, CNPq

P36 - THE EFFECTS OF EMBRYONIC EXPOSURE TO VALPROIC ACID ON THE DEVELOPMENT OF VOCALIZATIONS AND SOCIAL BEHAVIOR: A NEW AUTISTIC MODEL USING ZEBRA FINCH

DB

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Verbal communication is a key function often affected in several developmental neurological disorders, including autism spectrum disorder (ASD). In recent years, genomic approaches have revealed polymorphisms in ASD-linked genes. However, animal models approaching one gene at a time still fail to model broad spectrum disorders with a predominantly multigenic character such as ASD, and the species used, i.e. mouse and mouse, are not ideal for studying communication behaviors. Songbirds, on the other hand, are an important animal model for studying this behavior. Song learning and human speech acquisition share several characteristics, including a critical period for learning, and a circuit dedicated to the acquisition and production of vocal signals. Thus, songbirds can be an excellent model for studying neurobiological aspects related to speech in disorders such as ASD. In this work, zebra finch (Taeniopygia guttata) embryos were exposed to valproate (VPA) through intravenous injections. The chicks generated were exposed to only one tutor to evaluate the learning of the song. Although incomplete, our preliminary results indicate that VPA (5mg/kg) may alter vocal learning. This approach should contribute to a better understanding of how exposure to VPA during development results in communication defects in patients with ASD.
Funding: Instituto Serrapilheira, PROPESQ, CAPES.

P37 - ANALYSIS OF EEG MICROSTATE SEQUENCES TO STUDY SLEEP AND DREAMS

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Sleep and dreams are recurrent phenomena that intrigues researchers about its functions. The little knowledge about the neurophysiology of dreams makes its investigation harder. However, through specific electrophysiological patterns, sleep can be studied and classified in stages like N1, N2, N3 and REM. Nevertheless, the functions of these stages still are a matter of scientific investigation. This research project will try to investigate these functions by performing experiments involving videogames and sleep. During both activities, human male volunteers will be connected to an electroencephalography (EEG) equipment, which can measure electric signals produced by the brain. The brain signals of sleep and wakefulness will be compared, looking for similarities and its correlations with dream reports after sleeping for 2 hours. Comparing EEG data between sleep and wakefulness can be really hard, as those states are different in many fundamental ways. However, a growing number of scientific works are demonstrating the potential of an analysis method called EEG microstates to enable comparisons between many brain states. The method relies on previous discoveries about the brain. It has been shown that the distribution of electrical activity though the scalp can be summarized into 4 configurations, or states, with a small error. Because the duration of these states on average are on the range of 70 to 125 milliseconds, they are called microstates. With this rationale, this method transforms time series of many electrodes placed on the scalp into one sequence of 4 microstates. The sequences of these microstates and properties like duration, occurrences per second, and coverage percentage have already been shown to differentiate pathological states like schizophrenia, panic disorder and sleep stages like N2 from N1 and N3. This method will be applied to experimental data involving videogames and sleep. However, the experiments did not begin. For this, reason, this poster presentation is going to focus on the explanation about how the EEG microstate method works.
Funding: To buy EEG equipment and supplies, we had a funding from FUNPEC – Fundação Norte-Rio-Grandense de Pesquisa e Cultura.

P38 - PORTABLE DEVICES TO INDUCE LUCID DREAMS – ARE THEY RELIABLE?

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One of the main current challenges in lucid dreaming (LD) research is to develop a simple and reliable way to induce it. This is because, for most people, LD is very pleasurable but also very rare. Along with its hedonic nature, the potential clinical applications of LD – such as the treatment of recurrent nightmares in post-traumatic stress disorder (PTSD) – have attracted the attention of many high-tech companies, which have been launching portable LD-induction devices on the internet, some in crowdfunding platforms. These equipment capture brain waves for the online detection of rapid-eye-movement (REM) sleep, the sleep stage associated with typical dreaming. To induce lucidity, most devices provide visual and/or auditory stimuli without awakening the dreamer to serve as sensory cues, and some provide transcranial alternating current stimulation (tACS) of the frontal lobe. Here we reviewed 10 such devices: DreamLight, NovaDreamer, Aurora, Remee, REM dreamer, LucidCatcher, iBand, Neuroon, Aladdin and ZMax. We observed that only Neuroon, ZMax, iBand and Aurora provide minimal technical information on how their algorithm detects REM sleep

online, but none makes the data fully available. To date, only DreamLight has been empirically tested with published results. Better controlled validation studies are necessary to prove the effectiveness of LD induction devices.

P39 - ROLE OF THE CORTEX-HABENULA-RAFE CIRCUITRY IN AN AUTISM MODEL RAT'S SOCIAL BEHAVIOR

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Rats are eusocial animals that since the first weeks of life exhibit conspecifics directed behaviors. Among the most common behaviors are the emission of ultrasonic vocalizations in neonates, allo-grooming (conspecific cleaning) in infants, social play with vocalizations between juveniles, mating behavior with vocalizations, food preference transference and parental care. Despite the different types and contexts where they emerge, such behaviors are generated and regulated by a set of encephalic regions which activation dynamics varies according to the behaviors. Among these regions, we can highlight the hypothalamus (anterior hypothalamus, ventromedial hypothalamus and medial preoptic area), septum, prefrontal cortex (PFC) and midbrain nuclei (ventral tegmental area, VTA; locus coeruleus; raphe nuclei, RN and periaqueductal grey area) – the so called social brain network (SBN). The communication between these areas are essential for the proper expression of the social behaviors. Recent studies show that the lateral habenula plays an important role as a processing hub between the prefrontal cortex and the RN and VTA. Modulation of neural activity in the PFC and/or the lateral habenula significantly alters social behavior in rodents. However, little is known about the neuronal dynamics in the PFC-habenula-RN circuit. Therefore, our study aims to investigate the electrophysiological dynamics in this circuit in control juvenile rats and a rodent model of autism during social interaction tasks. Juvenile rats generated by prenatal exposure to valproic acid (VPA) will be individually monitored during postnatal development until postnatal day age 35 (PND35) (body weight, eye opening, neonatal vocalizations, olfactory memory and social recognition memory). At PND35, socially isolated animals and controls will be subjected to a social play task with an age- and sex-matched conspecific. Following the test, we will quantify the expression of the immediate-early genes c-fos and zif268 in the PFC, habenula, dorsal RN and ventral hippocampus. The same procedure will be applied to control animals. In a second set of experiments, electrophysiological and ultrasonic vocalization recordings will be carried out in juvenile rats during a social task. We will analyze oscillatory activity (LFP) and multiunit activity in the same previous regions and correlate with the behavior and vocalizations. Our preliminary results can be summarized as the development of a video-tracking system in real time to the extraction of behavioral parameters of the animal's behavior which allows us to carry out closed-loop experiments; recording and analysis of ultrasonic vocalizations from neonate animals; olfactory memory test and c-fos immuno-staining of brain tissue. Comparative results between the experimental and control groups will shown.

Funding: CNPq, CAPES

P40 - INVESTIGATING ZENK'S ROLE IN VOCALIZATIONS LEARNING AND MAINTENANCE.

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Memory formation requires gene expression triggered by neuronal activity. This response includes a series of activity-dependent genes that are thought to mediate the changes necessary for memory consolidation and maintenance. Among these genes,

zenk (a.k.a. egr1) was one of the first examples of a behaviorally driven gene and has been linked to memory formation in rodents. Nonetheless, the role of zenk in vocal learning, the exact behavior in which it was initially discovered as activity-dependent, remains unknown. To investigate the precise contribution of this gene for the acquisition and maintenance of song memories in zebra finches (*Taeniopigygia guttata*), we developed a dominant negative ZENK to manipulate the transcriptional activity of the endogenous protein, and identified a viral vector that efficiently infects the finch brain. Using these tools we found that normal ZENK activity is required for song maintenance in adults and song acquisition in juveniles. Moreover, our results show that ZENK blockade consistently leads to shortening of the song in manipulated birds compared to controls, suggesting that the maintenance of the tempo requires this activity dependent gene. Our findings provide for the first time a clear causal link between activity dependent genes and song learning and song stability. More importantly, they represent one of the first steps towards understanding the molecular processes involved in the acquisition, consolidation and reconsolidation of vocal signals, a process that is also required for human speech.

Funding: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)

P41 - LACK OF ORIENTATION PREFERENCE MAPS IN THE VISUAL CORTEX OF THE LARGE RODENT *DASYPROCTA LEPORINA*

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There is no evidence of orientation preference maps (OPMs) in rodent primary visual cortex such as in carnivores or primates. Nevertheless, orientation selective neurons have been found, though interspersed. Rodent data are mainly available for species with nocturnal or crepuscular habits and small brains, two factors that might contribute to develop a different functional architecture. Therefore, we investigated the functional properties of the primary visual cortex of agouti, a big rodent with diurnal habits, and a V1 size comparable to cats and small primates. We compared multi-site electrophysiological recordings using spatial arrays while visually stimulating with oriented gratings of several spatial and temporal frequencies in agoutis and cats. Although we detected highly orientation selective neurons with small receptive fields in agouti, lower selectivity than in cat recorded and analyzed in the same manner. In cats, compatible with continuous and modular orientation maps, orientation preference similarity decreased steadily between sites across the horizontal cortical axis. We found no such organization for agoutis, but a clustering of neurons with similar orientation preference for short ranges (< 250 μm). In conclusion, our results refute the conclusions of theoretical studies which pointed towards V1 size as a key parameter in determining the presence of OPMs, and are consistent with recent reports of orientation 'mini-columns' in mice, supporting that the rodents' interspersed organization is not random. Future research should aim to understand the circuits, which lead to small, selective receptive fields and great visual performance in agoutis while adopting a different functional architecture.

Funding: CAPES, CNPq

P42 - STEROLOGICAL ANALYSIS OF THE PRIMARY VISUAL CORTEX OF THE *DASYPROCTA LEPORINA*

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Theoretical studies hypothesized that the emergence of a columnar functional organization in the primary visual cortex (Area 17 or V1) could be related to the cortical volume, total cortical neurons or cell density in this region. It is very likely that the Dasyprocta species does not present large columns in their visual cortex. Several studies have used the Cavalieri method to estimate cortical volume, but there are no published studies which have calculated primary visual cortex's volume for Dasyprocta with this method. For Dasyprocta leporina there are no data on volume, neuronal density or cellular density of V1 at all. In this study we aimed to estimate the volume of Area 17 for the Daysprocta leporina. Our methods included area 17 volume estimation in 3 cerebral hemispheres using Nissl stained 50 µm thick sequential coronal sections and analyzing them with Stereo Zeiss Imager M.2 microscope and Stereo Investigator 10.0 software using Cavalieri stereological method. Our results are that Dasyprocta leporina's primary visual cortex has a volume of 545 mm^3 ± 42 mm^3, 25% ± 10% higher than described in a previous study for the Dasyprocta aguti. Because these are different species, there may be differences in the size of area 17. Also, the previously described animals had smaller visual cortex lengths in the macroscopic view in the anterior-posterior and latero-lateral axes than our animals. Our result indicates that large rodents could have a considerable V1 volume compared to other species such as cats and monkeys, without necessarily presenting columnar organization. Cellular and total neuronal density are paramount to infer about the arrangement of the V1 connections from a histological point of view.

Funding: This study was financed in part by the Conselho Nacional de Desenvolvimento Científico e Tecnológico - Brazil (CNPq).

(*) DB: Datablitz session.

ACKNOWLEDGMENTS

4th House Symposium of
the Brain Institute

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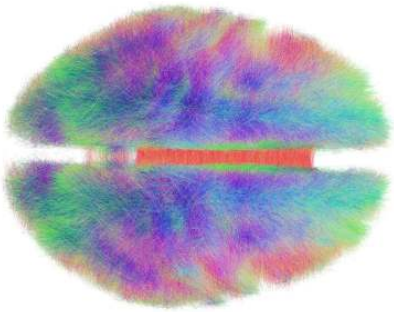

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