UNIVERSIDADE FEDERAL DO RIO GRANDE DO NORTE

INSTITUTO DO CÉREBRO

5TH HOUSE SYMPOSIUM

PROTECTING ICE FROM MELTING

INTERNATIONAL INSTITUTE OF PHYSICS

UFRN CAMPUS

NATAL

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60 ANOS

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GREETINGS

Another year has passed, and the Brain Institute at UFRN – fondly called "ICe" due to its name in Portuguese ("Instituto do Cérebro") – turned 8 years old (www.neuro.ufrn.br). The time has come to protect ICe from melting at its prodigious infancy, and to guarantee its continuous growth.

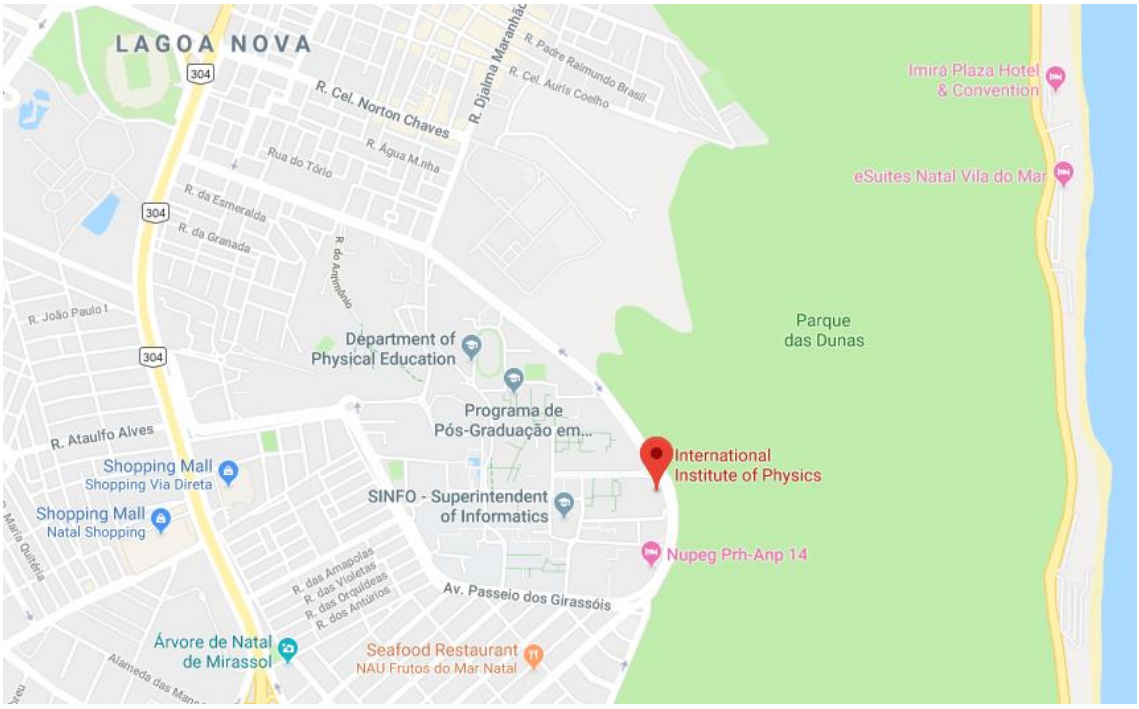
Amidst the severe cuts in Brazilian science budgets, the entire ICe community (from undergrads to graduate students, postdocs, technicians, PIs, secretaries, outsourced personnel, visiting scholars and collaborators) is looking forward to realizing the dream of moving into its permanent shelter soon: a brand new 5-story tall building (!) at UFRN campus. This years' theme – "protecting ICe from melting" – highlights our journey into a new home and our resistance in doing high-quality research in northeastern Brazil.

Our House Symposium is the yearly celebration of our existence and endurance, and the moment when the latest scientific discoveries of our research teams are shared with the community. It is also a great opportunity to mingle and open our doors to friends and collaborators in Natal and around the world, whom we also welcome to present their work.

Come join us in three exciting days of science, and let us all celebrate the beginning of the new ICe era at the bosom of UFRN!

The Organizing Committee

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



Program at a glance*

MONDAY, DECEMBER 2nd

13:30	Registration
14:15	Welcome and Introductory Remarks **Kerstin Schmidt** (Director of the Brain Institute)

Topic 1 – Vision & Vocalizations
Chair: Carolina Gonzalez

14:30	The visual gamma is now 30 years-old. Should we celebrate? **Sergio Neuenschwander**
15:00	What to expect? Perceptual priors implemented in early visual cortical circuits **Kerstin Schmidt**
15:30 – 16:00	**Coffee Break & Poster Session A**
16:00	Stability and instability of neuronal circuits and communication behaviors **Tarciso Velho**
16:30	Where is mummy? Dynamics of neonatal vocalizations in rats during maternal isolation **Rafael Bessa (Pereira Lab)**
17:00	Brain-wide imaging of the vocal communication network in a primate **Daniel Takahashi**

TUESDAY, DECEMBER 3rd

Topic 2 – Computational Neuroscience & Bioinformatics
Chair: Ignacio Gendriz

09:00	In silico structural study of neuronal ion channels modulation by general anesthetics **Letícia Stock (UnB)**
09:30	Molecular coevolution between neurotoxins and ion channels **Werner Treptow (UnB)**
10:00	**Data Blitz Session**
10:30– 11:00	**Coffee Break & Poster Session A**

11:00	Hippocampal-prefrontal interactions during decision-making **Lucas Tavares (Tort Lab)**
11:30	Pattern competition: a computational principle of memory **César Rennó Costa (IMD-UFRN)**
12:00 – 14:00	***Lunch break***

Topic 3 – Brain diseases & novel treatments
Chair: Bruna Landeira

14:00	Antero-posterior pattern of zika virus-derived microcephaly: a hypothesis for its origin and physiological consequences **Eduardo Sequerra**
14:30	The supramammillaro-dentate gyrus pathway: evidence for glutamatergic and GABAergic cotransmission and its reorganization in temporal lobe epilepsy **Monique Esclapez (INSERM)**
15:00	Transcriptional profile of adult brains and single neural cells identifies Alzheimer's disease genetic risk factors **Diego Marques Coelho (Costa Lab)**
15:30 – 16:00	**Coffee Break & Poster Session B**
16:00	Microscopic magnetic stimulation of neural tissue **George Nascimento (CT-UFRN)**
16:30	Anxiety-like behaviour induced by salicylate depends on age and can be prevented by a single dose of 5-MeO-DMT **Jessica Winne (Leão Lab)**
17:00	The antidepressant effects of ayahuasca: an update **Dráulio B de Araújo**

WEDNESDAY, DECEMBER 4th

Topic 4 – Swedish storm, sleep & memory
Chair: Andressa Radiske

09:15	Function of Dmrt3 spinal cord interneurons in locomotion **Jennifer Vieillard (Uppsala University)**

09:30	The functional role of Chrna2+ Martinotti cells **Anna Velica (Uppsala University)**
09:45	Hippocampal CA1 pyramidal cells heterogeneity: the deep and superficial **Lyvia Petiz (Uppsala University)**
10:00	Organization and function of OLMα2 cell circuits in the hippocampus **Angelica Thulin (Uppsala University)**
10:15	OLMalpha2 cells role in hippocampal mnemonic-emotional interactions **Samer Siwani (Uppsala University)**
10:30 – 11:00	**Coffee Break & Poster Session B**
11:00	Neuronal network of paradoxical (REM) sleep and its implication in learning and memory and sleep pathologies **Pierre-Hervé Luppi (Centre de Recherche en Neurosciences de Lyon)**
11:30	Semantic and affective measures of memory reverberation diverge at dream onset **Natália Mota (Ribeiro Lab)**
12:00 – 14:00	***Lunch break***

Topic 5 – Zebrafish, tinnitus & network circuits
Chair: Geissy Araújo

14:00	Neural mechanisms of behavioral individuality in zebrafish **Carlos Pantoja (UnB)**
14:30	Zebrafish: tool of great promise **Ana Luchiari (CB-UFRN)**
15:00	Zebrafish locomotion – from circuit to behaviour **Henrik Boije (Uppsala University)**
15:30 – 16:00	**Coffee Break**
16:00	Possibilities of tinnitus treatment for human patients with chronic tinnitus **Marine Rosa (UFPB)**
16:30	Activity dependent modulation of auditory networks in noise-induced tinnitus **Katarina Leão**
17:00	Inhibitory interneurons next to principal cells – what do they do? **Klas Kullander (Uppsala University)**
	Concluding Remarks – To be followed by a Happy Hour at Bar 54

* The Program at a Glance is subject to change

ORAL PRESENTATIONS

OR01 - THE VISUAL GAMMA IS NOW 30 YEARS-OLD. SHOULD WE CELEBRATE?

Sergio Neuenschwander (Brain Institute, UFRN, neuenschwander@neuro.ufrn.br)

In 1989, Gray et al. published a seminal article (4.7 K citations) on the synchronization of gamma responses in the visual cortex. Although the study was done in anesthetized cats, it addressed hard questions on Vision, with upshots to all cognitive sciences. How the brain encodes stimulus global properties? What are the mechanisms that coordinate distributed network activity underlying a single, unified percept? How to explain consciousness? After 30 years, several experimental studies in animals and human subjects found evidence that gamma is key to cognitive functions, such as visual binding, attention, and memory. However, many others failed to do so. As I will review in my talk, most evidence in support of the gamma synchronization hypothesis was based on studies that used simplified stimuli, such as gratings and bars. More naturalistic approaches led to diverging conclusions. Recently, In our laboratory, we showed that gamma is strong for optimally oriented gratings, but it is surprisingly absent during free viewing of natural images. These findings weaken the notion that gamma is necessary for visual encoding in natural conditions. Yet another possibility is that gamma synchronization is fundamentally volatile and non-stationary. Rapid fluctuations between coherent and incoherent states may be essential for controlling the flow of information in the brain. Beyond regular oscillations, such a complex, high-dimensional dynamics depends on large-scale, recurrent networks and may provide the computational framework necessary for perceptual binding, learning, and, ultimately, conscious experience. (Funding: CNPq; CAPES; UFRN).

OR02 - WHAT TO EXPECT? PERCEPTUAL PRIORS IMPLEMENTED IN EARLY VISUAL CORTICAL CIRCUITS

Kerstin E. Schmidt (Brain Institute, UFRN, kschmidt@neuro.ufrn.br)

Morphological and functional homologies between the lateral intrinsic and callosal networks in early visual areas are discussed. Both networks selectively link distributed neuronal groups with similar response properties and the actions exerted by callosal input reflect the functional topography of those networks. Reversible deactivation studies in cats strongly support that close to the vertical meridian representation callosal networks perpetuate intrinsic networks. Electrophysiological recordings and voltage-sensitive dye imaging demonstrate that both stimulus-driven and spontaneous activity of neurons that prefer potentially “midline crossing” features receive stronger influence by contralateral input. In particular, callosal connections seem to facilitate interactions between neurons with receptive fields along potential motion or (shape) trajectories crossing the visual field’s midline before a stimulus arrives. We propose that in cats, feature-selective lateral connections in general might exhibit a “cardinal bias” to interconnect neurons preferring vertical and horizontal contours. Those connections could support a spontaneously active network which pre-activates neurons along motion or shape trajectories frequently occurring in daily vision. We compare the cardinal bias of cats to the orientation and direction selectivity bias in a big rodent (Dasyprocta agouti). (Funding: UFRN).

OR03 - STABILITY AND INSTABILITY OF NEURONAL CIRCUITS AND COMMUNICATION BEHAVIORS

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

Insights into the function of neural circuits that control human speech development can be gained by studying songbirds as a model organism. Songbirds serve as a useful model because song-development and speech acquisition share several features, including a critical period of vocal learning, the requirement of intact hearing, the existence of social contingencies for normal learning, and a set of circuits dedicated for learning and production of vocalizations. Additionally, the small size and the fact that they breed well in captivity makes songbirds a tractable model for laboratory research. In the past few years, we have developed a series of tools and techniques that enable the manipulation of specific cell types within the song system as well as techniques such lentivirus-mediated transgenesis, to study song learning in a transgenic setting. Using these newly developed tools, we have successfully generated mutant zebra finches, a songbird species, that show abnormal vocal development and fail to completely consolidate their song. Interesting, these mutants also fail to express preference for the father song, indicating an altered social bond between father and progeny. In addition to transgenesis, we have also used genetic tools to manipulate specific neuronal classes to study the mechanisms involved in the maintenance of the song motor programs. More specifically, we have used a combination of acute and chronic genetic manipulations, as well as chemogenetics to perturb activity of individual neurons, coupled with calcium imaging in live behaving animals and extensive behavioral analysis of vocal signals. Our results indicate that the ensemble rather than individual units (neurons) are fundamental to generate stable motor outputs. (Funding: Instituto Serrapilheira; EDGE-NIH).

OR04 - WHERE IS MUMMY? DYNAMICS OF NEONATAL VOCALIZATIONS IN RATS DURING MATERNAL ISOLATION

Rafael Bessa (Brain Institute, UFRN, rafaelsbessa@neuro.ufrn.br)

Autism is a heterogeneous developmental disorder in which neural circuits involved in social cognition and sensory processing are dysfunctional. Vocal production plays a central role in social bonding in many mammalian species. Although not considered a communication mode acquired by learning, rat ultrasonic vocalizations (USVs) are produced at all developmental stages (from pups to adulthood), in distinct social contexts, conveys distinct emotional states and seem to have defined neurochemical routes. Pup USVs, in particular, are the earliest forms of emissions and occur when pups are found isolated from their mothers. Rodents exposed to valproic acid (VPA) during embryonic development reproduce many of the behavioral and physiological alterations observed as autistic endophenotypes. Mice prenatally exposed to VPA emit fewer USVs at postnatal day 8 (P8) as well as rats at P7 compared to controls, although there is still no study reporting the development profile of USVs in this model of autism. Our study, therefore, aimed to analyze the dynamic of USV production in VPA-treated rats from P7 to P21. Adult female Wistar rats received a single dose of VPA (500mg/kg, ip. in saline) at gestational day 12.5. At age P7, P14 and P21 pups were put in an acoustic isolated box with red light and an ultrasonic microphone (Dodotronics; Ultramic250K) positioned 18 cm above. For 300s, USVs were recorded using the software Audacity, with a sampling rate of 250 kHz. USVs were analyzed in MATLAB. We used an entropy-based method for USVs identification. After that we clusterized and classified the USVs using DeepSqueak, a deep learning-based method. Our results shown that VPA pups emitted less USVs in at P14, but no difference was found in P07 or P21. We also analyzed the total time that pups expended vocalizing. No difference was observed between VPA and control. With DeepSqueak we classified the USVs in 11 types using a supervised learning

method. We compared the relative frequency of occurrence for each type of USV at the ages investigated. From our USV classification, we found that control animals exhibit more types of USVs than VPA animals at P14. Our result showed that VPA-treated animal emmits fewer USVs and shows a less diverse vocabulary at P14 than control animals. (Funding: CAPES).

OR05 - DYNAMIC FUNCTIONAL ULTRASOUND IMAGING OF SOCIO-VOCAL NETWORK IN MARMOSET MONKEYS

Daniel Takahashi (Brain Institute, UFRN, takahashiyd@neuro.ufrn.br)

Vocal communication is the quintessential form of social interaction. Humans and other animals coordinate their social behaviors by producing and perceiving distinct vocalizations. Brain networks related to vocal communication include areas at the intersection of social behavior and vocal production-perception networks. Recent studies of primate vocal communication focused on lateral cortical regions, despite the fact that medial cortical and subcortical areas constitute the main vocal production and social behavior network (SBN). Hence, we aim to describe the brain-wide network underlying social communication focusing on the role played by medial cortical and subcortical areas. We use as our model the marmoset monkey, a highly vocal New World species. To image large-scale neural activity, we use functional ultrasound imaging which has a large spatial coverage and high spatio-temporal resolution. Furthermore, we built a stochastic dynamical systems model of vocal behavior that interacts with the marmoset in a closed-loop to fully control the vocal interaction and make quantitative predictions about brain dynamics during communication. We first show the existence of a medial brain system at the intersection of vocal production-perception and SBN; we call it the socio-vocal network (SVN). These areas differentially respond to affiliative vocalizations—contact, trillphee, and trill calls—produced in different contexts, exhibiting the highest and quickest response to contact calls. Given that the contact calls reflect the highest arousal state of the vocalizing animal, this is consistent with the hypothesis that SVN is related to the monitoring of others motivational state through vocalization. Second, through a closed-loop interaction between the computational model and a marmoset, together with large-scale functional imaging, we found that the marmoset anterior cingulate cortex (which is part of SVN) and the model's "SVN" are entrained. These results demonstrate what the SVN encompasses and its roles in vocal communication.

OR06 - IN SILICO STRUCTURAL STUDY OF NEURONAL ION CHANNELS MODULATION BY GENERAL ANESTHETICS

Letícia Stock (UnB, leticia.stock@gmail.com)

General anesthesia can be induced by chemically diverse molecules. Despite general anesthetics (GA) being routinely used and a fundamental asset to modern medicine, the molecular mechanism leading to the endpoint of general anesthesia remains unknown. GAs have been shown to modulate numerous membrane proteins. Yet, a complete understanding of how ligands modulate their protein receptors requires knowledge of their molecular bound-structure. The latter, has proven to be technically difficult to perform experimentally: although chemically unrelated, general anesthetics are typically small, mostly apolar compounds, with small masses and high dissociation constants. What is more, evidence suggests that modulation likely involves GA binding to multiple protein sites. One target of GAs, evidenced by both electrophysiology and in vivo experiments, is the neuronal voltage-gated potassium channel Kv1.2. Investigations on Kv1.2 modulation by the GA sevoflurane, suggest the molecule potentiates Kv1.2 by

binding to multiple independent sites, increasing channel's open-probability and maximum conductance. To clarify how GAs can modulate ion channels, we perform massive flooding molecular dynamics simulations. The molecular system consists of membrane-embedded Kv1.2 either in the open (conductive) or in the closed (non-conductive) conformation, both in the presence of fixed sevoflurane concentration. Control simulations are also performed in the presence of propofol, a volatile general anesthetic that does not modulate Kv1.2. Analysis show that while sevoflurane binds to both open and closed channel structures, the average bound number is consistently higher in the open conformation. Interestingly, propofol also binds to Kv1.2, though without any conformational dependence. Altogether, results support a structural premise of allosteric modulation, according to which small ligands are able to impact protein function by shifting conformational equilibrium of the receptors. From a thermodynamic perspective this can be explained by the more favorable binding of ligands to selected states – thus increasing their stabilization. The generality of the hypothesis is powerful as it could be used to help explain modulation of diverse set of systems. (Funding: CAPES; FAPDF).

OR07 - MOLECULAR COEVOLUTION BETWEEN NEUROTOXINS AND ION CHANNELS

Werner Treptow (UnB, treptow@unb.br)

Here, we present and discuss the contributions of coevolutive, evolutive and stochastic information in determining protein-protein interactions (PPIs) based on primary sequences of two interacting protein families. Specifically, under the assumption that coevolutive information is imprinted on the interacting amino acids of two proteins in contrast to other (evolutive and stochastic) sources spread over their sequences, we dissect those contributions in terms of compensatory mutations at physically-coupled and uncoupled amino acids. We find that physically-coupled amino-acids at short range distances store the largest per-contact mutual information content, with a significant fraction of that content resulting from coevolutive sources alone. The information stored in coupled amino acids is shown further to discriminate multi-sequence alignments (MSAs) with the largest expectation fraction of PPI matches – a conclusion that holds against various definitions of intermolecular contacts and binding modes. When compared to the informational content resulting from evolution at long-range interactions, the mutual information in physically-coupled amino-acids is the strongest signal to distinguish PPIs derived from cospeciation and likely, the unique indication in case of molecular coevolution in independent genomes. Applications to molecular interactions of neurotoxins and ion channels as an important case of molecular coevolution in independent genomes will be further presented. (Funding: CAPES; FAPDF).

DB

OR08 – DATA BLITZ SESSION

See poster abstracts with the "DB" mark on the left

OR09 - HIPPOCAMPAL-PREFRONTAL INTERACTIONS DURING DECISION-MAKING

Lucas Tavares (Brain Institute, UFRN, lucastavares@neuro.ufrn.com)

The hippocampus has been linked to memory encoding and spatial navigation, while the prefrontal cortex is frequently 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. However, the electrophysiological signatures associated with this interplay remain to be elucidated. To investigate the

dynamics of the hippocampal-prefrontal interactions, we have analyzed local field potentials (LFPs) previously recorded from rats performing a spatial alternation task in an 8-shaped maze (Fujisawa et al., 2008). We found that in this task, both theta (6-10 Hz) and beta (23-30 Hz) phase coherence peak around the choice point area of the maze. Also, that Granger Causality measures point to a hippocampus->prefrontal cortex directionality of information flow, peaking at starting areas of the maze. Additionally, we present spatially selective profiles of cross-frequency coupling within and between the two regions. In all, our results reveal maximum electrophysiological interactions between the hippocampus and the prefrontal cortex near the decision-making period of the spatial alternation task. These results corroborate the hypothesis that the dynamic interplay between these two regions is essential for cognitive processes. (Funding: CAPES).

OR10 - PATTERN COMPETITION: A COMPUTATIONAL PRINCIPLE OF MEMORY

César Rennó Costa (IMD, UFRN, cesar@imd.ufrn.br**)**

On the path for understanding the brain's processes, one needs to identify the algorithms that rule the observed phenomenology. As a classical case, cell assembly is a group of neurons with a shared spatiotemporal structure of the activation that has been associated with the representation of percepts and concepts in the brain. Two algorithms that transform cell assemblies, namely pattern completion and pattern separation, have been widely used to describe network functions and mnemonic processing. Inspired on a decade of modeling work of local brain networks, I reinterpret these algorithms as a competitive rule, coined as pattern competition. I use the new terminology to describe a series of experiments and observations within a unified and simple framework. (Funding: CNPq; BRAIN Initiative).

OR11 - ANTERO-POSTERIOR PATTERN OF ZIKA VIRUS-DERIVED MICROCEPHALY: A HYPOTHESIS FOR ITS ORIGIN AND PHYSIOLOGICAL CONSEQUENCES

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

In 2015, an outbreak of zika virus (ZIKV) in Brazil caused the birth of thousands of microcephaly cases. Although those children have a malformed prosencephalon, their rhombencephalon may have a normal development. Here, we tested the hypothesis that ZIKV entered the embryonic brain by infecting the amniotic fluid and subsequently the olfactory pathway, entering the brain through its anterior-most structure. In order to test that, we injected ZIKV in the amniotic fluid of E13 mice. 3 days post-infection (dpi) embryos displayed an infected olfactory epithelium but not the brain. At 6dpi, the olfactory bulb and brain were infected. Those data suggest that the pattern of ZIKV infection correlates with an entrance through the olfactory bulb. To estimate the physiological consequences of having malformed rhombencephalon, we analyzed computed tomography and electroencephalography (EEG) findings of 31 children with microcephaly. Children that had atrophy of rhombencephalic structures, like the cerebellum and brainstem, displayed epileptic activity in their EEG recordings, while 60% of these with normal rhombencephalon did not (Fisher's exact test; p= 0.0014, OR=33.8). These data suggest that the more posterior ZIKV-induced malformation is observed, the more severe brain physiological consequences for brain functions are seen. The understanding of the mechanisms through which ZIKV enters the embryonic brain will be important for the design of preventive strategies in infected pregnant mothers. (Funding: CAPES; ICGBE).

OR12 - THE SUPRAMAMMILLARO-DENTATE GYRUS PATHWAY: EVIDENCE FOR GLUTAMATERGIC AND GABAERGIC COTRANSMISSION AND ITS REORGANIZATION IN TEMPORAL LOBE EPILEPSY

Monique Esclapez (INSERM, monique.esclapez@univ-amu.fr)

In mesial temporal lobe epilepsy (MTLE), spontaneous seizures originate from a multi-structural epileptogenic zone, including several regions of the limbic system connected to the hippocampal formation. The supramammillary nucleus (SuM) is the main subcortical region innervating most limbic cortices including the dentate gyrus (DG). This hypothalamic nucleus could play a crucial in the control of several hippocampal-dependent activities and associated functions, including theta rhythms, sleep as well as emotional learning and memory, known to be altered in MTLE. We have shown in rat as in mouse, at the anatomical level and physiological level using optogenetic, that the neurons from the lateral region of the SuM (SuML) innervating the dorsal DG display a unique dual glutamatergic and GABAergic neurotransmittion phenotype. These SuML-DG neurons co-express markers for both glutamatergic (vesicular glutamate transporter 2; VGLUT2) and GABAergic (glutamate decarboxylase 65, GAD65 and the vesicular GABA transporter, VGAT) neurotransmission, establish asymmetric (excitatory) and symmetric (inhibitory) synapses on DG cells and co-release glutamate and GABA that simultaneously depolarize and hyperpolarize the DG granule cells. Selective activation of these SuML-DG neurons increase theta power and frequency as well as gamma power in the DG specifically during REM sleep and increase the activity of a subset of DG granule cells. We further demonstrated that this pathway is reorganized in experimental MTLE establishing additional and aberrant synaptic contacts on dentate granule cells (Pilocarpine model induced in rat or mouse). We will discuss whether the plasticity of the SuML-DG pathways contributes to the epileptogenic network in MLTE by triggering spontaneous seizures, according to the vigilance states of the animal.

OR13 - TRANSCRIPTIONAL PROFILE OF ADULT BRAINS AND SINGLE NEURAL CELLS IDENTIFIES ALZHEIMER'S DISEASE GENETIC RISK FACTORS

Diego Marques Coelho (Brain Institute, UFRN, diegomscoelho@neuro.ufrn.br)

Alzheimer's disease (AD) is the leading cause of dementia in aging individuals. Several studies have shown that 60-80% of AD attributable risk has an important genetic component. Therefore, the identification of AD risk factors is a fundamental step towards a comprehensive understanding of AD pathogenesis and to develop novel diagnostic assays and treatments. In recent years, genome-wide association studies (GWAS) and whole exome sequencing (WES) have revealed 45 genes/loci associated with the risk of developing AD. However, identifying candidate genes responsible for this association in some loci remains a major challenge. In this work, we hypothesized that the transcriptional profile of whole tissue and single-cells isolated from AD brains could contribute to isolate genes most likely associated with the disease. Thereby, using already published datasets, we found AD-related gene signatures throughout different brain areas. Moreover, we indicated alternative-splicing mechanisms that can possibly affect AD disease. We also highlighted that AD risk genes are expressed by different neural and non-neural cell types in the adult human brain. Co-expression networks reveal that these genes are highly associated with protein networks involved in synaptic transmission. Notably, co-expression networks are slightly different in AD and control subjects, likely reflecting changes in AD risk gene expression. (Funding: CAPES; IMD; UFRN).

OR14 - MICROSCOPIC MAGNETIC STIMULATION OF NEURAL TISSUE

George Nascimento (CT, UFRN)

Transcranial Magnetic Stimulation (TMS) is a non-invasive tool for electric stimulation in the brain which can cause neurons to fire, and gradually is becoming useful for the investigation and study of the human brain. The basic principles of TMS, an example of its application in neuroscience and complete design of a system for use in small animals will be shown. Our homemade system is able to deliver coil currents pulses up to 3,9kA, stimulus up to 119V/m and initial use of this technology to investigate the action of TMS at the cellular level and to dendric activity on the auditory cortex will be discussed. (Funding: CNPq; CAPES).

OR15 - ANXIETY-LIKE BEHAVIOUR INDUCED BY SALICYLATE DEPENDS ON AGE AND CAN BE PREVENTED BY A SINGLE DOSE OF 5-MEO-DMT

Jessica Winne (Brain Institute, UFRN, jessica.winne1@gmail.com)

Salicylate intoxication is a cause of tinnitus and comorbidly associated with anxiety in humans. In a previous work, we showed that salicylate induces anxiety-like behavior and hippocampal type 2 theta oscillations (theta2) in mice. Here we investigate if the anxiogenic effect of salicylate is dependent on age and previous tinnitus experience. We also tested whether a single dose of DMT can prevent this effect. Using microwire electrode arrays, we recorded local field potential in young (4-5- month-old) and old (11-13-month-old) mice to study the electrophysiological effect of tinnitus in the ventral hippocampus (vHipp) and medial prefrontal cortex (mPFC) in an open field arena and elevated plus maze 1 hr after salicylate (300 mg/kg) injection. We found that anxiety-like behaviour and theta2 increase (4–6 Hz) following salicylate pre-treatment only occurs in young (normal hearing) mice. We also show that theta2 and slow gamma oscillations increase in the vHipp and mPFC after salicylate injections in anxiety tests in a complementary manner. Finally, we show that pre-treating mice with a single dose of the hallucinogenic 5-MeO-DMT prevents anxiety-like behaviour and the increase in theta2, slow gamma after salicylate injection in normal hearing young mice. This work further supports the hypothesis that anxiety-like behaviour after salicylate injection is triggered by tinnitus and require normal hearing. Moreover, our results show that hallucinogenic compounds can be effective in treating tinnitus-related anxiety. (Funding: CNPq; CAPES; American Tinnitus Association).

OR16 - THE ANTIDEPRESSANT EFFECTS OF AYAHUASCA: AN UPDATE

Dráulio B de Araújo (Brain Institute, UFRN, draulio@neuro.ufrn.br)

Since 2006 our group has been investigating the effects of ayahuasca. Our studies aim to explore the basis of the acute and sub-acute effects of ayahuasca both in healthy controls and in patients with major depression. In a first open trial, seventeen patients with treatment-resistant depression attended a single dosing session with ayahuasca. Depression severity was accessed by two psychiatric scales (HAM-D and MADRS), before, during and after dosing. We also used Single Photon Emission Computed Tomography (SPECT) 8 hours after dosing to look for sub-acute changes of cerebral blood flow (CBF). A follow-up randomized placebo-controlled trial (RCT) was conducted in thirty-five patients with treatment resistant-depression and fifty healthy individuals. All participants were evaluated at baseline and one day after dosing to explore the effects of ayahuasca on a number of measurements, including psychiatric scales and questionnaires, and biochemical markers (cortisol, BDNF), and functional neuroimaging

(fMRI). Both the open-label and RCT showed a significant antidepressant effect of ayahuasca already 40 min after intake, which remained significant at all endpoints up to 21 days after dosing (open-label) and 7 days after dosing (RCT). Suicidality was also significantly reduced after dosing. We found basal hypocortisolemia and blunted awakening salivary cortisol response in patients with depression, compared to healthy controls. After dosing with ayahuasca, awakening salivary cortisol response was regulated to normal levels. We observed higher BDNF levels in both patients and controls that ingested ayahuasca when compared to placebo, and a significant negative correlation between BDNF levels and depressive symptoms in patients treated with ayahuasca. Evidence presented here offer good support for the antidepressant effects of ayahuasca when dosed in an appropriate setting. (Funding: CNPq; CAPES).

OR17 - FUNCTION OF DMRT3 SPINAL CORD INTERNEURONS IN LOCOMOTION

Jennifer Vieillard (Uppsala University, jennifer.vieillard@neuro.uu.se)

The vertebrate's locomotor CPGs are neuronal networks located in the ventral spinal cord and that are responsible for controlling the timing and patterns of movement. They play essential functions in the generation of the locomotor rhythm, the ipsilateral flexor/extensor coordination across the same or different joints in a limb and the left/right coordination between limbs. The Dmrt3-expressing interneurons are part of the locomotor CPGs. In Icelandic horses, a mutation in the Dmrt3gene allows the animal to perform an extra gait called pace. In mice, Dmrt3 is necessary to regulate the coordination of the limbs during swimming and running at high speed. To go further in the understanding of the function of the Dmrt3-expressing neurons within the locomotor CPGs, a monosynaptic retrograde tracing experiment was performed. We demonstrated that the Dmrt3 cells receive many inputs from the spinal cord especially from neurons located contralaterally. Interestingly, The Dmrt3 neurons also receive inputs from the brain, especially from nuclei involved in motor control and from the primary sensory afferents. This suggests that Dmrt3 neurons play an essential role at the interface between the sensory and the motor systems. (Funding: Swedish Research Council; Emil och Ragna Börjesons stiftelse).

OR18 - THE FUNCTIONAL ROLE OF CHRNA2+ MARTINOTTI CELLS

Anna Velica (Uppsala University)

OR19 - HIPPOCAMPAL CA1 PYRAMIDAL CELLS HETEROGENEITY: THE DEEP AND SUPERFICIAL

Lyvia Petiz (Uppsala University)

OR20 - ORGANIZATION AND FUNCTION OF OLMα2 CELL CIRCUITS IN THE HIPPOCAMPUS

Angelica Thulin (Uppsala University, angelica.thulin@gmail.com)

Accumulating research evidence is elucidating the differential roles of the dorsal and ventral hippocampal regions and their role in memory formation. However, less is known about intrahippocampal circuits in this respect. A specific subpopulation of hippocampal interneurons, the oriens-lacunosum moleculare (OLM) cells that express the cholinergic receptor subunit alpha 2 (OLMα2-cells), exhibit a graded distribution

and a different oscillatory activity along the dorsoventral hippocampus axis. OLMα2 cells are activated by fast ionotropic input via acetylcholine, but the sources of input, as well as the modulation of different oscillatory activities, remain to be determined. To reveal possible sources of input to OLMα2-cells, we performed retrograde monosynaptic tracing using G-protein deleted and entry receptor pseudotyped rabies virus. The preliminary results from these experiments indicate that OLMα2 cells mainly receive local inputs from pyramidal neurons and to a lesser extent inputs from other interneurons in stratum oriens and stratum radiatum. Long range connections seem to arise from the medial septum and diagonal band of Broca. Further studies are needed to confirm these results and to examine the differences over the dorsoventral hippocampus axis. (Funding: Stiftelsen för internationalisering av högre utbildning och forskning; STINT).

OR21 - OLMα2 CELLS ROLE IN HIPPOCAMPAL MNEMONIC-EMOTIONAL INTERACTIONS

Samer Siwani (Uppsala University, samer.siwani@neuro.uu.se)

Recent insight into the hippocampal longitudinal axis reveals a regional distinction on its mnemonic and emotional effects. Dorsal seems to be highly important for spatial and fear learning while ventral in anxiety related behaviors. Here, we investigate a microcircuit in the hippocampus that involves a subtype of interneurons called OLMα2 cells. When active, these cells facilitate LTP in the internal (CA3) inputs to CA1 and inhibits the external ECIII inputs. In our previous studies, we found that OLMα2 cell modulation influences distinct behaviors, depending on their dorso-ventral position. Dorsal and intermediate cells for instance has opposite effects on fear learning. Intermediate cells influences object learning while ventral affects anxiety. Further, we found that ventral OLMα2 cells drive hippocampal oscillations in the Theta II range. Which is known to appear during exposure to predator odor. We now aim to see whether these effects on fear, object learning and anxiety have similar underlying circuit mechanisms and behavioral phenotypes. Therefore, we will investigate whether these distinct phenotypes can be repeated by modulating OLMs in different positions along the dorso-ventral axis while recording LFPs. We will also investigate phenotypes in spatial learning and anxiety induced by visual stimuli. Our initial data indicates that the observations in anxiety might be replicated by stimulation of intermediate OLMα2 cells. Further, it seems that it does not involve visually induced anxiety and possibly other sensory stimuli that are provoked during elevated plus-maze. Although, further data collection is necessary to confirm these indications. (Funding: Swedish brain foundation; Swedish reasearch council).

OR22 - NEURONAL NETWORK OF PARADOXICAL (REM) SLEEP AND ITS IMPLICATION IN LEARNING AND MEMORY AND SLEEP PATHOLOGIES

Pierre-Hervé Luppi (CRNL, luppi@sommeil.univ-lyon1.fr)

Rapid eye movement (REM) sleep (also known as paradoxical sleep; PS) is characterized by EEG rhythmic activity resembling that of waking with a disappearance of muscle tone and the occurrence of REMs, in contrast to slow-wave sleep (SWS, also known as non-REM sleep) identified by the presence of delta waves. PH Luppi will report that the entrance from NREM to REM sleep is due to the intrinsic activation of REM-on hypothalamic MCH/GABAergic neurons. These neurons would inhibit during REM sleep a population of mesencephalic REM-off GABAergic neurons. This population of REM-off GABAergic neurons tonically inhibits during waking the glutamatergic neurons triggering the state of REM sleep localized in the pontine sublaterodorsal tegmental nucleus (SLD).

The exit from REM sleep would be induced by the inhibition of the REM-on GABAergic neurons by waking systems such as the pontine and medullary noradrenergic neurons and the hypothalamic hypocretin. In addition, PH Luppi will make hypotheses on the mechanisms responsible for REM sleep behavior disorder. He will propose that RBD is due to a neurodegeneration of the REM-on glutamatergic neurons triggering the atonia of REM sleep and localized in the SLD or that of the GABA/glycinergic premotoneurons localized in the ventromedial reticular formation and responsible for tonic hyperpolarization of motoneurons during REM sleep. Finally, PH Luppi will present new data on the cortical activation during REM sleep showing that only a few limbic structures known to be implicated in learning and memory are activated during REM sleep.

OR23 - SEMANTIC AND AFFECTIVE MEASURES OF MEMORY REVERBERATION DIVERGE AT DREAM ONSET

Natália Mota (Brain Institute, UFRN, nataliamota@neuro.ufrn.br)

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? Are they linked, or dissociated? What are the neural correlates of these transformations? To address 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 (WK), N1 or N2 sleep stages. We established an objective definition of 'Image Residue', as the formal semantic similarity between oral 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'. We compared these grounded measures of two distinct aspects of the 'day residue' within participants to randomly-generated values calculated across participants. We found that Image Residue persists throughout the transition to sleep, increasing during N1 in proportion to time spent in this stage. In contrast, the progression of sleep gradually neutralizes the Affect Residue, which decreases in proportion to time spent in N1 and reaches a minimum during N2. We also investigated the correlations between Image and Affective Residue and EEG power during wake, N1 and N2. In agreement with the semantic results, EEG imagetic and affective aspects of the 'day residue' diverge at dream onset. The results show that the imagetic and affective aspects of the 'day residue' diverge at dream onset. (Funding: CNPq; CAPES; FACEPE; FAPESP; Austrian Science Fund Project).

OR24 - NEURAL MECHANISMS OF BEHAVIORAL INDIVIDUALITY IN ZEBRAFISH

Carlos Pantoja (UnB, cpantoja@gmail.com)

Selection of behavioral traits should alter the genetic underpinnings of neural activity. However, it is unclear how rapid, stable and widespread these changes can be. Here, we examined brain-wide patterns of activity with extracellular signal-regulated kinase (ERK) staining in larval zebrafish selected over two generations for extreme differences in the habituation of the acoustic startle response (ASR). In animals selected for high habituation, sound stimuli evoked stronger activation of fear-processing brain areas and caudal hypothalamus, while low habituation-selected animals displayed stronger spontaneous brain activity in fear-processing centers. The effect of behavioral selection on caudal hypothalamus neurons was reproduced in independently selected lineages

with in vivo calcium imaging. Behavioral studies revealed that ASR habituation differences co-segregated with spontaneous swimming phenotypes, but not visual startle responses. Furthermore, high- and low-habituation larvae differed in stress responses as adults. Thus, short-term selective pressures on behavior can induce substantial differences in brain activity, dragging along unrelated behaviors as co-segregating traits. (Funding: Brain & Behavior Research Foundation; NARSAD Young Investigator Grant; Max Planck Society).

OR25 - ZEBRAFISH: TOOL OF GREAT PROMISE

Ana Luchiari (CB, UFRN, analuchiari@yahoo.com.br)

The (zebra) fish belongs to the most diverse class of vertebrates and yet present the core mechanisms of several more elaborated physiological and behavioral responses observed in mammals. These features help to answer questions regarding how organisms evolved but also how they function. In this sense, the zebrafish has met the ideal balance between the system complexity and practical simplicity, which gave it popularity and put it in a position of model organism that is boosting the biomedical research, mainly the ones focusing on brain and behavior. In my talk, I will present the zebrafish advantages and disadvantages and discuss how it can be a useful model to be added to the short list of biomedical models.

OR26 - ZEBRAFISH LOCOMOTION – FROM CIRCUIT TO BEHAVIOUR

Henrik Boije (Uppsala University, henrik.boije@neuro.uu.se**)**

There is a gap in our understanding of how neural activity translates into behaviour. By analysing elementary circuits we can provide a foundation for grasping the vast complexity of our brains. One such circuit, the spinal locomotor network, creates rhythmic output to muscles and coordinate left/right alternation. However, it is still largely unknown how this network orchestrates different locomotor speeds and movement patterns. A population of interneurons was recently found to be crucial for the transition between different locomotor patterns, gaits, in horses and mice. We use zebrafish as a model, which allows for unique in vivo analyses, to reveal the development, circuitry and function of these gait-interneurons. Given the newly discovered speed dependent microcircuits in zebrafish, and the locomotor phenotype in mammals, we investigate if gait-interneurons act as a gearbox to facilitate speed and gait transitions. Our preliminary data reveals a role for gait-interneurons within the zebrafish locomotor network, which places the research project in a unique position to investigate how hard-wired neural circuits are coordinated to generate flexible outputs. We use in an array of techniques and a holistic approach, spanning the formation, function and behavioural output of a neural network, to investigate how complex traits are encoded by participating neurons. (Funding: Beijer foundation; Ragnar Söderberg foundation; Swedish research council).

OR27 - POSSIBILITIES OF TINNITUS TREATMENT FOR HUMAN PATIENTS WITH CHRONIC TINNITUS

Marine Rosa (UFPB)

OR28 - ACTIVITY DEPENDENT MODULATION OF AUDITORY NETWORKS IN NOISE-INDUCED TINNITUS

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

Abnormal neuronal activity is associated with a majority of neurological disorders. For the auditory system, excessive noise and thereby excessive neuronal activity, can generate a continuous phantom sound, referred to as tinnitus. Chronic tinnitus perception can be loud and is often associated with stress, anxiety, depression, and decreased quality of life. Up to date there are no efficient treatments for tinnitus, which partially reflects the poor understanding of what subtype of auditory neurons generate and drive abnormal auditory activity. Here, using a mouse model of noise-induced tinnitus and in vitro and in vivo electrophysiology we are targeting subtypes of neurons of the cochlear nucleus, the believed origin of tinnitus, and the auditory cortex, correlated with the perception of tinnitus, to elucidate how noise-overexposure can persistently alter firing of certain populations. We have found that tinnitus-like behavior can be abolish by chemogenetically decreasing neuronal activity of CamKII2 alpha positive dorsal cochlear nucleus neurons. Next, we have found that cortico-cortical type B pyramidal cells of the primary auditory cortex layer 5 have increased firing 5-8 days following noise-overexposure, suggesting that tinnitus may be maintained intrahemispherically. We also investigate how tinnitus may alter attention to sound, and how this can be manipulated pharmacologically using an attention enhancer such as nicotine, and a possible attention disruptor such as cannabis extract. Here, preliminary data show noise-overexposed animals to display more double peaks of auditory evoked-potentials in a test for auditory sensory filtering, suggesting that tinnitus perception may recruit larger network activity of sound evoked responses compared to control mice. Interestingly, cannabis extract rich in delta9-THC may restore normal auditory evoked potentials of adult tinnitus animals. On the contrary, cannabis extract may generate tinnitus-like behavior in young mice, high-lighting the importance of a mature nervous system for beneficial effects of cannabis extracts in treating tinnitus perception. Taken together, tinnitus pathophysiology appears to alter neuronal activity of several distinct cell populations and carries components of limbic regulation that affects attention to sound. (Funding: The American Tinnitus Association; CNPq; CAPES).

KEYNOTE LECTURE

OR29 - INHIBITORY INTERNEURONS NEXT TO PRINCIPAL CELLS – WHAT DO THEY DO?

Klas Kullander (Uppsala University, klas.kullander@neuro.uu.se)

Learning and memory depend on several brain structures and a variety of cell types within these structures. That inhibitory interneurons participate in mnemonic processes is undisputed; however, defined roles for identified interneuron populations are still scarce. Oriens lacunosum-moleculare (OLM) interneurons are positioned to control the flow of information into CA1. In particular, a subpopulation of OLM cells genetically defined by the expression of the nicotinergic receptor α2 subunit has been shown to gate information carried by either the temperoammonic pathway or Schaffer collaterals in vitro. Cortical disinhibition has recently arisen as an important mechanism for information flow during complex behavioral tasks. Different subtypes of GABAergic inhibitory interneurons connect to each other, for example, a subpopulation of GABAergic cells that express vasoactive intestinal polypeptide (VIP) selectively innervates inhibitory interneurons, including OLM interneurons. Disinhibition is in such cases a possible outcome of interneuron-to-interneuron signaling, depending on the

activity state of the second inhibitory interneuron. We have used genetic targeting of specific inhibitory interneuron cell types labeled by Chnra2, which have allowed for a characterization of the cellular composition and function of possible disinhibitory circuits. I will discuss recent findings in learning and memory circuits and the possible role of OLM cells as well as in cortical circuitry and the possible role of Martinotti cells (Funding: STINT/CAPES).

POSTER SESSION A (MONDAY AFTERNOON & TUESDAY MORNING)

DB **DATA BLITZ PRESENTER**

P01 - BRINGING SLEEP FUNCTIONS INTO ARTIFICIAL NEURAL NETWORKS

DB

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Sleep is known to enhance behavioral performance on memory-dependent tasks. However, the underlying mechanisms are unknown. In this project, we use a machine learning paradigm to evaluate different theories of how sleep persistently change the connectivity between neurons with an impact on behavior. We constructed an artificial neural network and trained it to recognize different patterns in known public datasets. We could evaluate the effectiveness of our proposed sleep algorithms by checking whether the quality of the training is maintained or enhanced by sleep. A key aspect of our model is that natural neural networks are strikingly sparse, whereas artificial neural networks usually are fully connected. We propose that sleep regulates connectivity, allowing mnemonic processing equivalent to a fully connected network in a sparse network. The algorithm includes the cyclic sleep stages of REM and non-REM sleep. The core strategy is that during REM, we selectively prune synapses, whereas, during non-REM sleep, we induce synaptogenesis. Previous studies and our preliminary results show that sparse neural networks can learn as much or even better than dense networks, depending on factors like network dimension and the task. Now, we show that for the limits of connectivity found on biological neural networks, where the number of memories is close to the storage capacity, such an algorithm is even more critical to enhancing the cognitive capability of the brain. In such conditions, however, we face a harder challenge to set the proper parameters for the algorithm to work correctly.

Funding: Google Latin America Research Award 2017, Superintendência de Tecnologia da Informação - UFPB

P02 - MODULATION OF AUDITORY EVENT-RELATED POTENTIALS AFTER CANNABIS EXTRACT AND NICOTINE ADMINISTRATION IN TINNITUS MICE

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Tinnitus is a constant perception of a sound without an external source commonly described as "ringing in the ears". A fundamental question of tinnitus is whether it increases the level of attention to a sound, since it can be related to emotionally negative effects such as stress, anxiety, irritability, lack of focus, insomnia and depression. An important component of attention is sensory filtering, a pre-filtration of sensory stimuli from the environment. To study the role of attention to tinnitus perception, we exposed mice to loud narrow-band noise for 1 hr (90dB sound pressure level, 9-11 kHz) to generate tinnitus perception, or sham procedures for control mice. Mice were routinely evaluated for hearing threshold and tinnitus perception and next we recorded auditory event-related potentials using implanted chronic intra-hippocampal arrays in the right dorsal hippocampus in awake, freely moving control and tinnitus mice. We analyzed the evoked potential generated between 20~300ms after a paired-click stimulation paradigm. Normally, the second click responses are smaller in

magnitude, thereby suggested to produce auditory habituation (sensory filtering). Next, to study auditory attention, we provoked auditory sensory filtering with a single dose of a classic enhancer of attention, nicotine (1mg/kg); and Cannabis extract, a compound that is associated with decreased attention. The amplitude and latency of both negative and positive components of the event-related potentials were analysed before and after nicotine, cannabis extract and nicotine+cannabis extract administration. Preliminary results suggests that nicotine may improve N40 sensory filtering (difference between negative peak at 40 ms latency of the first and second click) amplitude and latency in tinnitus but not in control animals. Interestingly, cannabis extract may abolish N40 doublet responses (double peak) in tinnitus mice but not in control mice. The doublet classically suggest contribution of both inhibitory and excitatory populations, and here cannabis extract appears to silence the additional population response more frequently seen in tinnitus mice. More experiments are necessary to further dissect such mechanisms and confirm if there is a significant effect of tinnitus on sensory filtering amplitude and latency. This study aims to provide an electrical signature/biological marker for tinnitus perception that could potentially be translated to a signature picked up by electroencephalogram (EEG) in tinnitus patients, as well as, provide insights on tinnitus treatment.

Funding: CAPES, CNPq, American Tinnitus Association

P03 - CAMKIIα+ DORSAL COCHLEAR NUCLEUS NEURONS ARE NECESSARY FOR TINNITUS PERCEPTION

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Noise-induced tinnitus is a phantom sound, perceived without a physical source, caused by over-exposure to loud noise. The dorsal cochlear nucleus (DCN), a region known to integrate somatosensory and auditory pathways, has been identified as a potential key structure in the generation of phantom sound perception. Here, we decrease activity of the Calmoduline Kinase II alpha (CaMKIIa) positive DCN neurons to investigate their role in tinnitus perception. Mice were over-exposed to loud noise (90dBSPL, 1h, followed by 2h of silence) to induce tinnitus. Auditory brainstem responses (ABRs) and gap prepulse inhibition of acoustic startle (GPIAS) test were recorded two days before and two weeks after noise over-exposure to assure tinnitus induction (significant decrease in GPIAS response, $p = 0.003$, $n = 12$ mice) without permanent hearing loss. Activity of CaMKIIa+ neurons in the DCN was decreased by expressing and activating Gi-coupled human M4 Designer Receptors Exclusively Activated by Designer Drugs (hM4Di DREADD). Animals were retested on the following day in the GPIAS test but under effect of a systemic clozapine-n-oxide (CNO, 0.5mg/kg) administration. We found a decrease in tinnitus-like responses when CaMKIIa+ DCN neurons activity was decreased ($p = 0.018$, $n = 12$ mice), while the control group (control virus; CaMKIIa-YFP + CNO) showed no improvement in GPIAS responses ($p = 0.105$, $n = 6$). In another set of experiments, we administered CNO 30 minutes before the noise over-exposure to decrease activity of CaMKIIa+ DCN neurons ($n = 3$ experimental and 2 control mice) and preliminary results suggests that lowering CaMKIIa+ neurons activity can also prevent tinnitus induction. Our results suggests that CaMKIIa+ cells in the DCN may have a role in maintaining tinnitus perception in mice.

Funding: CAPES, CNPq, American Tinnitus Association

DB

P04 - COMPLEX NETWORK APPROACH TO THE NEUROSCIENCE OF PSYCHEDELIC PHENOMENA

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The theory of complex networks applied to real systems have made impactful and lasting discoveries in the past few decades. From social relations and air traffic to the internet itself, complex networks are ubiquitous throughout nature and can be used to model a range of different systems. The theory's recipe consists of taking a system and representing it as a structure of nodes and connections between pairs of such nodes. In this work, we take functional magnetic resonance imaging data of the human brain to represent it as a complex network system, in which the neural activity of cortical regions and the correlations between pairs of such regions are the nodes and connections, respectively, of the network structure. We then apply the machinery of statistical physics to investigate the neural correlates of the altered states of consciousness induced by the psychedelic brew ayahuasca, to which we find, among typical topological metrics, a higher network entropy of both the degree and geodesic distance distributions when compared to that of a normal waking consciousness, suggesting an increased variability of functional patterns during the psychedelic experience.

Funding: CAPES, CNPq, DFG (HO4695/3-1; Collaborative Research Center 910)

P05 - TEMPORAL EVOLUTION OF PATHOLOGICAL HIGH-FREQUENCY OSCILLATIONS AND ITS RELATION TO SLEEP SPINDLES AND INTERICTAL SPIKES ACTIVITY IN ANIMAL MODELS OF EPILEPSY

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Characterized by spontaneous and recurrent seizures, temporal lobe epilepsy (TLE) is one of the most common forms of epilepsy. Seizure initiation and spread involve structures of the limbic system, including networks within the hippocampal formation. Cell death, neuroinflammation, and abnormal synaptogenesis in this region contribute to the appearance of pathological high-frequency oscillations (pHFO) in CA1 and dentate gyrus. Despite 20 years since its first description, the temporal evolution of this paroxysmal activity during epileptogenesis is poorly described. In this project, we propose to characterize the occurrence and spectral profile of pathological high-frequency oscillations in CA1 and dentate gyrus after status epilepticus induced by intrahippocampal administration of pilocarpine or kainic acid in mice. Preliminary results suggest that pHFOs appear in the very first induced seizures and do not subside during the latent period. Further analysis will demonstrate whether spectral components of this pathological oscillation mature and which are the correlations between them and other physiological brain oscillations as sleep spindles, interictal spikes, and REM sleep theta activity.

Funding: CAPES, CNPq, Finep, Propesq-UFRN

DB

P06 - DECREASED ELECTROCORTICAL TEMPORAL COMPLEXITY DISTINGUISHES SLEEP FROM WAKEFULNESS

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In most mammals, the sleep-wake cycle is constituted by three behavioral states: wakefulness (W), non-NREM (NREM) sleep, and REM sleep. These states are associated with drastic changes in cognitive capacities, mostly determined by the function of the thalamo-cortical system. The intra-cranial electroencephalogram or electocorticogram (ECoG), is an important tool for measuring the changes in the thalamo-cortical activity during W and sleep. In the present study we analyzed broad-band ECoG recordings of the rat by means of a time-series complexity measure that is easy to implement and robust to noise: the Permutation Entropy (PeEn). We found that PeEn is maximal during W and decreases during sleep. These results bring to light the different thalamo-cortical dynamics emerging during sleep-wake states, which are associated with the well-known spectral changes that occur when passing from W to sleep. Moreover, the PeEn analysis allows to determine behavioral states independently of the electrodes' cortical location, which points to an underlying global pattern in the signal that differs among the cycle states that is missed by classical methods. Consequently, our data suggest that PeEn analysis of a single EEG channel could allow for cheap, easy, and efficient sleep monitoring.

Funding: PEDECIBA, ANII (FCE 1 2017 1 136550), CSIC (I+D-2016-589), CSIC group grant (CSIC2018 - FID 13 - Grupo ID 722)

P07 - SUBVENTRICULAR ZONE NEUROBLAST SWITCH ITS NEURONAL TYPE DIFFERENTIATION AFTER KAINIC ACID INJECTION

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Adult subventricular zone (SVZ) cells give rise to different olfactory bulb (OB) neuronal types/subtypes. It has been suggested that the fate-determination of these neurons relies on spatial morphogenetic signals for the stem cells within the SVZ niche. It is not clear though, if this positional information is instructive or determinant to the neuronal type differentiation. In this work, we stimulate kainate (KA) receptors in neuroblasts en route to the OB to assess the plasticity of these cells outside the SVZ. We used DCX-CreERT2::GFP mice, to fate map post-mitotic neurons in the SVZ-OB system. Mice received three daily doses of tamoxifen before surgery and on the fourth day, were injected with KA or vehicle in a coordinate close to the striatal part of the rostral migratory stream (RMS). After 36 hours, the glial tube surrounding the migratory neurons in the RMS is disorganized close to the injection site and neuroblasts ectopically migrate to the surrounding parenchyma. However, multiple neuroblasts maintain their migration to the olfactory bulb, where they differentiate into bona fide OB neurons. Notably, however, we observed a shift in the proportions of different OB neuronal subtypes after 30 days. While the proportion of granular cells is increased, the fraction of Tyrosine Hydroxylase (TH)+ neurons in the glomerular layer is decreased in KA injected animals compared to controls. These data, suggest that KA injection is sufficient to change neuronal type differentiation by SVZ neuroblasts and that the positional information they receive in the SVZ is instructive but not determinant for neuronal subtype specification.

Funding: CAPES

P08 - SEEING NON-EXISTENT MOVEMENTS: A NOVEL PSYCHOPHYSICAL PARADIGM TO STUDY THE EFFECT OF COLLINEARITY ON APPARENT MOTION

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Psychophysics is a quantitative investigation of perceptive or evoked response due to an external and physical stimulus. Besides the wide range of applications and the several contributions in the understanding of perceptive processes, the development of novel psychophysical paradigms is almost scarce by decades. Motion Quartet (MQT) is one of the currently established protocols to study apparent motion in the context of bistable motion, once that it is well known the effects of long-range interhemispheric connection during the MQT task. On the other hand, the collinearity effect is a basic visual feature responsible for visual integration and perceptual grouping. When the MQT is presented centrally in the visual field the observers are more likely to perceive vertical motion, possibly due to the complex interhemispheric connection required to process horizontal motion, which leads to natural vertical facilitation. Knowing that collinearity effects during the MQT task were never tested, the aim of this work is to investigate the possible counter-facilitation effect of collinear stimulus during a MQT task. Thus, we recorded both electroencephalographic activity and behavior during two different conditions: vertical distance increment with constant horizontal distance (VH) and horizontal distance increment with constant horizontal distance (VH). Each condition had three subgroups: horizontal and vertical Gabor patch (5 c.p.d) and control stimuli (dots with 50% of Gabor patch size) with vertical (CV) and horizontal (CH) increments. All stimuli had 4 deg and the subject was 57 cm away from the screen. We recorded EEG data of one subject using a 68 electrode system during all MQT protocols. The data was analyzed offline using Analyzer 2.2 and Matlab using the following steps: common reference, IIR bandpass filter (0.5 - 100Hz), notch filter at 60 Hz, semi-automatic artifact inspection, ICA, epoch segmentation based on each stimuli presented on the screen, and intertrial-coherence performed on Matlab to determine long-range interhemispheric coherence using left-right pairs of electrodes (O1-O2, PO3-PO4, PO7-PO8). Behaviorally we determine the Parity Ratio (PR) using the average distances of perceptual-switch in each of the six protocols. Surprisingly, we found the lowest PR in the HH group (0.85). This indicates a strong collinear effect of the horizontal Gabor patch while increasing the horizontal distance. Electroencephalographic analysis indicates stimulus-related differences in interhemispheric phase-synchrony. EEG result is also congruent with behavior measuring, once the HH group showed the highest coherence score on the interhemispheric pairs of electrodes PO3-PO7 (0.52) and PO7-PO8 (0.54). We conclude that PR and interhemispheric coherence can be modulated by either vertical and horizontal Gabor patch, with a strong effect on horizontally-directed Gabor.

Funding: CAPES

P09 - THE EFFECT OF NOISE-INDUCED TINNITUS ON MEMBRANE PROPERTIES OF DIFFERENT CELL CLASSES OF THE AUDITORY CORTEX

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Tinnitus is a condition characterized as a perception of sounds such as ringing of the ears when there is no acoustic external stimuli. Tinnitus perception is not harmful, but it can lead to severe psychological stress, anxiety and depression. Several studies indicate the auditory cortex as a potential target for transcranial magnetic/direct

current stimulation to alleviate tinnitus perception, yet little is known of how tinnitus alters cortical circuits. Here we investigate cellular populations of layer 5 (L5) of the primary auditory cortex (A1) in a mouse model of noise-induced tinnitus. L5 pyramidal cells (PCs) were subdivided into putative corticofugal projecting type A, or contra-lateral projecting type B PCs, post hoc. We found that membrane properties were different between younger (P16-23) and mature cells (P38-52), and therefore we opted to only include animals ≥1 month of age for noise-overexposure (4-20kHz, 90dB, 1,5 hrs). Passive and active membrane properties between the two PC subtypes were compared for control and tinnitus-like animals. We also used transgenic Chrna2-cre mice to investigate inhibitory Martinotti cells between the experimental groups. We found that noise overexposure did not change passive membrane properties of either type A or type B PCs when examined 5-8 days later. Instead we found type A PCs to fire with a significantly lower firing frequency in response to positive current injections (150pA) following noise overexposure (control A: 20,3±1,8Hz, n=11, noise-overexposed: 16,1±1,2Hz, n=19, p=0.050), while contrarily type B PCs significantly increased steady state firing frequency (Control B: 13,3±1,3Hz, n=13, noise-overexposed: 19,5±2,4Hz, n=22, p=0,048). Interestingly, preliminary data from Martinotti cells from noise-overexposed animals show a higher initial firing frequency than control (control M: 70,05±6,5Hz, n=8, noise-overexposed: 80,5±3,4Hz, n=12) and steady state frequency (control M: 20,35±4,4Hz, noise-overexposed: 33,5±4,9Hz). Since Martinotti cells are specifically connected to type A PCs through recurrent inhibition, this could suggest that Martinotti cells protects type A PCs from acoustic over-activity. Here we have identified cortical neurons affected by noise-induced tinnitus that may add to the understanding of tinnitus mechanisms, crucial for improving treatments such as transcranial magnetic stimulation.

Funding: CAPES, CNPq and American Tinnitus Association

P10 - INTRAUTERO INJECTION OF ZIKV LEADS TO OLFACTORY EPITHELIUM AND BRAIN INFECTION IN A TEMPORAL FASHION THAT SUGGESTS AN ANTERIOR ENTRANCE

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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 vírus through the embryonic olfactory system, which is in direct contact with the amniotic liquid. Objective: The aim of this project is to verify if ZIKV infects the olfactory epithelium, and subsequently the brain, after its injection in the amniotic fluid. In addition, we want to establish a method for the ablation of the olfactory epithelium in order to inhibit/reduce ZIKV entrance in the brain. Methods: Mice are obtained from the Brain Institute animal facility and infected animals are maintained at the Tropical Medicine Institute, UFRN. We are using a ZIKV lineage isolated in Pernambuco in the year 2015. We inject ZIKV in the amniotic liquid of E13 mice and verified infection at 3 days post infection (dpi), 6dpi and 12dpi by using an antibody (4G2) that recognizes the viral envelope protein. For the OE ablation test, postnatal P3 mice are being used by injecting ZnSO4 (0.17M) into the right nostril (approximately 5µl) and saline into the control group. One day later, ZIKV is injected into the nasal route that previously received ZnSO4 or saline. Partial Results and Conclusions: ZIKV injection in the amniotic

fluid caused ZIKV infection in the OE at 3dpi but not 1dpi. The percentage of embryos infected in the OE was higher than those with a infected brain both at 3 and 6 dpi. We observed that ZnSO4 injection successfully kills most of the OE and its projections to the OB. We also observed that intranasal injection of ZIKV in P3 mice leads to OE infection at 6 dpi. 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 expression pattern of ZIKV in the brain suggests that the virus is spreading through the differentiating neurons and its processes. Future experiments will aim to establish if the killing of OE cells prevent or mitigate ZIKV brain infection.

Funding: CAPES, CNPq, ICGEB

DB

P11 - ESTABLISHMENT OF A LABORATORY COLONY OF SIMULTANEOUS HERMAPHRODITE FISHES KRYPTOLEBIAS HERMAPHRODITUS AND KRYPTOLEBIAS OCELLATUS FOR THE STUDY OF REPRODUCTIVE AND AMPHIBIOUS BEHAVIOR

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The genus Kryptolebias is the only known group of vertebrates in which individuals have both male and female germ cells at the same time, with self-fertilization capabilities (simultaneous hermaphroditism). Previous studies have shown that these animals have a low level of heterozygosity, which make them an interesting model because they depend solely on epigenetic variability for plastic responses to the environment. In order to establish a colony in laboratory, we evaluated the presence of eggs in the gonads of fixed animals in formaldehyde and found that only animals larger than 20 mm of standard length have eggs. Thus, 38 K. hermaphrodites larger than 20 mm were collected form the mangrove of the Aquaculture Technological Center of UFRN, in Extremoz, RN. The animals are stored in individual plastic containers for 10 months to acclimate, and observed for oviposition and self-fertilization, which occurred 13 times during the observation time. All eggs were laid between June and September, suggesting a seasonality for oviposition for this specie. Four of these embryos or larvae remain alive. Among the plastic responses presented by K. hermaphroditus, is the capability of staying outside the water. The emersion time was measured during 10 minutes in an arena with 3 wells of brackish water separated by a dry area cover with cork. We observed that all animals moved through dry environment. The mean time outside the water was 9.8% with high variability (standard deviation = 8.6%, n=13) and the time spent has no correlation with animal size. We also observed terrestrial behavior starts in larvae; at least 29 days post eclosion. For testing if the terrestrial behavior can be motivated by the presence of other fish in the pond, we tested if chemical signals from the conspecific or predator (Guavina guavina) alter time spent outside water. In order to do this, we added water from containers of conspecific or predator to the well where the tested animal was allocated. Both conditioned waters did not change time spent outside the water or latency to first exit to dry cork (n=15 each). In order to have a near group with a different reproductive behavior, we collected 11 specimens (5 males and 6 hermaphrodites) of Kryptolebias ocellatus from a mangrove at Barra de Guaratiba, Rio de Janeiro. This species produces a much higher proportion of males (males in K hermaphroditus are extremely rare) and present genetic indications of sex between individuals. There are no behavioral studies with this species so far and for the first time we observed terrestrial behavior. The present study indicates that it is possible to maintain and obtain new animals for the establishment of K. hermaphroditus and K. ocellatus clonal laboratory colonies. In addition, we show

that this species presents a remarkable amphibious behavior, which can be an important model for the study of anatomical and physiological plasticity.

Funding: No funding

P12 - DIFFERENTIAL MODULATION OF DELTA AND THETA OSCILLATIONS IN THE RAT HIPPOCAMPUS ACROSS SUCCESSIVE TREADMILL RUNNINGS

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Neuronal networks in the rodent hippocampus oscillate in many different and sometimes coexisting frequency rhythms according to behavioral states. While theta (5-10 Hz) oscillations are prevalent during active behaviors and also during REM sleep, hippocampal delta (1-4 Hz) oscillations occur mostly in quiet behaviors and non-REM sleep. These two rhythms are traditionally viewed as mutually exclusive, and often used to characterize respectively "online" and "offline" states of the hippocampus. To investigate the modulatory effect of running speed on hippocampal delta and theta oscillatory responses, we recorded local field potentials (LFP) from hippocampal CA1 area of rats executing successive bouts of running in a computer-controlled treadmill under crescent or constant speeds (permit number 061.069/2017). Animals were trained to perform 48 bouts of running on the treadmill (20 seconds) under a consecutive protocol of crescent (1,1.5, and 2 cm/s^2) and constant speeds (20, 30 and 40 cm/s) in one day session. We also investigated full sessions where animals executed at least 35 bouts of running on the treadmill (15 seconds) under constant speed (30 cm/s). We observed the emergence of strong delta oscillations while the rats executed treadmill runs under crescent speeds, which became remarkably periodic above speeds of 30 cm/s. The amplitude and frequency of delta oscillations increased significantly across constant speed protocols of 20, 30 and 40 cm/s. In contrast, theta oscillations were prominent throughout all protocols of constant running speeds, but the power of theta band was not significantly different. In addition, while we observed a significant increase in the power of delta band along successive bouts of running under constant speed (30 cm/s), we also observed that the power of theta band significantly decreased along the bouts of running. In summary, our results show that running speed strongly modulates delta oscillations in the rat hippocampus, and that successive bouts of running inversely affect delta and theta oscillations. We suggest that delta and theta rhythms coexist in the rat hippocampus, and that their differential modulation may be important for signaling the development of fatigue along running exercise.

Funding: CAPES, CNPq

P13 - EFFECT OF CANNABINOIDS ON NOISE INDUCED TINNITUS PERCEPTION

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Tinnitus is an auditory pathology characterised by phantom sounds described as ringing or hissing sound by humans, which origin remains unknown. In addition, tinnitus can also be described as an auditory epilepsy due to hyperactivity in different auditory regions i.e. the dorsal cochlear nucleus and the auditory cortex. There is a growing interest to treat epilepsy with cannabinoid compounds, and therefore recent studies aim to evaluate tinnitus treatment with cannabinoids. Different groups show contradicting results, in a way that cannabinoids could either increase or even induce tinnitus, or cannabinoids did not change tinnitus perception. Due to small number of

publications in this area, especially models of noise-induced tinnitus, this project aims to evaluate the effect of a THC-rich cannabis extract after noise overexposure (tinnitus induction) in mice. So far, preliminary data shows that the extract (100 mg/kg, usually used for epilepsy experiments) actually seems to promote tinnitus-like behaviour in young (P30-35) sham (n = 3) and young noise overexposed (n = 9) mice using the gap-prepulse inhibition of acoustic startle test. Further experiments will compare the effects of the extract at more mature age (P75) and we will also test whether a ten times lower dose of the extract (10 mg/kg) decreases tinnitus-like behaviour and anxiety-like behaviour using the elevated plus maze and open field test.

Funding: The American tinnitus Association, CNPq, CAPES

P14 - QUANTITATIVE PHOSPHOPROTEOMIC ANALYSIS ACROSS THE SLEEP STAGES IN RATS

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Sleep comprises two principal stages, knowing as 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 molecular changes and neuronal activities. Those aspects could be evaluated by proteins expressed in the specific brain areas. To explore memory consolidation linked by sleep, here we investigate the molecular basis of sleep phases in the hippocampus (Hp) and primary somatosensory cortex (S1) using quantitative proteomic analysis in the bottom-up shotgun mass spectrometry in a two-dimensional liquid chromatography-tandem mass spectrometry setup in the MSE mode with label-free quantification. The brain were collected from rats exposed to novel objects (10 min), called group +, or no objects, group -, then kept awake for 30 minutes and finally killed after period rich in SWS or REM. Our preliminary analysis indicate that the brain proteome of these rats exhibits difference in modulation of phosphoproteins identified by STY tags (modification with phosphoryl). The initial approach has been conducted comparing the phosphoproteomic profile of the treatments and regions (SWS+ x SWS-, REM+ x REM-, REM+ x SWS+ and REM- x SWS-), specifically the protein abundance and protein function. Comparison of the treatments identifies 90 mostly modulated phosphoproteins, related mainly with synaptic function, actin-microtubule regulation, DNA-RNA related, Protease-phosphatase-kinase, cell death, cell membrane and other protein regulation function. Interestingly, the modulation of phosphoproteins in Hp and S1 under novelty exposition indicates an abundance shift generated by SWS phase in both regions. When analyzing compared modulated phosphoprotein, according to enrichment analysis of the gene ontology and biological pathways we could identify that in S1 modulated phosphoproteins related to cytoskeleton and kinases. Furthermore, the principal functions modulated in Hp were linked to nuclear function. We believe that the profile of protein modulation is a potential guidance of the progressive disengagement of the memories of the hippocampus and engagement of the cerebral cortex during sleep stages. In conclusion, we produced a significant amount of data that is under analysis using a variety of bioinformatics approaches and manual annotation. The identification of key molecules that are modulated by sleep stages could provide us significant insights on the mechanism that underlies reverberation, storage, and propagation of memory traces during sleep.

Funding: CAPES

DB

P15 - LSD BOOSTS OBJECT-LOCATION MEMORY: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER STUDY

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Serotonin 2A (5-HT2A) receptors play an important role in cognitive processes like learning and memory. Psychedelic substances, such as lysergic acid diethylamide (LSD), mediate their effects mainly through agonist action on those 5-HT2A receptors and, furthermore, seem to induce neuroplasticity. Therefore, LSD might exert a beneficial effect on memory performance. The objective of this study was to examine the effects of a medium dose of LSD on sub-acute memory performance. In a randomized, double-blind, placebo-controlled, counterbalanced, crossover study, we applied a medium dose of LSD (50 micrograms) to 25 healthy participants. To examine visuospatial memory performance, a 2D object location task was applied before substance administration (learning) and 24h afterwards (memory). If controlling for Body Mass Index (BMI), LSD significantly increased memory performance compared to placebo ($F(1,20) = 7,846$; $p = 0.011$), while there were no order effects. Effect size was medium. Interestingly, the beneficial effect of LSD on object location memory was only pronounced if controlling for BMI, whereas a higher BMI was related to stronger memory consolidation under LSD, compared to placebo. These results indicate that an even smaller and weight adapted dosage might exert stronger pronounced effects. Altogether, our findings suggest that a single dose of LSD may boost memory capacity which emphasizes the therapeutic potential of psychedelic substances.

Funding: CAPES (Finance Code 001)

P16 - AN INVESTIGATION OF CA1 AND DG DELTA OSCILLATIONS IN RESPONSE TO SYSTEMIC ADMINISTRATION OF THE NMDAR ANTAGONIST KETAMINE

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The investigation of intracerebral oscillatory activity generated by populations of neurons has provided advances in our understanding of brain function in normal and pathological conditions. Recent reports have used systemic administration of the NMDA receptor antagonist ketamine as an animal model to study schizophrenia. These studies revealed the disturbance of normal oscillatory activity in many brain areas like the thalamus, prefrontal cortex, and also in the hippocampus. For instance, the amplitude of low-frequency oscillations in the delta band (1-4 Hz) increases in the hippocampus. However, it is still unclear whether specific subareas of the hippocampus are equally affected. Our aim was to investigate the amplitude modulation of delta oscillation in CA1 and Dentate Gyrus (DG) of the rat hippocampus in response to the systemic administration of saline and three subanesthetic doses of ketamine (25 mg/kg, 50 mg/kg e 75 mg/kg). As preliminary results, we found that the CA1 and DG delta oscillations are modulated by NMDAr antagonist ketamine in a dose-dependent manner.

In addition direct comparison of delta power among CA1 and DG with locomotion speed lower than 5cm/s showed no statistical difference. These findings suggest that differential responses of delta oscillations in hippocampal subregions may characterize an animal model of schizophrenia.

Funding: CNPq

P17 - SOFTWARE DEVELOPMENT FOR THE DETECTION OF ULTRASONIC VOCALIZATIONS: STUDYING EARLY-LIFE SEPARATION CALLS IN A RODENT MODEL OF AUTISM

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Vocalization in mammals is an essential skill for social interaction. It communicates and co-regulates internal states related to threat and affective contact between individuals. Although rats vocalize in the audible range (up to 20 kHz), ultrasonic vocalizations (USVs; 20-100 kHz) are the ones used for conspecific communication, during maternal separation, juvenile play, threat encounters and courtship. During postnatal development, separation calls (~40 kHz) are commonly produced by neonates when isolated from the dam/nest, leading to maternal rescue. Atypical vocalization patterns have been taken as a signal of abnormal neural circuit development in animal models of autism. In this study, we developed a software for the detection and refinement of USVs that runs in MATLAB environment and, can be use as input to supervised and unsupervised classifiers in DeepSqueak software. The software was used to detect neonatal USVs produced by Wistar rats (control and autism model) at PND7-PND21 ages. USVs were recorded by a digital microphone (Ultramic250k; sampling rate=250 kHz; A/D 16 bits; Dodotronics). Audio recordings were acquired using Audacity software (GPLv2 license) and each vocalization file (5 min; ~150MB; .wav format) was stored in hard disk. The USV detection algorithm is based on Shannon entropy, in which entropy drops represent increase in informational content in a given region of the audio spectrum. To do that, the algorithm searches low-entropy regions in the audio spectrogram, both in time and frequency, obeying a predefined threshold. As in many threshold-based detection methods, the efficiency of the algorithm depends on the signal-to-noise ratio of the audio. The software allows for parameter adjustments and manual refinements a posteriori. Since this process takes time, we developed a graphical user interface (GUI) to aid detection and optimize analysis. The GUI is modular, comes with predefined settings and has navigation tools that allows the user to decide between true (inclusion)/false (exclusion) USVs and to define the USV time-frequency box. In case of a true detection, the user can fine-tune USV margins and confirm the detection. In case of a false detection, the interface allows the user to delete it using keyboard shortcuts. The GUI also allows the user to include undetected (false negative) USVs. The software outputs the following measurements: USV onset time (s), offset time (s), duration (min), minimum frequency (kHz), maximum frequency (kHz), bandwidth (kHz), average power (mV2) and sinuosity (based on DeepSqueak from USVs) in a .mat variable. For a selected set of USVs, the GUI also generates plots of its audio recording, spectrogram contour and entropy values. In addition, it calculates the performance of USV edge detection computing the mean square error of min_frequency, max_frequency, onset time and offset time) by comparing the auto detection to the user redefinition. After refinement, the program computes the accuracy, precision, sensitivity and specificity of detection.

Funding: CNPq, CAPES, UFRN

P18 - INVESTIGATION OF DIRECT AND INDIRECT EFFECTS OF INFLAMMATION DURING THE CNS DEVELOPMENT

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Several pathologies, from infectious diseases to metabolic syndromes, can cause an inflammatory response in the organism. This occurs through pro-inflammatory cytokines release through activation of immune system. During pregnancy the inflammatory process can be detrimental to embryonic nervous system development. Recent studies that evaluate infections and chronic inflammation during the gestational period in rodents showed that these process cause microglia activation and neural alterations in the offspring such as a decrease in the amount of neural progenitors. The immune response effects on neural cells could be direct or indirect . In the direct effect, there is cytokines activity in their respective receptors present in the neural cells. However in the indirect effect the microglia acts as a mediator during inflammation altering the physiology of neural cells. Therefore, the direct and indirect effects of inflammation on central nervous system (CNS) development can be studied using an in vivo model - an animal model of maternal chronic inflammation. We propose in this project the establishment of an inflammatory model to analyze the effects on neuronal migration and dendrite genesis arising from the chronic inflammatory process during the development of the CNS in mice. Thus, through these analyzes, we aim to identify neural changes and new therapeutic strategies that may help to reduce the damage caused by inflammation during the gestational period.

Funding: CAPES, CNPq

DB

P19 - THE CANNABIS STRAIN MATTERS FOR THE ANTICONVULSANT EFFECT?

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The use of Cannabis-derived products as an alternative treatment in refractory epilepsies has been increasing worldwide. In Brazil, Cannabis sp. is an outlawed species, on the other hand, in recent years some patients have obtained Brazilian court authorization to grow the species and prepare their own medicine. Thus, patients have acquired seeds without observing the cannabinoid content of these strains. From a regulatory point of view, there is no guidance on how these extracts are prepared and which strains should be preferably used to treat epilepsy. Here, we tested two Cannabis extracts from different strains: one extract is rich in tetrahydrocannabinol - THC (XT-THC) and another rich in cannabidiol – CBD (XT-CBD) in pilocarpine-induced status epilepticus (SE) using mice (#013/2016 – CEUA/UFRN). Our results suggest that XT-THC (THC:CBD, ratio = 11:1) attenuate pilocarpine-induced SE. This dose-response suppression of behavioral seizures by THC-rich extract (472.5 mg/kg, i.p., n = 6) compared to vehicle (10 mL/kg, i.p., n = 13) ($p<0.05$, Kruskal-Wallis test) was similar to the one observed after diazepam administration (5 mg/kg, i.p., n = 6) (p = 0.80, Mann Whitney test). Behavioral analysis also indicated that low doses of XT-THC (4.72 mg/kg, i.p., n = 7) increased generalized seizure-related behaviors (such as rearing and falling, wild running and jumping) but did not change the measured ictal parameters. We have adjusted the CBD dose in XT-CBD, in order to compare with the effects observed on XT-THC. Surprisingly, low doses of XT-CBD (4.72 mg/kg, i.p., n = 5) reduced ictal-related behavior, generalized seizure duration, and Racine scale than compared to the vehicle ($p<0.05$, Kruskal-Wallis test), this dose did not differ from the observed effect for XT-THC 472.5 mg/kg on Racine scale (p = 0.79, Mann Whitney test). It is important to note that high doses of XT-CBD (216.6 gm/kg, i.p., n = 4) caused a deep depression in the

animals that led to hypothermia and cardiac arrest. Ongoing experiments are focusing on the electrophysiological evaluation of these extracts during intrahipocampal pilocarpine-induced SE for quantifying electrographic seizure latency and duration, as well as pathological high-frequency oscillations dynamics. Together, these results demonstrate that Cannabis antiepileptic effects can be related mostly to CBD-rich extracts. Future assays with CBD alone will elucidate whether this effect depends solely on CBD or might be shared by some others types of cannabinoids.

Funding: CAPES, FINEP, UFRN

P20 - SEROTONERGIC PSYCHEDELICS EFFECTS ON HIPPOCAMPAL AND PREFRONTAL ELECTROPHYSIOLOGY IN RATS

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The psychoactive effects of classic psychedelics depend on serotonergic receptors 5-HT2A and 5-HT1A, but little is known about their neurophysiological effects. Here we set out to investigate the effects of 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) and N, N-diethyllysergamide (NN-LSD), two potent serotonergic agonists, on local field potentials (LFP) recorded from the hippocampus (HP) and prefrontal cortex (PFC) of rats. Rats were surgically implanted with a cannula in the lateral ventricle and tungsten (50µm) multi-electrode arrays in the HP and PFC. Experimental sessions consisted of baseline recordings for 1h, injected i.c.v or i.p with 5-MeO-DMT or NN-DLS, and recorded for 2-3h or 9h. Electrophysiological signals were recorded with IntanRHD2000, behavior was recorded with CinePlex, and data were analyzed using customized Matlab routines. Behavioral alterations were observed ~15 min after drug injection, including increased locomotion, increased space occupancy, and the occurrence of stereotyped behaviors such as wet dog shaking, and uncoordinated locomotion. Similar to results from previous studies, LFP alterations were detected in the PFC and the HP. For DMT experiments, while power in the gamma band (LG, 30-100 Hz) and theta band (5-10Hz) decreased in both regions within the first 15 min, power in the delta (0.5-5 Hz) band showed no significant change. Moreover, coherence between PF and HP is increased in the gamma band, and tended to increase also in the theta and delta band. On the other hand, for NN-DLS experiments theta power showed a tendency to increase in the HP. Next, we compared the changes caused by 5-MeO-DMT and NN-DLS to the regular electrophysiology of the sleep-wake cycle. State map analysis revealed that both substances promoted a shift in the spectral profile typical of waking towards that of the intermediated sleep (between SWS and REM sleep) or WK to sleep transitory region, despite the fact that the animals remained overtly awake. Altogether, the results are novel and promote a better understanding of the neurophysiological alterations caused by psychedelics.

Funding: CAPES, CNPq, UFRN

POSTER SESSION B (TUESDAY AFTERNOON & WEDNESDAY)

DB

P21 - EFFECT OF MENSTRUAL CYCLE ON MOTOR FUNCTION

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Many studies have shown that motor functions such as muscle strength and motor performance may vary throughout the menstrual cycle. For example, maximum muscle strength increases during the follicular phase and falls after ovulation. The fine motor skill increases in the luteal phase and decreases in the follicular phase, the opposite may be observed for gross motor skill. There is evidence that these variations are the result of the action of sex hormones, especially estrogens and progesterone, whose blood concentration varies throughout the menstrual cycle. Studies with transcranial stimulation show that the corticospinal tract can be more strongly excited and inhibited in the late follicular phase as compared to the luteal and menstrual phase. However, it is not known at what level of the corticospinal tract (whether in the motor cortex, medulla or motor plate) sex hormones exert their actions and whether these actions have implications for motor functions. The present study, which is being developed, has investigated the effect of hormonal oscillations throughout the menstrual cycle on the sensorimotor cortex and performance during motor imaging practice, suggesting the modulation of female sex hormones on the central component of motor control. The study was conducted with 30 women (10 analyzed) aged between 18 to 30 years with regular menstrual cycle. They were submitted to the Manual Laterality Recognition Test (MLRT) in three different phases of the menstrual cycle (menstrual, late follicular and luteal). The MLRT is a test to identify the laterality (right or left) of hands presented in different orientations on a computer screen. To be most successful in the test, volunteers should engage in the motor imaging process, where they mentally rotate their hand (right or left) in search of congruence with the presented hand. Blood was also collected at each phase of the cycle to monitor hormonal dosages. The menstrual phase was defined as the bleeding period of the cycle, the late follicular phase was defined between the 9th and 12th day of the cycle and the luteal phase was estimated using the increase of LH levels before ovulation. The Friedman test was used to compare the response time between the phases of the menstrual cycle. The differences found were explored with multiple comparison tests with Tukey correction. The MLRT analysis showed differences between the phases of the menstrual cycle ($x^2(2) = 19.63$; $p < 0.001$). Response time in the late follicular phase was significantly shorter than in the menstrual ($p = 0.01$) and luteal ($p < 0.001$) phases. No difference was observed between the menstrual (low estrogen and progesterone levels) and follicular (high estrogen level) phases for hands that were presented without rotation (0°). However, the difference was evidenced for hands with 180° rotation ($p = 0.02$), where the response time was shorter for the menstrual when compared to the follicular phase. These results suggest that the performance in purely cognitive motor test varies depending on the phase of the menstrual cycle and that estrogens seem to play a key role in this process, since the mental rotation of the hand needed to perform the task seems to be facilitated at the moment that estrogen levels are lower (menstrual phase) or associated with higher progesterone levels (luteal phase). MLRT performance was similar to that found for fine motor skill tests. These results suggest that variations in motor functions during the menstrual cycle may be caused by the modulation of female sex hormones on the central nervous system, especially the sensorimotor cortex.

Funding: CAPES

DB

P22 - INTEROCEPTION AS A MEDIATOR OF LOWER ANXIETY LEVELS AFTER MINDFULNESS TRAINING

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Mindfulness training (MT) describes a collection of attentional practices designed to cultivate attentional skills such as awareness, in an effort to renegotiate maladaptive self-referential tendencies. Interoception is the process of how the nervous system feels senses, integrates, stores, predicts and represents information about the state of the inner body at the conscious and unconscious levels. This ability has been related to emotional regulation and its psychopathology is involved in many conditions such as anxiety-related disorders. Here we report the results of a brief MT intervention regarding a randomized control condition over interoception, anxiety and mindfulness. Our results show consistent improvements within the group after MT but not in control group in interoception measurements (Mindfulness: V=23, p=0.001, r=0.33, CI: -0.603/-0.01 Control: V=99, p=0.89, r=0.01, CI:-0,306; 0,318) and anxiety (Mindfulness: V=148, p=0.03, r=0.31, CI: 0,027; 0,576; Control: (V=115, p=0.72, r=0.07, CI: -0,245; 0,383). Additionally, a causal mediation showing the negative correlation between interoception and anxiety scores after the MT is described. According to these results, a brief MT increases interoception sensibility, but not the accuracy, and this change leads to a reduction in anxiety state scores in a healthy adult population. Importantly, the change in interoception sensibility can be seen in regulatory aspects of interoceptive sensibility, representing how the body is used for self-regulation purposes. To our knowledge, this is the first study that shows the potential acute effect of a brief mindfulness-based attentional training on interoception and its relation with anxiety and possible applications in daily life.

Funding: CAPES

P23 - ANXIETY TRAIT IS RELATED TO MINDFULNESS LEVELS IN NON-MEDITATORS

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Investigations regarding mindfulness meditation have been increasingly prevalent, mainly due to its reported important psychological effects. However, researches often focus on mindfulness training rather than an individual approach to difference. To understand the influence of individual difference of mindfulness trait on measures of wellbeing, we analyzed self-reported measures of anxiety (State and Trait Anxiety Inventory), perceived stress (Perceived Stress Scale), affect (Positive Affect and Negative Affect Schedule), mindfulness trait (Five Facets of Mindfulness Questionnaire) and state (State Mindfulness Scale) and plasma cortisol. The sample consisted of university students, with no previous experience in meditation and yoga (n=40, mean age: 24.15+3.61 years old, 20 females). We used k-means to classify the levels of mindfulness trait, with the number of k clusters set to 2, as suggested by several indexes provided by NbClust package available in R software. Based on previous report showing that the “observe” facet of Five Facets of Mindfulness Questionnaire is not reliably measured in non-meditators, we used a four-factor model from this questionnaire, removing “observe” from the total score and excluding this facet from clustering analysis. The grouping variables (total score and facets “describe”, “non-judge”, “act with awareness” and “non-react”) were previously standardized on z-

scores, and after clustering centers were above mean for a cluster (then named High Mindfulness, n=16) and below the mean for the other (so-called Low Mindfulness, n=24). Further, we performed a stepwise (backward) logistic regression using clusters as a binary outcome and Akaike Information Criteria for variable selection. Only perceived stress (logit= 2.02, p= .02), anxiety trait (logit= -3.97, p= .002) and plasma cortisol (logit= 1.15, p= .04) were significant classifiers of mindfulness trait, although mindfulness state (logit= .88, p= .06) has been also maintained in the selected model. We then compared these variables between clusters using multivariate analysis of variance and found a multivariate effect (Pillai= .47, F(1,38)= 7.82, p< .001), but only anxiety trait reached statistical significance (F(1,38)= 12.82, p< .001; others: p> .1). This result corroborates the literature regarding the inverse relationship between higher mindfulness trait and anxiety measures , but failed in replicate the inverse association between the high trait and other measures, such as negative affect and perceived stress, and finding a positive association between the high trait and positive affect. We conclude that individuals with no experience in meditation but with high level of mindfulness trait have lower anxiety trait than low mindfulness individuals.

Funding: CAPES

P24 - ESTABLISHING A NEW RODENT MODEL OF AUTISM BY INTRAUTERINE EPIGENETIC MODULATION IN RATS

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The epigenetic modulator and anti-epileptic drug valproic acid (VPA) is a known environmental risk factor for the development of autism spectrum disorder (ASD). The rat ASD model generated by a single intraperitoneal injection of VPA in pregnant females at gestational day 12 (E12) is well established and has been used by our and other research labs to study various aspects of ASD, such as behavior, neurophysiology and cellular features. Given its face, construct and prediction validity, this model is an invaluable tool for preclinical research. In this project, our aim is to refine two aspects of the model: its variability and penetrance of autistic-like traits. For that, we intend to generate a new ASD model by intrauterine administration of VPA, in which we will be able to precisely control the concentration of drug exposed to each embryo. Our goal is to find the optimal dose of VPA in which there is minimal fetal reabsorption and teratogeny, with maximum homogeneity and severity of the autistic endophenotype. To do so, we will perform a medial laparotomy on pregnant dams at E12 (when the embryos are undergoing the end of primary neurulation) to expose the uterine horns, enabling single-embryo injections. Each embryo will receive a single VPA injection of 1-8 µmoles into the amniotic fluid. Controls will receive saline injection instead. Once finished the injections, female dams will have their muscle and abdominal skin sutured and pregnancies will be allowed to proceed undisturbed. Following vaginal delivery, we will analyze the number of fetal reabsorptions (difference between the number of injected embryos and pups at term) and teratogenic effects in newborn pups, such as syndactyly, polydactyly and facial abnormalities. During postnatal development, we will also analyze maternal separation-induced ultrasonic vocalizations at postnatal ages (P) 7, P14 and P21, locomotor activity, stereotypical behavior in the open field test (P21, P30), and social interaction (P35). At P36, the animals will be euthanized and their brains collected for histological assays. All data will be compared to saline-injected controls (generated by the same project) and to intraperitoneally-VPA injected animals (from previous data of our lab).

Funding: CNPq, CAPES, UFRN

P25 - LATENT SEMANTIC ANALYSIS IN THE POETRY OF RAUL GOMEZ JATTIN

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Raul Gógez Jattin was a renowned Colombian poet that suffered from chronic mental disorders. Raul´s live was marked by a troubled childhood, and social preconceptions due the fact that he was homosexual and drug user. The quality of his poetry, along with his mental state makes his work valuable for psychiatric investigation. The principal objective of the present research is to assess Raul's work as case study, but in a quantitative way. To fulfill this goal, we use Natural Language Processing (NLP) and Machine Learning (ML) tools. Raul´s poems published in seven different books were compared with controls (contemporary Colombian poets free from mental illness, n = 20). For comparisons were computed the semantic similarity from poems to target words selected heuristically (n = 99). Each unit of text (poems or individual target words) used in the study was converted to vectors by a word embedding tool (FastText applied on Spanish corpus). Next, was computed the semantic similarity (cosine similarity) between poem vectors and target word vectors, resulting a Similarity Matrix (rows representing poems, columns representing target words). Based on the Similarity Matrix three main results can be highlighted. First, was trained a classifier based on Discriminant Analysis to separate between Raul´s and control´s poems. The mean accuracy for the classifier on bootstrap sampling was 0.74. This result suggests that by using a computational model Raul´s poems can be correctly distinguished from controls in approximately 75 % of the cases. Second, the target words were ranked based on its capacity to discriminate between the two groups of poems, Fisher Score was used as ranking metric. The top five ranked words were: 'Psiquiatra', 'Padre', 'Homosexual', 'Loco' and 'Culpa'. These words are related to Raul´s psychiatric condition, sexual orientation and maybe the pressure that he felt from his social environment. Third, we perform a correlation analysis between the semantic similarity for target words from Raul´s poems and its date (taking the publication date as reference). The words with significant correlation ($p < 0.05$) were: 'Escapar', 'Infierno', 'Prisión', 'Carcel', 'Ira' for positive correlation and 'Humor' with negative correlation. This is consistent with the fact that Raul write in some poems that he was prisoner of a jail of health, which seems to increase with the pass of years. In contrast, his mood tends to decrease until his last days. In general, results suggest that NLP and ML could be effectively used to quantitative assessment of written poetry. The findings also agree with previous studies indicating that computational tools are valuable complement for traditional approaches on psychiatry research.

Funding: PNPD–CAPES

P26 - EFFECTS OF A GAMING INTERVENTION WITH STUDENTS FROM DIFFERENT SOCIOECONOMIC STATUS

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Recent findings show that children from low-socioeconomic (SES) tend to have reduced performance on several tasks involving working memory, attention and executive control. In addition, researchers argue for the effectiveness of training of these same cognitive skills as a way to ameliorate children's EF skills as well as scholastic outcomes. To investigate that, we trained 61 low-SES children for 5-7 weeks with games focused on practicing executive functions and compared their performance with that of 60 age-matched high-SES and also trained peers on measures of executive functions and reading. Our results demonstrate a general effect of SES for the dependent variables. Furthermore, our findings demonstrate a positive near transfer effect on a working

memory and a selective attention test and a far transfer effect on the words and pseudowords reading measure.

Funding: CAPES

DB

P27 - EFFECTS OF AYAHUASCA ON BIOCHEMICAL PARAMETERS OF A PLACEBO-CONTROLLED CLINICAL TRIAL FOR MAJOR DEPRESSION

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Ayahuasca is an Amazonian psychedelic beverage prepared by the slow decoction of the Banisteriopsis caapi root vine together with the leaves of the shrub Psychotria viridis. B. caapi contains ß-carboline alkaloids (harmine, tetrahydroharmine, and harmaline) that act as reversible inhibitors of monoamine oxidase (MAO)-A, whereas P. viridis is rich in N,N-dimethyltryptamine (DMT), a hallucinogenic tryptamine that acts as a 5-HT1A/2A/2C agonist. Ayahuasca has been used in therapeutic trials, mainly to psychiatric disorders as major depression, posttraumatic stress disorder (PTSD), antisocial behavior and drug dependence. However, it is not known the consequences of Ayahuasca on biochemical parameters, both in control as well as in depressive patients. To fill this gap, we conducted a double-blind randomised placebo controlled trial, collecting a series of tests and assessments one day before and one day after a single dosing session with ayahuasca. Here we show results from general hematological and biochemical parameters of 28 patients with major depressive disorder and 42 healthy volunteers. We preliminary observed no significant alterations in both control and depressive groups compared to placebo, which suggests that ayahuasca is clinically safe.

Funding: CNPq

DB

P28 - SEEING NON-EXISTENT MOVEMENTS: A NOVEL PSYCHOPHYSICAL PARADIGM TO STUDY THE EFFECT OF COLLINEARITY ON APPARENT MOTION

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Psychophysics is the quantitative investigation of perceptive or evoked responses during external stimulation. Despite its wide range of applications and contributions to the understanding of cognitive processes, new paradigms are rarely introduced. The Motion Quartet (MQT) is one of the currently established protocols to study apparent motion. It is a bistable stimulus that leads to the percept of either vertical or horizontal motion. Interestingly, when the MQT is presented in the central visual field the observers are more likely to perceive vertical motion. This bias was attributed to the longer integration time required to process horizontal motion through interhemispheric connections. It is known that the presence of collinear contours facilitates perceptual grouping. Previous work in our lab has demonstrated that also visual interhemispheric connections implement this psychophysical Gestalt criterium as they link neurons of the same orientation preference and with collinearly aligned receptive fields. We thus hypothesize that horizontal collinear (as opposed to non-colinear) contours should facilitate perceptual grouping across the visual field's midline and thus bias bistable motion. Therefore, we propose a new not yet examined version of the MQT paradigm introducing Gabor patches of collinear gratings in its four elements. We test whether the „natural“ facilitation of vertical motion perception during a MQT task can be counter-balanced. To this aim, we recorded both electroencephalographic activity and

behavior during two different conditions: vertical distance increment with constant horizontal distance (VH) and horizontal distance increment with constant horizontal distance (VH). Each condition had three subgroups: horizontal and vertical Gabor patch (5 c.p.d) and control stimuli (dots with 50% of Gabor patch size) with vertical (CV) and horizontal (CH) increments. All stimuli had 4 deg diameter and the subject was 57 cm away from the screen. We recorded EEG data of one subject using a 68 electrode system during all MQT protocols. The data was analyzed offline using Analyzer 2.2 and Matlab using the following steps: common reference, IIR bandpass filter (0.5 - 100Hz), notch filter at 60 Hz, semi-automatic artifact inspection, ICA, epoch segmentation based on each stimuli presented on the screen, and acros trial-coherence performed on Matlab to determine long-range interhemispheric coherence using left-right pairs of electrodes (O1-O2, PO3-PO4, PO7-PO8). Behaviorally, we determined the Parity Ratio (PR) using the average distances of perceptual-switch in each of the six protocols. Surprisingly, we found the lowest PR in the HH group (0.85). This indicates a strong collinear effect of the horizontal Gabor patch while increasing the horizontal distance. Electroencephalographic analysis indicated stimulus-related differences in interhemispheric phase-synchrony. The EEG result was also congruent with the behavior data, once the HH group showed the highest coherence score on the interhemispheric pairs of electrodes PO3-PO7 (0.52) and PO7-PO8 (0.54). Our preliminary data indicate that PR and interhemispheric coherence during the MQT paradigm can be modulated by both vertical and horizontal Gabor patches, with a strong effect of colinearly aligned horizontal Gabors to bias the horizontal motion percept across the visual field's midline.

Funding: CAPES

DB

P29 - CANNABINOID MODULATION OF FRONTO-AMYGDALOID NEURONAL ACTIVITY DURING EMOTIONAL TRANSFER IN A RODENT MODEL OF AUTISM

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Background: Empathy is the ability to recognize and introspect someone else's emotions. It is an important aspect of social behavior in mammalian species that is dependent on the observer's attention, motivation and past experiences. Recent studies demonstrate that rats display emotional contagion, a proxy for empathic responses, and observational learning. In the brain, the amygdala plays a central role in the processing of social information, enhancing the salience of social sensory stimuli and assigning affective valence and autonomic responses via its connections through the hypothalamus. In this region, CB1 cannabinoid receptors are restricted to cholecystokinin-positive GABAergic neurons and play an important role regulating emotional processing. Considering that social interaction and affective responses are critically affected in autism, we hypothesize that cannabinoid modulation could improve some of these behaviors. Objective: Our aim is to evaluate the cannabinoid modulation of emotional transfer response of rats model of autism (VPA model) and the neuronal activation of fronto-amygdaloid circuits using immediate-early gene expression and extracellular multi-unit activity. Methods: VPA rats will be generated by fetal exposure to valproic acid. Controls will be treated with saline. After birth, pup development will be monitored from postnatal day (P) 1 to P21 (weight gain, eye-ear opening and ultrasonic vocalizations). At P21, animals will be tested in the open field to measure locomotion, exploration and grooming, and subsequently weaned. At this time, they will be housed in pairs (matched by sex) and assigned to four experimental groups that will be taken to the empathy test: VPA (observer) watching a familiar (demonstrator) rat receiving shock (VS+); VPA watching a familiar rat without shock (VS-); Control watching a familiar rat receiving shock (CS+); Control watching a familiar rat without shock (CS-). In a fist phase of the project (at P35-45), the animals will be tested for emotional contagion (empathy test). Each rat will observe a familiar animal

receiving a set of 5 foot-shocks and behavioral responses (freezing, social approach, yawning, grooming, vocalization) will be acquired by a video camera/ultrasonic microphone and quantified in all animals. In two new groups (CS+C and VS+C), we will test the modulatory effects of systemic administration of cannabidiol on the behavioral responses of the observer. Here, the animals will receive an injection of cannabidiol (30, 60 mg/Kg, i.p.) 30 min prior to the empathy test. Ninety minutes after the test the animals will be perfused and the brains collected for the analysis of immediate-early gene expression (zif268; c-fos). In a second phase of the project, the animals will be implanted with recording electrodes in the amygdala, prefrontal cortex and hippocampus before the empathy test and following recovery, electrophysiological recordings will be conducted before and during the empathy test. On the following day, brain activity will be recorded during a social interaction test with the familiar demonstrator partners. Brain activity (local field potentials and unit recordings) will be analyzed between groups. At P42, the animals will be perfused and the brains collected to confirm electrode placement.

Funding: CAPES, CNPq, UFRN

P30 - TOWARDS A ROLE OF 5-MEO-DMT IN ANXIETY-RELATED CIRCUITS

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Anxiety is a worldwide prevalent circuitopathy. Several factors can influence circuits mismatches. Finding elements that can rescue the optimal function of circuits is an important way to treat it properly. Here, we sought to verify how 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), the main active compound of Amazon plants traditionally used by native people, can affect anxiety-related circuits through a novel approach based on glutamate-driven neuroplasticity. In this study, we are investigating the effect of 5-MeO-DMT on anxiety-related gene expression and if it modules the expression of important genes involved in hippocampal plasticity and neuronal activity by dissecting and performing RT-qPCR from specific subregions, such as Dentate Gyrus and ventral CA1, related to anxiety behavior. In addition, we found that treated mice exhibited less anxious behavior and lower corticosterone levels compared to control. We also characterized their electrophysiological profile through in vitro recordings. Taken together, these findings may open doors for further studies and point 5-MeO-DMT as a new therapeutic opportunity.

Funding: CAPES

DB

P31 - GAMMA AND ENTRAINMENT IN THE CAT RETINA: TWO FACES OF THE SAME PHENOMENON?

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Gamma responses in the retina are transmitted to the lateral geniculate nucleus and the cortex and are thought to encode stimulus size and continuity. Here, we measured the coherence for single-cell gamma responses in the retina and lateral geniculate of the cat. During halothane anesthesia, synchronous gamma oscillations were robust for cells of the same polarity. To our surprise, however, gamma oscillations were reduced as halothane levels were lowered, and were absent under ketamine. In follow-up experiments, we recorded from the LGN of awake cats (N= 2), which were subsequently anesthetized with ketamine followed by halothane. Gamma oscillations appeared only when halothane was added to the anesthesia protocol. 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 activity. These latter findings indicate that endogenously generated oscillations in the early visual system may shorten the representation of fast-changing stimuli. Overall, our results do not support the hypothesis that fast gamma oscillations in the retina play a role in natural vision. The very synchronization mechanism in the retina responsible for the powerful entrainment of activity by a periodic stimulus may also lead to fast oscillatory dynamics in the retinal circuits under halothane anesthesia.

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P32 - ZBTB20 EFFECT OF NEURAL SPECIFICATION DURING CEREBRAL CORTEX DEVELOPMENT

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Understanding the regulatory mechanisms controlling the fate decisions of neural stem cells is crucial to comprehend mammalian central nervous system development in health and disease. Important progress has been made towards the identification of cellular and molecular mechanisms controlling the generation of neuronal diversity. However, still little is known about the origin of astroglial cells. In literature has been saw that the Zbtb20 gene have a important function in the astrocyte specification, supplied a basic understanding of how intrinsic mechanisms govern the production of astrocytes from precursor cells and the generation of astrocyte diversity. Thus, it was suspected that overexpression of Zbtb20 in cortical progenitors change the proportion of neurogenesis and gliogenesis during development. To elucidated our hypothesis we utilized videomicrocopy analysis to evaluated division cycles features and cells phenotypes generated with or without Zbtb20 overexpression in cortical progenitors. Using time-lapse videomicroscopy to made a photo sequence of cultivated cells in vitro, that allowed us track cell line and possible effects in experimental group. Our data indicate don't have change in neural (NeuN+) generation between control and experimental groups. However, when evaluated culture post-mitotic cells, there is a significant decrease in no express GFAP or NeuN cells, in experimental group. Hereafter, we pretend investigate which cell type this would be. Dedicate to study like that is add what is understood about the regulation these cells, given that that regulation is related to neurological diseases.

Funding: CNPq, CAPES

DB

P33 - ANALYSIS OF ELECTROENCEPHALOGRAPHIC MICROSTATES AND DREAM CONTENT TO EVALUATE THE INFLUENCES OF SLEEP ON BEHAVIOR DURING A PREY AND PREDATOR SIMULATION

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Sleep is a mental and corporal state that is important for the elimination of toxins generated by metabolism and for the consolidation of memories. It is a very conserved state throughout animal evolution, being present in all species of reptiles, birds and mammals ever studied. Due to its high evolutionary preservation, it is presumable that sleep has influenced the constitution of the different behaviors found in animals. For example, were the distinct prey and predator habits influenced by sleep? And by dreams? Scientific research has not yet found robust differences in prey and predator

sleep. However, research possibilities in humans may be a potential source of discovery in this area. First, because human beings can communicate to us the dreams they had. In addition, complex tasks can be crafted using video games that simulate various situations that would otherwise be difficult to do. In this sense, experiments were performed with 17 pairs of volunteers, who came simultaneously to the laboratory and had their brain activity recorded by electroencephalography (EEG). During registration the pair played an electronic game for 45 minutes, then slept for 2 hours and then played again for another 45 minutes. In the game, one of the participants acted as prey and the other as a predator. The prey could hit the opponent with punches only, while the predator could hit with punches and a firearm. Therefore, the predator had the advantage in the dispute, as it is in nature. EEG signals were analyzed using a technique called microstates. It classifies the recording time as a sequence of four electrical activity distributions, called microstates "A", "B", "C" and "D". Dream reports from participants that dreamed were also assessed using a technique known as cosine similarity. This technique evaluates the semantic distance of a text to a keyword, generating a metric that indicates how similar the meaning of the text words is to the keyword. Thus, we evaluated how similar dream reports were to some keywords. One of the words tested was the word “game”, which is a way of analyzing how much the participants dreamed about the game. Some significant results were found. Of these, we highlight the positive correlation found between the percentage of time covered by microstate A and the difference in the number of predator deaths between game 2 and game 1. This correlation was found both by assessing the differences in microstate properties between game 2 and game 1 (rho: 0.5, p: 0.048), as evaluating these properties during sleep (rho: 0.5, p: 0.043). A negative correlation was also found between the distance of dream reports for the word game and the difference in the number of deaths between game 2 and game 1 for prey (rho: -0.7, p: 0.004). These results indicate that brain activity and dream content influence the behavior of individuals subjected to both prey and predator roles. The activity of microstate “A”, characterized by a higher activity of the temporal cortex, impairs the predator performance. On the other hand, dreaming about the game promotes better prey performance. Additional analyzes will be performed to understand these results.

Funding: FINEP

DB

P34 - EFFECT OF ZIKA VIRUS CONGENITAL INFECTION OVER FETUS-TO-MOTHER MICROQUIMERISM

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The Brazilian Health Ministry has detected an outbreak of births of microcephaly patients that was correlated with the zika virus (ZIKV) epidemic that happened in 2015. Despite ZIKV’s role in the origin of brain malformations have been also tested experimentally, little is know about the cellular mechanisms involved in the lesions observed. According to Health Ministry, 4.121 cases of microcephaly were notified in 2015 and 8.610 in 2016. Although a reduction occurred in number of cases throughout the following years, 1.657 notifications were reported in 2018 confirming it's relevance. Therefore, it is important to keep investigating what actually happens in pregnant women when they are infected with ZIKV in order to mitigate the effects. It is known that during pregnancy several changes happen in the woman's body, including a bidirectional exchange of a small number of cells between the mother and child, called microchimerism. This cell traffic begins around fourth week of gestation and the probability of finding offspring's cells in mother's blood increase as the pregnancy continues. However, even years after giving birth, those cells might still be found in the woman's blood. Events such as infections during gestation may result in a production of reactive antibodies against fetal antigens. Here, we hypothesize that ZIKV induces fetal

cell migration to the mother's blood. This migration activates the maternal immune system to react against fetal brain. Therefore, this study aims to verify if an induction of fetal cell traffic occurs from fetus to mother in the presence of ZIKV, working as a base for further studies regarding how pregnant´s immune system get activated when infected. In order to do that, we will use a transgenic mouse line that expresses EGFP constitutively in all their cells (beta-actin promoter + CMV enhancer). Crossing a heterozygous EGFP male mouse with C57BL/6J females, we obtain wild type mothers with pregnancies of EGFP embryos. Here, we show that EGFP positive and negative cells in the blood are separable by flow cytometry. In order to measure physiological microchimerism, we will work with 3 groups. In one of those, we will inject ZIKV in the amniotic fluid on embryonic day 13 (E13), while the others will be two controls, non injected with uterus exposure and inactivated virus injection (Mock). Blood samples from all groups will be collected from the maternal tail lateral vein. Those samples will be collected one day before C57BL/6J females are put together with EGFP males (E-1), but also those samples will be collected in E7, E13, E14, and P0. In this experimental design, half of the embryos do not inherit EGFP; and therefore, we can analyze microchimerism between siblings. PCR analysis are also meant to me done on brain and liver from mothers of all groups to test for persistent fetal cells in the mother. Our preliminary results show that with this experimental design we are able to observe fetal cells passing to the maternal blood.

Funding: CNPq, ICGEB

P35 - A SINGLE DOSE OF N,N-DIETHYLLYSERGAMIDE CAN IMPROVE LEARNING IN YOUNG AND ADULT RATS, WHILE OLD RATS N,N-DIETHYLLYSERGAMIDE PLUS EXPOSURE TO ENRICHED ENVIRONMENT

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Background: Learning and memory decay with aging, in correlation with loss of synapses and decreased plasticity. Exposure to an enriched environment (EE) enhances learning & memory in aging rodents. Previous studies have shown that serotonergic psychedelics promote synaptic plasticity and can cause changes in brain function that persist long after the acute effects. We set out to assess whether different protocols of administration of the serotonergic agonist N,N-Diethyllysergamide can modulate learning in rats of different ages. Methods: Young (2 months), adult (8-10 months) and old (12-18 months) Wistar rats were treated with N,N-Diethyllysergamide. Animals received 0.13mg/kg of the drug via intraperitoneal injections, were housed individually, with an interval of 6 days without treatment before exposure to an object recognition task (ORT). In addition, old rats injected with saline or N,N-Diethyllysergamide were exposed to EE for 6 days (3h/day) and housed in groups of 5 animals between the last injection and ORT. The ORT was composed of training and test session (30 minutes interval). Two identical objects (assembled using LEGO™ pieces) were used for the training session, with 12 edges and vertices each, for the training session one of the objects was replaced by an object with 14 edges and vertices. Results and Conclusions: Young animals treated with saline spent in average 58.57±9.06% of the test session exploring the new object, while young animals treated with N,N-Diethyllysergamide spent in average 67.95±13.13($p = 0.05$) of the test session exploring the new object. Novel object exploration in adult rats increased significantly ($p = 0.008$) from 44.16±7.49% (saline) to 62.65±5.07% (N,N-Diethyllysergamide), but N,N-Diethyllysergamide treatment did not change ORT performance in old rats unexposed to EE ($p = 0.5$). Notably, old animals treated with N,N-Diethyllysergamide and then exposed to EE spent proportionally more time exploring the new object (62.24±7.41%), than old rats treated with saline and exposed to EE (52.77±6.96%, $p = 0.05$). All animals

exposed to EE performed better than old animals unexposed to EE (48.14±4.55%). The results suggest that N,N-Diethyllysergamide improves learning and/or novelty preference, and that old animals can be cognitively enhanced by a combination of N,N-Diethyllysergamide and EE.

Funding: CAPES, CNPq, UFRN

P36 - CHARACTERIZATION OF THE INTERACTION EFFECTS BETWEEN PHARMACOLOGICAL MODELS OF ALZHEIMER'S DISEASE AND PSYCHOSIS: EFFECTS OF CHRONIC KETAMINE TREATMENT IN STREPTOZOTOCIN INJECTION ALZHEIMER'S DISEASE MODEL

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Alzheimer's disease (AD) is the leading cause of dementia and the most prevalent neurodegenerative disease in the elderly population affecting about 40 million people worldwide. Among these patients, nearly 41% develop psychosis (P), which presents a more intense aggression, agitation and abrupt cognitive decline compared to patients without psychosis. In this context, patients with AD and P are treated with antipsychotics, which alleviate some of the positive symptoms of psychosis. However, this treatment increase the risk of cerebrovascular disease, accentuated cognitive impairment and the mortality rate. In the present project, we used intracerebroventricular (i.c.v.) streptozotocin (STZ) infusion for AD model and chronic intraperitoneal (i.p.) treatment with non-competitive NMDA-type L-glutamate receptor antagonists, ketamine chloridate (KET) for P model. Objective: (A) To characterize the behavioral and histological changes generated by the STZ-induced AD model (B) Test the hypothesis that chronic KET treatment would accentuate STZ-induced cognitive impairment and histological changes corresponding to DA+P model. Methodology: Adult Wistar were divided into four groups underwent (1) i.c.v. streptozotocin, (2) i.p chronic KET treatment or (3) combination of STZ followed by chronic KET treatment. The animals' performance in working spatial memory (SWM) in 8-arm radial maze and novel object recognition (NOR) tasks were evaluated. These groups were dupliclated: one for SWM and the others 4 for NOR. Additionally, we tested motor sensory filter, locomotion, neuronal density with hematoxylin eosin (HE), brain-derived neurotrophic factor (BDNF) and immediate gene expression (Zif-268) in circuits relevant to memory processing and injured in AD. Results: Our findings indicate that STZ compromises SWM, measured 20 days after its application. The vehicle group obtained an average error of 14.94 ± 0.66 and the STZ group 18.94 ± 1.08 (nVei = 18 and nSTZ = 16, test t-Student; T=-3,224; df=32, p<0,001). NOR was also impaired after 27 days of STZ infusion, demonstrated by the rate of exploration of the new object relative to the familiar. While the vehicle group reached a rate of 67.73 ± 4.83 the STZ group totaled 53.78 ± 4.10 (nVei = 7 and nSTZ = 11). Additionally, STZ had decreased neuronal density in the entorhinal cortex by 12% (vehicle: 162.07 ± 7.13 neuron / mm^3 and STZ: 143.59 ± 3.42 neuron / mm^3; nVei = 7 and nSTZ = 8 – p=0.03, one-way ANOVA post hoc Tukey) as analyzed by HE staining. There was a statistically significant difference between group with only STZ (n=8) compared with only Ket (n=6) group (p = 0.034, one-way ANOVA post hoc Tukey) in the entorhinal of the left hemisphere, as well as in the right limbic region (p = 0.019, one-way ANOVA post hoc Tukey) in BDNF. Also, there was a difference on Zif-268 in the right cingulate between control group (n=6) and STZ (n=8) only group (p = 0.037, one-way ANOVA post hoc Tukey), in the left cingulate between group with Ket (n=6) compared to the group with STZ and Ket (n=7) (p=0.03, one-way ANOVA post hoc Tukey).

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DB

P37 - THE ALTERNATION OF STATIC AND DYNAMIC UNRESPONSIVE STATES IN OCTOPUS INSULARIS IS ANALOGOUS TO THE SWS/REM SLEEP CYCLE

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The combination of body quiescence and skin pattern changes displayed periodically by Sepia officinalis, as well as the high threshold for arousal upon stimulation and increased brain activity in quiescent Octopus vulgaris, have been interpreted as evidence in cephalopods of a state analogous to the rapid-eye-movement sleep (REM) observed in higher vertebrates. Skeptics still argue that animals were possibly awake because i) responsiveness was not tested in Sepia officinalis, and ii) Octopus vulgaris studies did not specify body patterns during the arousal threshold test. To address these questions we quantified behavioral states and their transitions, and measured reaction times after sensory stimulation in 4 adult specimens of Octopus insularis. Two quiescent unresponsive states (median reaction time: 50 s) were detected in tandem, the first analogous to slow-wave sleep (SWS) with long duration, uniformly white skin and closed pupils, and the second analogous to REM, with short duration (median 40.8 s), dynamic skin patterns and moving pupils. The REM-like state was periodic (63.6% of allrecurrences between 22-42 min, mode 32 min), and occurred after the SWS-like state (82% of all transitions). The results confirm the existence in cephalopods of a cycle analogous to the SWS/REM alternation in higher vertebrates.

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P38 - CONNECTIVITY OF DMRT3 SPINAL INTERNEURONS

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Locomotion is coordinated by neuronal circuits in the spinal cord called central pattern generators (CPGs). Doublesex and mab-3 related transcription factor 3 expressing cells (Dmrt3 cells) are spinal cord inhibitory interneurons that are necessary for normal CPG function and limb coordination. We used monosynaptic circuit tracing with glycoprotein deleted rabies virus to retrogradely label Dmrt3 input cells in mice. Our data shows that Dmrt3 neurons receive inputs from the primary sensory afferents located in the dorsal root ganglia. To identify what subtype of sensory neurons these input cells belong to, the tissue was analysed immunohistochemically. We demonstrate that Dmrt3 neurons are innervated by neurons that are immunopositive for both parvalbumin and calbindin, markers for proprioceptive neurons.

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P39 - ELECTROPHYSIOLOGICAL CHARACTERIZATION OF MARTINOTTI-ALPHA2 CELLS IN L5 OF THE PRIMARY MOTOR CORTEX

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The primary motor cortex (M1) is an area in the frontal lobe, critical for the planning and execution of movement. Among the 74.000 neurons that can be found in M1, 15% are GABAergic interneurons, which are important to maintain the excitatory-inhibitory balance in neuronal networks and modulate cortical output of excitatory neurons. Martinotti cells (MCs) are one abundant cross-laminar type of GABAergic interneurons in M1, positive for somatostatin and mainly defined by their ascending axon collaterals to layer 1, where they target distal dendrites of pyramidal cells (PCs). MCs in layer 5 express the nicotinic acetylcholine receptor alpha2 subunit (MC-alpha2), which can be labelled by crossbreeding Chrna2-cre mice with a reporter line. Our study aims to investigate the electrophysiological properties, morphology, distribution and shape of axonal arborizations of MC-alpha2 cells. Therefore, we obtain whole-cell recordings from MC-alpha2 cells in current clamp mode. Our analysis demonstrated that two subtypes of MC-alpha2 cells in M1 exist. Both type A and type B MC-alpha2 are small multipolar neurons with an ovoid soma, situated in layer 5 and sending their axons mainly to cortical layer 1. Electrophysiological characteristics of type A MC-alpha2 cells showed a high action potential threshold, an adapting firing pattern and a nearly linear current-frequency relation. Compared to this, type B MC-alpha show the opposite character. They have a low action potential threshold, a strong Ih mediated sag, rebound action potentials and a stagnating current-frequency relation. As a future plan, we will explore the intra-laminar connectivity between MCs-alpha2 and PCs through paired patch recordings, as well as optogenetic manipulation of MC-apha2. Thereby, we try to elucidate the connection between type A and B MC-alpha2 cells and PCs, if they favour thick or thin tufted PCs and at which compartment of the PC dendrite they connect to. In conclusion, this work shows that M1 layer 5 MC-alpha2 has two subtypes with distinct electrophysiological parameters, however more experiments are needed to answer if the subtypes present distinct roles and how they influence the output behaviour of nearby PCs.

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P40 - INVESTIGATING THE ROLE OF OLMA2 INTERNEURONS IN THE HIPPOCAMPUS

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Hippocampal interneurons are a diverse population of cell types that participate in memory processes. However, the specific function of the different populations remains poorly understood. Oriens lacunosum-moleculare α2 (OLMα2) cells are a subpopulation of hippocampal interneurons that specifically express the cholinergic receptor nicotinic α2 subunit. They act as a gate switch controlling the internal and external inputs to the hippocampus. In this project, we aim to characterize the role of OLMα2 interneurons in the hippocampus. For this purpose, we will investigate the inputs to OLMα2 along the dorsoventral axis by using retrograde monosynaptic tracing. This study will be complemented by investigating the role of the neuropeptide Nociceptin, implicated in memory and stress response, in OLMα2 cells. The gene coding for this peptide will be conditionally knocked out using the CRISPR/Cas9 system. Our preliminary results reveal some input cells to OLMα2 interneurons, which will be analysed by subsequent immunohistochemistry to identify the different cell populations. We have produced a mouse line with approximately 40% of OLMα2 cells expressing Cas9 that will be

transfected with the plasmid containing sgRNA to conditionally knockout Pnoc. This study will help to better understand the hippocampal circuitry, crucial knowledge to prevent or treat disorders characterised by memory impairment.

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