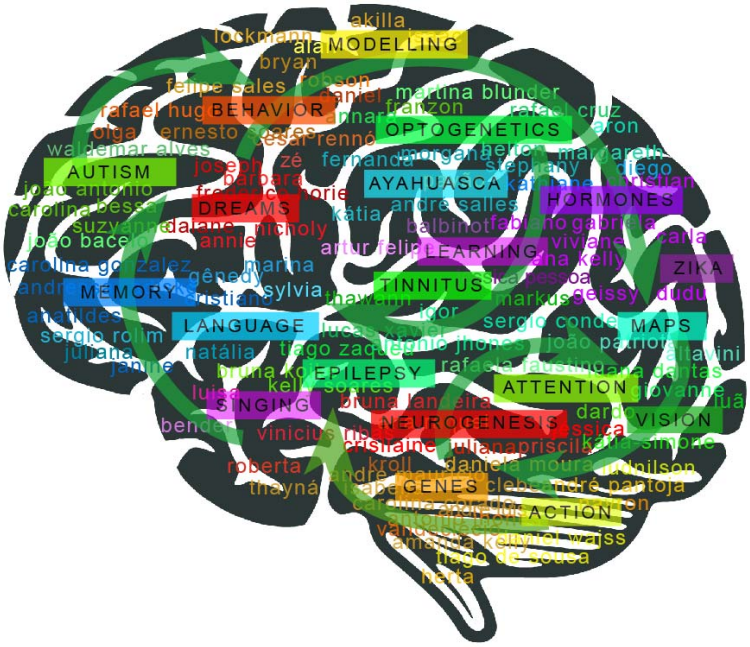
UNIVERSIDADE FEDERAL DO RIO GRANDE DO NORTE

INSTITUTO DO CÉREBRO

HOUSE SYMPOSIUM 2016



BRAIN MATTERS:

THE BRAIN IN A NUTSHELL

CAMPUS UFRN

NATAL

GREETINGS

It is a great please to welcome you to the Second House Symposium of the Instituto do Cérebro (ICe) of the Universidade Federal do Rio Grande do Norte. The motto "the brain in a nutshell" expresses the efforts of the different groups of the ICe to understand the organization and function of one of the most complex forms of matter of the universe, the brain.

It is the perfect opportunity to get to know the latest findings and discoveries of our research teams. In this respect, the Program brings interesting topics spanning from cellular reprogramming to new diagnostic tools in psychiatry, visual and auditory physiology, experimental approaches towards neurological disorders and new insights on learning and memory.

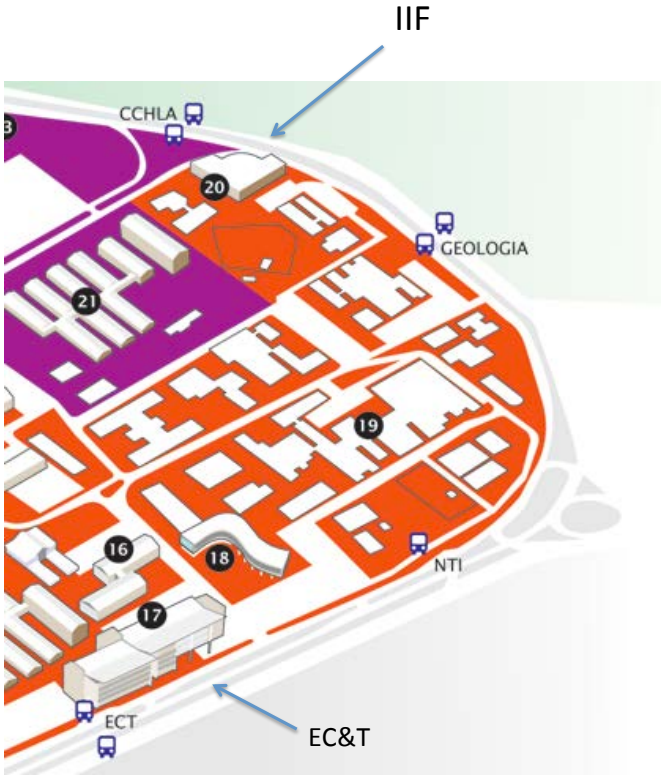
This year, the symposium is taking place at the new building of the International Institutes of Physics of the UFRN. Thus, the House Symposium stretches its borders towards other spaces of the university, aiming to boost transversal knowledge between different areas of expertise. We are also happy to welcome prof Gilad Silberberg from Karolinska Institute and prof Korbinian Möller from Leibniz-Institut für Wissensmedien, who kindly accepted our invitation for delivering the keynote lectures. The participation of Dr. Gilad and Dr. Korbinian reflects the effort of the ICe to increase international collaborations in a period of political turmoil with apparent long-term impacts for national science and technology policies.

The topics covered by the symposium reflect the diversity of the research interests of the Institute: 20 oral presentations and 30 posters. This event was made possible with the unconditional support of the central administration of the university, through its direct financial support of the educational, scientific and administrative activities of the Institute, and most important, by all the staff of the ICe, who definitely makes this neuroscience center unique in the world!

We wish you a pleasant meeting, full of discoveries and a good time!

The Organizing Committee

Venue: International institute of Physics auditorium, UFRN
http://www.iip.ufrn.br/ (IIF = IIP, please see in fig below)



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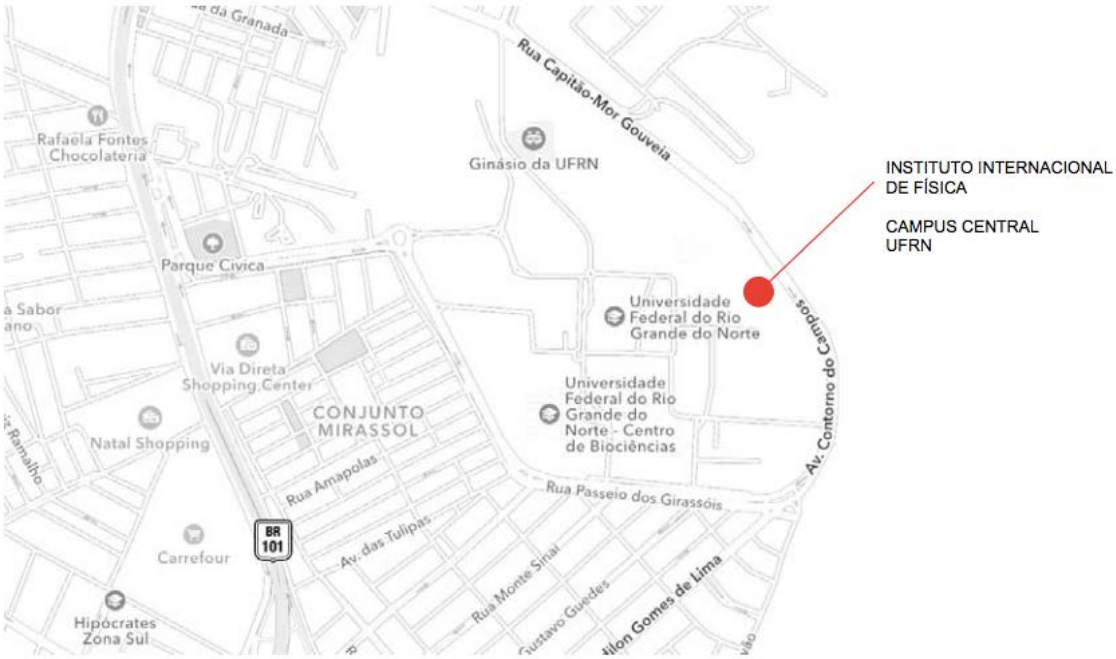

PROGRAM AT A GLANCE *

MONDAY, NOVEMBER 28		TUESDAY, NOVEMBER 29	
08:30 – 09:10	Registration	**Topic 3 - Neurological diseases Chair: Daiane Golbert**	
09:10 – 09:30	Welcome (Sidarta Ribeiro)	08:30 – 09:00	Kelly Soares
Topic 1 – Coding and rhythms Chair: Katarina Leão		09:00 – 09:30	Daniela Moura
09:30 - 10:00	Diego Laplagne	09:30 – 10:00	Rodrigo Romcy-Pereira
10:00 – 10:30	André Lockmann	10:00 – 11:00	Coffee & Poster Session 2
10:30 – 11:30	Coffee & Poster Session 1	11:00 – 11:30	Annie C. Souza
11:30 – 12:00	Richardson Leão	11:30 – 12:00	Dmitry Melnikov (IIP)
12:00 – 12:30	Markus Hilscher	12:30 – 14:00	Lunch break
12:30 – 14:00	Lunch break	**Topic 4 – From cellular mechanisms to behavior and back Chair: Janine Rossato**	
Topic 2 – Pharmacological and behavioral manipulation of the CNS Chair: André Salles		14:00 – 14:30	Gustavo de Souza
14:00 – 14:30	Dardo Ferreiro	14:30 – 15:00	Tarciso Velho
14:30 – 15:00	Sergio Neuenschwander	15.00 – 16:00	Coffee & Poster Session 2
15:00 – 15:30	Fabio Novaes (IIP)	16:00 – 16:30	Gênedy Apolinário
15:30 – 16:30	Coffee & Poster Session 1	16: 30 – 17:00	Andressa Radiske
16:30 – 17:00	Fernanda Palhano	17:00 – 18:00	Keynote Lecture I: Gilad Silberberg
17:00 – 17:30	Geissy Lima	18:00 – 18:15	Mini-break
17:30 – 18:30	Cocktail and music at sunset Fabio Soren Presgrave and students	18:15 – 19:15	Keynote Lecture II: Korbinian Möller
		19:15 – 19:30	Closing remarks

*** The Program at a Glance is subject to change.**

MONDAY, NOVEMBER 28, 2016

09:00 OPENING AND INTRODUCTORY REMARKS
Sidarta Ribeiro (Director of the Brain Institute)

Topic 1 – Coding and rhythms
Chair: Katarina Leão

09:20 SENSORIMOTOR RHYTHMS IN THE RAT
Diego Laplagne (Laplagne group)

09:50 RESPIRATION-COUPLED NETWORK OSCILLATIONS IN THE HIPPOCAMPUS
André Lockmann (Tort group)

10:20 – 11:20 Coffee & Poster Session 1 (MONDAY)

11:20 TO MOVE OR TO CRY: TYPE ONE AND TYPE TWO THETA ACTIVITY IN THE HIPPOCAMPUS
Richardson Leão (Leão R group)

11:50 THE DIFFERENTIAL EXPRESSION OF Ih IN OLMα2 CELLS ALONG THE DORSO-VENTRAL AXIS OF THE HIPPOCAMPUS
Markus Hilscher (Leão K group)

12:30 – 14:00 Lunch break

Topic 2 – Pharmacological and behavioral manipulation of the nervous system
Chair: André Salles

14:00 ABOUT THE EVOLUTION OF ORIENTATION COLUMNS IN VISUAL CORTEX: DIFFERENCES BETWEEN RODENTS AND CARNIVORES
Dardo Ferreiro (Schmidt group)

14:30 HOW GRATING STIMULI DO BIAS OUR CONCEPTS ON CORTICAL GAMMA SYNCHRONIZATION
Sergio Neuenschwander (Neuenschwander group)

15:00 UNRAVELING THE PHYSICS OF GRAVITATIONAL WAVES
Fabio Novaes (International Institute of Physics)

15:30 – 16:30 Coffee & Poster Session 1 (MONDAY)

16:30 PSYCHOBIOLOGICAL AND CLINICAL RESEARCH WITH AYAHUASCA
Fernanda Palhano (Araújo group)

17:00 EFFECTS OF BRIEF MINDFULNESS MEDITATION INTERVENTION ON STRESS PHYSIOLOGICAL MARKERS
Geissy Lima (de Sousa group)

17:30 Music entertainment by Prof Fabio Soren Presgrave and students at sunset
Musica Brasileira ao cair da tarde com UFRN Cellos

TUESDAY, NOVEMBER 29, 2016

Topic 3 - Neurological diseases
Chair: Daiane Golbert

08:30 USING ASTROCYTES AS DISEASE-MODIFYING TREATMENT FOR TEMPORAL LOBE EPILEPSY
Kelly Soares (Queiroz group)

09:00 REPROGRAMMING OF NEURONAL FATE BY KAINIC ACID ADMINISTRATION IN MOUSE HIPPOCAMPUS
Daniela Moura (Costa group)

09:30 ELECTROPHYSIOLOGICAL DYNAMICS OF LIMBIC SEIZURES IN TWO ANIMAL MODELS OF TEMPORAL LOBE EPILEPSY
Rodrigo Romcy-Pereira (Pereira group)

10:00 – 11:00 Coffee & Poster Session 2 (TUESDAY)

11:00 INVESTIGATION OF THE NEUROPHYSIOLOGICAL EFFECTS OF 5-METOXI-DIMETHYLTRYPTAMINE (5-MEO-DMT)
Annie C. Souza (Ribeiro group)

11:30 FIELD THEORY, TOPOLOGY AND FOLDING PROTEINS
Dmitry Melnikov (International Institute of Physics)

12:30 – 14:00 Lunch break

Topic 4 – From cellular mechanisms to behavior and back
Chair: Janine Rossato

14:00 PROTEOMIC CHARACTERIZATION OF BRAIN ABSCESS AND EMPYEMA CLINICAL CASES
Gustavo de Souza (S De Souza group)

14:30 STABILITY AND INSTABILITY OF NEURONAL CIRCUITS AND COMMUNICATION BEHAVIORS
Tarciso Velho (Velho group)

15:00 – 16:00 Coffee & Poster Session 2 (TUESDAY)

16:00 POSTACQUISITION STABILIZATION OF MEMORIES AFTER RETRIEVAL IN WATER MAZE REQUIRES NMDA RECEPTOR ACTIVITY
Gênedy Apolinário (Bevilaqua group)

16:30 PRIOR CONFLICTING KNOWLEDGE IS CRITICAL FOR AVERSIVE MEMORY RECONSOLIDATION
Andressa Radiske (Cammarota group)

Keynote Lecture I:
17:00 NEURAL MICROCIRCUITS UNDERLYING MULTISENSORY INTEGRATION IN THE MOUSE STRIATUM
Gilad Silberberg (Karolinska Institute, Stockholm, Sweden)

18:00 Mini-coffee break

Keynote Lecture II:
18:15 CONSIDERING WHITE MATTER IN NUMERICAL COGNITION
Korbinian Möller (Leibniz-Institut für Wissensmedien, Tübingen, Germany)

19:15 Closing remarks

ORAL PRESENTATIONS

RAT NEUROETHOLOGY AT HIGH TEMPORAL RESOLUTION

Diego Laplagne

Neuronal activity evolves fast—in the order of tens of milliseconds. Behavior of humans and other large vertebrates appears to evolve at slower time scales. In contrast, the natural behavior of small rodents, the most widely used animal model for neurophysiology of behavior, is richly structured at those fast scales. A striking example of this is the family of sensorimotor rhythms executed by rats and mice during active exploration: sniffing, whisking, vocalization, head movements and locomotion, which are typically periodic at 6–10 Hz. These rhythms are inevitably linked to vast neuronal activity distributed across the brain, originating from motor pattern generators and sensory areas. In our lab, we have started a program to monitor behavior in freely moving rats performing innate behaviors in laboratory settings. Simultaneously recorded variables so far include video tracking, ultrasonic vocalizations, respiration, whisker EMG, head accelerometry and high-speed video. We record all these with the high temporal resolution that will be needed to correlate behavioral components with the rapidly evolving neural activity that underlies them. I will present results showing how the different sensorimotor rhythms interact at various time scales. Our observations point to a model where each motor plan can be independently generated, but they typically couple during active behavior. This coupling is flexible, such that the synchronization between motor plans quickly changes as the rat transitions through distinct behavioral modes.

RESPIRATION-COUPLED OSCILLATIONS IN THE RAT HIPPOCAMPUS

André Lockmann

During slow-wave sleep and deep anesthesia, the rat hippocampus displays a slow oscillation (SO) that follows "up-and-down" state transitions in the neocortex. There has been recent debate as to whether this local field potential (LFP) rhythm reflects internal processing or entrains with respiratory inputs. To solve this issue, here we have concomitantly recorded respiration along with hippocampal, neocortical, and olfactory bulb (OB) LFPs in rats anesthetized with urethane. During the course of anesthesia, LFPs transitioned between activity states characterized by the emergence of different oscillations. By jointly analyzing multisite LFPs and respiratory cycles, we could distinguish three types of low-frequency hippocampal oscillations: (1) SO, which coupled to neocortical up-and-down transitions; (2) theta, which phase-reversed across hippocampal layers and was largest at the fissure; and (3) a low-frequency rhythm with largest amplitude in the dentate gyrus, which coupled to respiration-entrained oscillations in OB and to respiration itself. In contrast, neither theta nor SO coupled to respiration. The hippocampal respiration-coupled rhythm and SO had frequency <1.5 Hz, whereas theta tended to be faster (>3 Hz). Tracheotomy abolished hippocampal respiration-coupled rhythm, which was restored by rhythmic delivery of air puffs into the nasal cavity. These results solve the apparent contradictions among previous studies by demonstrating that the rat hippocampus produces multiple types of low-frequency oscillations. Because they synchronize with different brain circuits, however, we postulate that each activity pattern plays a unique role in information processing.

TO MOVE OR TO CRY: TYPE ONE AND TYPE TWO THETA ACTIVITY IN THE HIPPOCAMPUS

Richardson Leao

The dorsal and ventral hippocampus have been linked to cognition and emotion-related functions, respectively. Since both regions display prominent oscillatory activity, different neuronal oscillations could underlie their functional dichotomy. Type 1 theta oscillations arise in the dorsal hippocampus during movement and exploratory behavior and are independent of cholinergic transmission. In contrast, type 2 theta depends on acetylcholine and appears when animals are exposed to emotionally laden contexts, such as predator odor tests. However, despite its involvement in emotions, type 2 theta has never been related to the ventral hippocampus. Here we show that optogenetic activation of oriens-lacunosum moleculare (OLM) interneurons in the ventral hippocampus drives type 2 theta and increases risk-taking behavior in response to predator odor. These results contribute to an understanding of how the two theta types associated with different regions support distinct hippocampal functions.

THE DIFFERENTIAL EXPRESSION OF Ih IN OLM 2 CELLS ALONG THE DORSO-VENTRAL AXIS OF THE HIPPOCAMPUS

Markus Hilscher, Klas Kullander, Richardson Leao & Katarina Leao

Oriens-lacunosum moleculare (OLM) cells are a class of hippocampal interneurons known to gate information arising from the entorhinal cortex and CA3 in CA1. These neurons are have been shown to express somatostatin (Som+) and the cholinergic receptor, nicotinic, alpha 2 (Chrna2+), where Chrna2 is the most specific OLM cell marker in the intermediate/ventral CA1 up to date. OLM cells are also important players in the generation of theta oscillations. These neurons show strong spike phase lock with theta oscillation and modeling studies have suggested that OLM cells can synchronize clusters of pyramidal cells and basket interneurons. We perfomed whole-cell current- and voltage-clamp recordings in the dorsal and ventral hippocampus and show that passive and active electrophysiological properties of OLM cells differ along the dorsal to ventral axis. Dorsal OLM cells generated more hyperpolarization-activated current (Ih) than ventral OLM cells, indicating a difference in the expression of the hyperpolarization-activated cyclic nucleotide-gated (HCN) channels. Furthermore, both dorsal and ventral OLM cells showed electrical resonance at theta frequencies, with dorsal OLM cells resonating in distinct frequency bands than ventral OLM cells. The resonance frequency was extracted from the impedance amplitude profile, i.e. the voltage response to a Chirp current stimulus, which consisted of a linearly increasing (1 Hz/s) sine wave with constant amplitude. This protocol was run under the application of tetrodotoxin to block action potentials. While at near-threshold potentials Ih was not active, at hyperpolarized potentials this current contributed to theta-resonance and could be suppressed with the HCN channel blocker ZD7288. In summary, our data suggests that dorsal OLM cells differ from ventral OLM cells through the generation of Ih and that this current contributes to the electrical resonance in OLM cells at theta frequencies.

VISUAL RESPONSE PROPERTIES IN CAT AND AGOUTI VISUAL CORTEX

Dardo N. Ferreiro, Sergio A. Conde-Ocazionez, Luã C. de Souza and Kerstin E. Schmidt

In contrast to carnivores and primates, the rodents studied so far show no evidence of a columnar organization of neurons with similar response properties in V1. However, highly orientation selective neurons have been found in all of the examined species. This opens up

the question whether the connectivity underlying the emergence of such specialized cortical response properties follows a different blueprint in animals with interspersed as compared to those with columnar organization. Furthermore, rodent data are only available for species with nocturnal or crepuscular habits and small brain sizes, two factors that could contribute to develop a different architectural blueprint. Thus, we set out to compare the cortical functional architecture between carnivores and a big rodent of diurnal habits, and comparable visual cortex size to that of small primates and carnivores. To this end, we performed multi-site electrophysiological recordings from both anesthetized cat (Felis catus domestica) and agouti (Dasyprocta aguti) visual cortex. Stimuli consisted in contrast reversing checkerboards and oriented gratings. We characterized and compared the visual response properties to several spatial and temporal frequencies of stimulation, in V1 neurons of both species. Moreover, we were able to detect orientation and direction selective single-unit responses in V1 of agouti. Our preliminary data suggests that big diurnal rodents as agouti do not exhibit the degree of clustering of iso-orientation selective units as observed in carnivores.

HOW GRATING STIMULI DO BIAS OUR CONCEPTS ON CORTICAL GAMMA SYNCHRONIZATION

Sergio Neuenschwander

Vislab, Brain Institute - UFRN, 59056-450 Natal, Brazil.

Gamma oscillations have been implicated in perceptual binding and visual attention. So far, most of the evidence has been derived from analysis of responses to moving gratings. However, a key step for understanding whether gamma contributes to visual processing is to obtain data during free viewing of ecologically meaningful scenes. Recent studies using a more naturalistic approach in the visual cortex led to diverging conclusions. In humans, gamma was absent from ECoG responses to natural images and noise. Similarly, analysis of spiking activity in V1 of capuchin monkeys revealed strong beta but no gamma components in responses to pictures. An analysis of ECoG signals in the macaque showed, on the contrary, surprisingly strong gamma responses to static images. Here we record spiking and local field potential signals from V1 of capuchins in response to gratings and natural stimuli during both maintained fixation and free viewing. Our results show that large gratings capable of activating selectively the cortex induce strong and stable gamma oscillations (from 48 to 89 Hz, over 3 monkeys), confirming previous results in the macaque and humans. In contrast, gamma is absent from free viewing of natural images and movies presented on a monitor screen. Similar results were obtained with real world scenes, such as viewing of other monkeys, humans or real objects. Overall, our findings weaken the notion that gamma is necessary for visual processing and question its role in attention.

UNRAVELING THE PHYSICS OF GRAVITATIONAL WAVES

Fabio Novaes (International Institute of Physics, Natal)

On September 14th, 2015, 100 years after the publication of Einstein's General Theory of Relativity, the first gravitational waves were detected on Earth as a result of the collision of two black holes. This feat was achieved by both of the twin Laser Interferometer Gravitational-wave Observatory (LIGO) detectors, separated by 3000 km distance. In this seminar, we will discuss the physical properties of gravitational waves and the challenges involved in measuring this signal.

PSYCHOBIOLOGICAL AND CLINICAL RESEARCH WITH AYAHUASCA

Fernanda Palhano, Draulio de Araújo

Psychedelic research has gained strength in recent years. Several centers around the world are investigating how these substances interact with the brain, leading to cognitive, affective and perceptual changes and probing their potential use in treating psychiatric disorders. Ayahuasca is a psychedelic herbal beverage traditionally used by indigenous cultures of the Amazon region and later introduced in urban centers through syncretic religions. Since 2014 we initiated a randomized placebo controlled trial to evaluate the antidepressant effects of ayahuasca. Fifty healthy controls and 29 treatment resistant depressed patients were evaluated using a parallel design. The antidepressant effects have been evaluated with Hamilton-D and Montgomery-Asberg Rating scales that assess severity of depression before, during and monthly until six months after the treatment session, in which they received ayahuasca or placebo. Besides the antidepressant effect of ayahuasca, this project was also designed to evaluate its acute and subacute effects on some biological markers. During the treatment session (acute effects) volunteers were evaluated by electroencephalography, psychiatric scales, questionnaires and salivary cortisol measures. To evaluate the subacute effects were carried out the following measures 24h before and 24h after the treatment sessions: psychiatric scales, neuropsychological tests, speech evaluation, functional magnetic resonance imaging, polysomnography and biochemical measures, including cortisol, brain-derived neurotrophic factor and some interleukins. During this presentation, we will present details of the project and some preliminary results regarding the acute and antidepressant effects.

EFFECTS OF BRIEF MINDFULNESS MEDITATION INTERVENTION ON STRESS PHYSIOLOGICAL MARKERS

Geissy L L Araújo and Maria B C Sousa

Mindfulness based stress reduction programs are composed by activities involving attentional training. These programs benefit healthy and clinical populations by increasing abilities as emotion regulation, resilience, attention and self-awareness. Brief mindfulness meditation interventions (1-6 days) have been used as alternative to the standard program (8 weeks) to prevent drop out during the period of research or treatment. Some stress physiological measures show important changes after 3 days of practice. Cortisol levels, blood pressure, heart rate variability and electrodermal activity are the main common markers used in this field. In this presentation, we are going to show some literature data about the impact of a brief intervention in those physiological markers. Besides that, we will present preliminary results of electroencephalographic records correlated with the performance of sustained attentional task, interoceptive tasks and acute stress test, both before and after 3 days of mindfulness meditation intervention.

USING ASTROCYTES AS DISEASE-MODIFYING TREATMENT FOR TEMPORAL LOBE EPILEPSY

Kelly Soares Farias; Chouchane, M.; Ribas, V; Costa, M. R.; Queiroz, C. M.
Brain Institute, Federal University of Rio Grande do Norte (UFRN), Natal, Brazil

Astrocytes are involved in the extracellular homeostasis by buffering K+ concentration, metabolizing neurotransmitters, controlling neuronal firing and synchronization and contributing to the blood-brain barrier. Under pathological conditions, astrocytes may change their morphology in order to compensate abnormal function, being referred to as activated astrocytes (a.k.a., reactive gliosis). This phenomenon is commonly observed in brain

regions associated with seizure generation and spread, although its role in abnormal synchronization is unknown. While astrocytes can enhance potassium and glutamate-related metabolism, sustained long-term reactivation can lead to neuronal dysfunction. Temporal lobe epilepsy (TLE) is the most common form of epilepsy and is usually associated to refractoriness. TLE is characterized by extensive cell death (hippocampal sclerosis), synaptic reorganization (mossy fiber sprouting) and reactive gliosis. Here, we hypothesize that transplantation of immature astrocytes in chronically epileptic hippocampus would reduce epileptiform activity, including the occurrence of electrographic and behavioral seizures. To test this hypothesis, animals made epileptic by the systemic injection of pilocarpine (which induced status epilepticus, SE) were unilaterally transplanted with green fluorescent protein-positive (GFP+) astrocytes into the hippocampus 30 days after the SE. Group assignment was made according to SE behavioral severity and spontaneous epileptiform activities (interictal spikes, high-frequency oscillations, full-blown seizures) were recorded in both (treated and untreated) hippocampi using chronically implanted multi-electrodes. Viable astrocytes were identified in the host hippocampus seven months after transplantation and were mainly localized at the hilus of the dentate gyrus and fimbria/fornix. Cells or tissue clusters indicative of tumor were not identified. Epileptiform electrographic activity was recorded in 75% of control animals (SE-control, N= 6/8) and in 60% of experimental animals (SE-astro, N=6/10; chi-square=0.45 p>0.05). Spontaneous seizure frequency was highly variable between animals (18 vs 13 recorded seizures in SE-control and SE-astro groups, respectively) and no difference was observed between groups (seizures/hour: 0.06±0.02 vs 0.03±0.01, SE-control and SE-astro, respectively). Astrocytes grafting did not change seizure duration (64.5 ± 3.5 s vs 74.3 ± 6.6 s, for SE-control and SE-astro groups, respectively). Also, we did not observe any difference in the morphology, periodicity or frequency of hippocampal interictal spikes (IIS) between experimental groups and/or treated hemisphere. Interestingly, however, astrocyte transplantation significantly reduced behavioral seizure severity (scores: 5.4 ± 0.2 vs 4.1 ± 0.4; for SE-control and SE-astro, respectively; $p < 0.05$, Mann-Whitney test). Our results support the therapeutic use of immature astrocyte transplants in TLE. Future experiments are needed to elucidate the mechanisms by which astrocytes attenuate behavioral seizure severity.

REPROGRAMMING OF NEURONAL FATE BY KAINIC ACID ADMINISTRATION IN MOUSE HIPPOCAMPUS

Daniela M.S. Moura, Claudio M. Queiroz, Marcos R. Costa
Brain Institute, UFRN, Brazil

Dysfunctional neural networks lead to seizures. In mice, intrahippocampal kainic acid (KA) induces hallmarks of temporal lobe epilepsy, such as hippocampal sclerosis, synaptic reorganization and long-lasting epileptiform activity. Despite generalized cell death in the hippocampus, granule cells in the dentate gyrus are spared. Interestingly, KA increases cell proliferation in the subgranular zone of the dentate gyrus, but it is not accompanied by a proportional increase in neurogenesis. This suggests that newly generated cells either undergo cell-death or adopt alternative phenotypes than neurons. To evaluate this possibility, we mapped the fate of hippocampal cells after KA using conditioned doublecortin-dependent expression of green fluorescent protein (GFP). Consistent with previous findings, histological analysis of the hippocampus showed bilateral cell death and ipsilateral dispersion of granule cells. We observed a significant increase in GFP+ cells in both ipsi and contralateral dentate gyrus. Remarkably, however, in the ipsilateral dentate gyrus most GFP+ cells adopted glial morphologies and expressed the astrocytic protein GFAP.

Conversely, in the contralateral side GFP+ cells differentiated into granule cells displaying ectopic positioning and basal dendrites. These results suggest that primary and secondary epileptic foci differently affect progenitor cells. Moreover, they indicate that KA can reprogram a population of progenitor cells within the dentate gyrus to switch their fate towards astrocytes. These results explain the paradoxical observation of increased proliferation and reduced neurogenesis in this animal model. Further studies will be necessary to determine the consequences of this abnormal differentiation to the generation of epileptic seizures.

NEUROCIRCUITRY DEVELOPMENT, SPLICING REGULATION AND TRAIT HERITABILITY IN ANIMALS PRENATALLY EXPOSED TO VALPROIC ACID: A NEW TOOL IN THE STUDY OF AUTISM

Rodrigo N Romcy-Pereira

Laboratory of Neural Circuit Plasticity – Brain Institute (UFRN)

Autism (or autism spectrum disorders, ASD) is a neurological condition that impairs sensory, cognitive and social functions. Although with a strong genetic component, environmental factors affecting the formation of neural circuits during brain development can lead to autism. Since the first anecdotic reports of autistic children born from women taking valproic acid (VPA) during pregnancy in the mid-90's to the most recent studies in a cohort of 650.000 children showing increased risk for autism development, evidence have accumulated on the effects of VPA on neurodevelopment. Here, I will present the most recent findings from our lab and others on the behavior and molecular aspects of the abnormal development of neural circuits in the VPA model of autism.

INVESTIGATION OF THE NEUROPHYSIOLOGICAL EFFECTS OF 5-METOXI-DIMETHYLTRYPTAMINE (5-MEO-DMT)

Souza, A. C.; Lopes-dos-Santos, V.; França, A.; Moradi E, Tort, A.B.L.; Leão, R.; Ribeiro, S.

Serotonergic hallucinogens are widely found in nature and are well known for their capability of altering states of consciousness. More specifically they can be defined as substances that: 1) promote altered thought, mood and perception, without causing physical addiction, craving, or any relevant physiological alteration, nor cognitive deficits, amnesia or delirium; 2) have psychoactive effects dependent on activation of 5-TH2A receptors; and 3) are perceived by rats as DOI (2,5-dimetoxi-4-iodoamfetamina) in a discriminative task. Here we set out to investigate the behavioral and electrophysiological effects of a serotonergic hallucinogen in freely behaving rats. Specifically, we assessed the effects of 5-MeO-DMT at different doses and administration pathways, with electrophysiological recordings in the hippocampus. Preliminary observations indicate that rats show increased alertness following the administration of 5-MeO-DMT with no clear increase of locomotion. Theta oscillations emerged during this induced behavioral state, lasting for ~15 minutes, and their power was significantly higher than the expected by speed. More specifically, during non-locomotion periods, normalized theta power seems to persist for a prolonged period of time, suggesting that increased theta is not likely to be a consequence of augmented locomotion. Moreover, DMT-induced theta oscillations failed to present amplitude-phase modulation with high frequency oscillations (HFOs), which was strongly present in control experiments with saline injections. Altogether, the preliminary results suggest that 5-MeO-DMT disrupts the coordination between hippocampal theta waves and high frequency oscillations, which could be an indication that it might alter normal information flow within the hippocampus.

FIELD THEORY, TOPOLOGY AND FOLDING PROTEINS

Dmitry Melnikov (International Institute of Physics, Natal)

In modelling the process of protein folding coarse graining methods are commonly used. The main idea behind these methods is to replace the complex details of the molecular structure of a protein by a collection of more "coarse" building blocks. In quantum field theory such an approach is named renormalization - it instructs us to describe the large scale phenomena by an effective theory, which does not hold memory of irrelevant features that small scale dynamics possesses. One of the research directions of the group at the IIP deals with effective theories of folded proteins and application of modern methods of mathematical physics to understand basic properties of proteins' natural state.

PROTEOMIC CHARACTERIZATION OF BRAIN ABSCESS AND EMPYEMA CLINICAL CASES

Bjørnar Hassel[1] , Gustavo A. de Souza[2], Daniel Dahlberg[3]

[1]Department of Complex Neurology and Neurohabilitation, Oslo University Hospital; [2]The Brain Institute, UFRN; [3]Department of Neurosurgery, Oslo University Hospital

The biochemical composition of pus from brain abscesses has been little studied. Pus could influence the surrounding brain tissue and the course of infection. We analyzed the proteome of the extracellular fluid of pus from 47 brain abscesses, i.e. the supernatant after centrifugation. As a control, we also analyzed subdural empyemas from 16 patients, collected during routine brain surgeries. Overall, 1379 proteins were present in at least one brain abscess sample; of which 288 proteins were identified in all samples. Among the latter, our data shows that proteins participating in immune response, originated from neutrophils, macrophages and eosinophils, are enriched in pus. Matrix metalloprotrases are particularly abundant in pus, which suggests that abscesses might cause further cellular damage to the tissues neighboring the area.

STABILITY AND INSTABILITY OF NEURONAL CIRCUITS AND COMMUNICATION BEHAVIORS

Tarciso Velho

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 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.

POSTACQUISITION STABILIZATION OF MEMORIES AFTER RETRIEVAL IN WATER MAZE REQUIRES NMDA RECEPTOR ACTIVITY

Gênedy Apolinário

Spatial learning requires hippoca.mpal NMDA receptors activity. Although studies have shown that rats treated with AP5, a NMDA receptor antagonist, poorly learn the water maze task, few reports described the role of these receptors on spatial memory reconsolidation. Using adult male Wistar rats, trained in different versions of the water maze task, we found that AP5 infusion into dorsal hippocampus right after a probe test related to a reference memory task does not affect its persistence, on the other hand, its infusion after a reversal learning protocol prevents rats to express reverse memory but not original. Moreover, AP5 infusion after a delayed matching-to-place task, in which new memory encoding was required each day, blocks the persistence of the last learned place. Our results show that sensitivity to AP5 was observed only when the training protocol involves new memory encoding.

AVERSIVE MEMORY RECONSOLIDATION REQUIRES PRIOR CONSOLIDATION OF CONFLICTING NON-AVERSIVE KNOWLEDGE

Andressa Radiske

Reactivation can render consolidated memories labile again, making them prone to incorporate new information through a gene-expression and protein synthesis dependent restabilization process referred to as reconsolidation. Disruption of reconsolidation usually produces amnesia. However, some memories are particularly resilient to reconsolidation blockers, indicating that this process is not a pervasive quality of memory but happens only when a still loosely defined set of conditions occurs. Using behavioral, pharmacological, biochemical and electrophysiological tools we demonstrated that prior consolidation of non-aversive information is essential for aversive memory reconsolidation.

KEYNOTE LECTURES

NEURAL MICROCIRCUITS UNDERLYING MULTISENSORY INTEGRATION IN THE MOUSE STRIATUM

Gilad Silberberg (Karolinska Institute, Stockholm)

The basal ganglia are traditionally studied with focus on their motor functions, however they receive sensory inputs from the entire neocortical sheet, including primary sensory areas. Our aim is to elucidate the functional properties of cortical and striatal neural circuits underlying sensory and motor processes. I will present in-vivo work demonstrating bilateral and multimodal sensory integration by individual striatal neurons in the healthy and dopamine-depleted striatum. I will also present recent data from our lab pertaining to the synaptic organization of the striatal microcircuitry, focusing on the connectivity between the different types of striatal interneurons.

CONSIDERING WHITE MATTER IN NUMERICAL COGNITION

Korbinian Möller (Leibniz-Institut für Wissensmedien, Tübingen, Germany)

Numerical cognition is a clear case of multi-modal and distributed processing within the human brain. There is accumulating evidence indicating that it involves a fronto-parietal neural network. However, so far, the majority of studies investigating this network focused on grey matter cortex areas and largely neglected white matter connections involved in numerical cognition. In my talk, I will suggest a generalizable account on the anatomo-functional associations as well as the connectivity of representational codes underlying numerical cognition as proposed by the currently most influential model of numerical cognition. Therefore, we evaluated the neural networks subserving number processing in healthy adult participants but also brain-damaged patients with regard to both grey matter localizations as well as white matter tracts. Thereby, we (1) specified additional memory-related grey matter cortex areas crucial for arithmetic fact retrieval (e.g., the hippocampus) and (2) identified important white matter connections between the anatomo-functional instantiations of representations involved in numerical cognition. These specifications of brain connectivity augment the Triple Code Model of number processing and calculation with respect to how grey matter areas associated with specific number-related representations may work together in numerical cognition.

POSTER SESSION 1 (MONDAY)

001 - ELIMINATION OF EARLY BORN NEURONS AFFECTS THE SPECIFICATION OF LATE BORN NEURONS IN THE CEREBRAL CORTEX

Landeira, B.S, Araújo, J.A de M., Costa, M. R.

The cerebral cortex of mammals is histologically organized into different layers of excitatory neurons that have distinct patterns of connections with cortical or subcortical targets. During development, these cortical layers are established through an intricate combination of neuronal specification and migration in a radial pattern known as "inside-out": deep-layer neurons are generated prior to upper-layer neurons. In the last few decades, several genes encoding transcription factors involved in the sequential specification of neurons destined to different cortical layers have been identified. However, the influence of early-generated neurons in the specification of subsequent neuronal cohorts remains unclear. To investigate this possible influence, we induced the selective death of cortical neurons from layer V and VI before the generation of layer II, III and IV neurons. Next, we evaluate the effects of ablation of early born neurons on the phenotype of late born neurons by BrdU-chasing. Our data shows that one-day after ablation, layer VI neurons expressing the transcription factor TBR1 are newly generated while virtually no neuron expressing TBR1 was generated in the same age in control animals. This suggests that either progenitors or neurons destined for superficial layers suffer interference from the selective death of neurons in deep layers, changing their specification. We also observed that while TBR1-positive neurons are located exclusively in deep cortical layers of control animals, many TBR1-positive neurons are misplaced in superficial layers of ablated animals, suggesting that the migration of cortical neurons could be controlled independently of neuronal phenotypes. Interestingly, this increase in the generation of Tbr1-expressing neurons was not observed when we induced neuronal cell death in vitro, suggesting that tissue organization is important for signaling between post-mitotic neurons and progenitors. Altogether, our data indicate the existence of a feedback mechanism of control between early-generated neurons and progenitors involved in the generation of granular and supra-granular cortical neurons. This mechanism could help to control the number of neurons in different layers and contribute to the establishment of different cortical areas.

002 - REPROGRAMMING OF DIFFERENT CELL TYPES INTO NEURONS THROUGH A COCKTAIL OF SMALL MOLECULES

Ana Raquel Melo de Farias, Marcos Romualdo Costa

Recently, many techniques have been described to generate neurons that could be used in cell-based therapies to neurodegenerative diseases or acute central nervous system injuries. One of such techniques is the lineage reprogramming of differentiated cells into neurons, either directly or indirectly. However, most protocols for lineage reprogramming rely on the expression of ectopic genes, which could lead to other unexpected transcriptional changes in the reprogrammed cells. To circumvent this possibility, we here evaluate the possibility to reprogram different cellular types - astrocytes from mouse cortex and mesenchymal stem-cells isolated from human umbilical cord (hUCMSC)- into neurons through the use of a cocktail of small molecules in the cell culture medium. This cocktail contains molecules associated with different cellular pathways, including gene expression regulation, neurogenesis modulation and cell cycle control, and it has been previously shown to reprogram fibroblastos into neurons. To assess the cellular phenotype after treatment of

astrocytes and hUCMSC cultures with small molecules, we evaluated the expression of neuron-specific proteins, morphology and gene expression by immunocytochemistry and RT-qPCR. Our preliminar data show that astrocytes and, to a lower extent, hUCMSC adopt morphologies and gene expression compatible with a neuronal phenotype, indicating that small molecules can be used to reprogram those cell populations.

003 - DIRECT LINEAGE REPROGRAMMING OF MÜLLER GLIAL CELLS INTO NEURONS.

Guimarães R, Leão R and Costa MR

Instituto do Cérebro, Universidade Federal do Rio Grande do Norte

Worldwide approximately 32.4 million people suffer from blindness. This happens due to loss of neurons with advancing disease. The development of cell-based therapies aiming at restoration of retinal neuronal circuits are a promising approach to treat these diseases. An important cell therapy tool highlighted in recent years is the lineage reprogramming of somatic cells. This technique allows the reprogramming of a differentiated somatic cell into another cell type. In terms of degenerative diseases in the retina, a group led by Dr. Thomas Reh recently demonstrated the ability to reprogram Müller gilal cells (MGC) into neuronal progenitors. In this work, we study the possibility to reprogram the MGC directly into neurons using the pro-neural genes Ascl1 and Neurog2. MGCs were purified from C57 / Bl6 mice retina at the age of 7 postnatal days (P7) in the presence or absence of epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF). Afterwards, cells were nucleofected with the plasmid carrying either the gene Neurog2, Ascl1 or controls containing only the gene for reporter protein RFP. After thirteen days of culture, cells were fixed and processed for immunocytochemistry, allowing the microscope observation and quantification of reprogramming efficiency. Next, optogenetic techniques were used to evaluate the electrical functionality of neurons reprogrammed from MGC. All procedures were done in accordance with national and international laws and were approved by the local ethical committee (048/2014). Four to seven days after nucleofection, we started to observe morphology changes in Neurog2 or Ascl1 expressing MGCs. These changes, characterized by decreasing cell body and extending long and fine processes, indicate that MGC underwent lineage reprogramming into neurons. To confirm the neuronal phenotype, reporter-positive cells were assessed for the expression of class III beta-tubulin after 13 days in vitro. We observed that 77.19% and 26.33% of cells purified in the presence of EGF/bFGF or in the absence of these mitogens, respectively, expressed betaIII-tubulin after nucleofection with Neurog2, Expression of Ascl1 in MGC expanded in the presence or absence of growth factors led to the expression of betaIII-tubulin in, 26.54% and 9.81% of cells, respectively. Virtually every cell showing neuron morphology also expressed the neuronal microtubule associated protein 2 (MAP2). After a month in culture, neurons reprogrammed with Neurog2 were able to express calcium-sensitive protein GCAMP5 under the control of the human synapsin promoter, suggesting a robust functional maturation. Indeed, calcium-imaging experiments revealed fast fluctuations in the GCAMP5 fluorescence, suggesting that the reprogrammed neuron is depolarizing. Our results show that MGCs can be lineage-converted into functional neurons by expression of a single pro-neural factor. Future experiments should clarify the identity of reprogrammed neurons.

004 - ACTION OF ACUTE AND CHRONICLE ELECTRIC STIMULATION OVER NEURONAL TYPE SPECIFICATION OF ADULT SUBVENTRICULAR ZONE PROGENITORS

Carvalho BS; Cunha-Pereira C; Moura DMS; Sequerra EB; Costa MR

The Subventricular zone (SVZ) is the site of adult neurogenesis to the olfactory bulb (OB). SVZ progenitors generate mainly two types of interneurons that integrate in the OB: granular and periglomerular (PG) neurons. These cells can also be further subdivided based on the expression of the proteins calbindin, calretinin or tyrosine hydroxylase. The mechanisms that lead to the specification into these neuronal types are unknown. In the spinal cord neurogenesis, neurotransmitter identity is specified according to early spontaneous electrical activity in progenitor and precursor cells. This electrical pattern guide master transcription factors expression and the differentiation in a particular subtype. Manipulation of electrical activity can change de fate of progenitors and derived neurons. We hypothesize that the specification of SVZ-OB interneurons could also be influenced by electrical activity. To test this hypothesis, two experiments were designed to manipulate the cell electricity either acutely or chronicly. First, DCX-Cre-ER2/lox-GFP mice were injected with Kainic Acid (KA) or PBS in the neuroblasts migratory route to the bulb. Tamoxifen was injected 4 days after to label immature neuroblasts affected by KA and perfusion was performed 45 days after KA injection. In a second set of experiments, wild type mice were injected with a retrovirus containing the RNA for the expression of NaChBac, a bacterial sodium channel that increases electric activity. This channel is fused with the GFP that labels the infected cells. To control this experiment, a mutated non-functional version of the NaChBac channel was used. Cell identity was analyzed 45days after injection. Our preliminary results suggest that the neuroblasts stimulated by the acute approach differentiate into TH+ PG neurons at the expense of Calbindin+ PG phenotype.

005 - POSTNATAL BRAIN MYELINATION IN AN ANIMAL MODEL OF AUTISM INDUCED BY PRENATAL EXPOSURE TO VALPROIC ACID

Araujo-Sousa, C & Romcy-Pereira, RN

Mammalian brain circuits are formed through the interaction between timely regulated genetic and environmental signals during development. These signals control synaptic formation, synaptic pruning and myelination that are processes required for the maturation and establishment of the adult neural connectivity. In developmental disorders, such as autism, deficits in these processes may lead to abnormal communication between neurons leading to maladaptive behaviors, including sensory disturbances, restricted interests, stereotyped movements and epilepsy. A recent transcriptome study from our lab indicate that infant VPA (valproic acid)-treated rats (a developmental model of autism) have altered expression of synaptic genes and reduced expression of myelin-related genes in the frontal cortex, suggesting possible molecular mechanisms for the behavioral deficits observed in these animals. In accordance to studies on white matter alterations in autistic patients, abnormal myelin formation in VPA animals could underlie deficits in motor control (hyperactivity), sensory processing (abnormal sound processing) and neuronal excitability (increased susceptibility to epilepsy). Therefore, the aim of this study was to investigate the myelination pattern in the forebrain of VPA-treated rats at different postnatal ages (infant: P15, adolescent: P30 and adult: P60), in order to find patterns of brain misconnections. For that, VPA animals were generated by injecting pregnant rats with 500 mg/Kg i.p. VPA or saline on embryonic day 12.5 (E12.5). Analysis of myelin integrity is being conducted by two different approaches: (1) histological quantification of the thickness and myelin staining

intensity of the major forebrain white matter tracts (corpus callosum, anterior commissure, fimbria and internal/external capsule) using the myelin-specific stain Fluoromyelin®; and (2) gene expression analysis of structural myelin genes (Mobp, Plp1, and Mag) in dissected samples of the frontal cortex by quantitative real-time PCR.

006 - POSTNATAL SENSORIOMOTOR DEVELOPMENT IN THE VPA RAT MODEL OF AUTISM

Olga E. Rodriguez-Sierra, Waldemar A. Silva-Neto, Rodrigo N. Romcy-Pereira

Autism Spectrum Disorder (ASD) is a developmental disorder, highly heterogeneous, with a diagnosis mostly centered around social and communication deficits. However, sensory and motor disturbances are also widely present among individuals with ASD. From a developmental perspective, sensoriomotor processes are the building blocks from which the adult mind emerges. Hence, recent theories of ASD propose that these –often overlooked – sensorimotor disturbances are critical to understand their more characteristic symptoms. The relationship between sensorimotor processes and social interaction during early development remain elusive and difficult to study since we lack reliable biomarkers that can point out individuals at risk of ASD. Animal models of autism offer an alternative approach to study early sensorimotor processes at different developmental stages. In the present study, we injected pregnant rats with valproic acid (VPA) to induce an autistic-like disorder in their offspring. From PD1-PD15, we monitored their sensory and motor development of VPA and control rats using an assay of behavioral tests. After PD15, we assessed social interaction in pairs of siblings until PD21 in VPA and control groups. The longitudinal experimental design was implemented not only to study developmental dynamics between groups but also the variance within subjects across time.

007 - SPONTANEOUS OSCILLATORY ACTIVITY AND EVOKED POTENTIALS IN THE BARREL CORTEX OF NEONATAL RATS EXPOSED TO VALPROIC ACID IN UTERO

Maciel, Suzyanne Xavier & Romcy-Pereira, Rodrigo Neves

Laboratory of Neural Circuit Plasticity – Brain Institute (UFRN)

Sensory processing is a key component of cognitive and emotional functions. Both of which are critical for the expression of social behaviors. When brain regions devoted to encode information coming from the environment undergo abnormal development, individuals can display non-adaptive behaviors as the result of altered integration of sensory inputs into the cognitive and emotional networks. In autism and schizophrenia, for example, atypical behaviors are thought to be the expression of developmental dysfunctions in some of these brain circuits. In order to explore the time-course of such dysfunctions, we will take advantage of the protracted postnatal maturation of cortical circuits (from birth to PND30), in rodents, as a time-window to study the dynamics of neuronal activity maturation. We will investigate patterns of spontaneous local field potentials and evoked neuronal responses (field oscillations, fPSPs) induced by whisker stimulation in the barrel cortex (the vibrissae somatosensory cortex) of a rodent model of autism at distinct postnatal ages (PND5-6 and PND13-15). Pharmacological manipulation of GABA transmission will be used to probe the critical period for transition to the inhibitory action of GABA. Our experiments will use rats prenatally exposed to valproic acid (VPA), as it is known that human fetuses exposure to VPA have an increased risk to develop autism in humans and rats exposed to VPA show a set of phenotypic features that resemble autism (autistic endophenotypes). Our main goal is to evaluate the electrophysiological maturation of cortical activity in these animals assessing

incomplete or inadequate transition to mature electrical patterns of activity. Our findings may help to characterize early electrophysiological dysfunctions in the cortex of animals exposed to VPA in utero, which can be used as a proxy for the human case.

008 - EMBRYONIC BRAIN INVASION BY ZIKA VIRUS THROUGH THE OLFACTORY NERVE

Sequerra EB; Landeira B; Mesquita Y; Morais IC; Araujo JMG, Jeronimo SM; Costa MR

During last months of 2015, Brazil went through an outbreak of microcephaly cases, later identified as being caused by zika virus (ZIKV) infection. The analysis of 27 patients from Natal revealed that the frequency of anterior, telencephalic, abnormalities were higher than those on caudal structures, like brainstem and cerebellum. Little is known so far about the biology of the infection of the embryonic brain by ZIKV and no data is available to help to interpret this antero-posterior pattern. The data available in the literature show that 1- ZIKV is present in the amniotic liquid and 2- the virus is highly neurotrophic. We here then hypothesize that ZIKV is infecting the brain through one of the few neuronal populations the amniotic fluid touches, the olfactory epithelium. For testing that, we injected ZIKV in the amniotic fluid of E12 embryos and gave them different survival times. Our preliminary data shows that ZIKV is still detectable in the amniotic fluid for 24 hours but not 6 days after infection (dpi). We also show that ZIKV infects the olfactory epithelium and is transported to the olfactory bulb in less than 6 days. At 6 dpi, the olfactory bulb displays a high number of infected cells while more caudal structures, like the cortical plate, do not. These data suggest that the olfactory nerve and/or the migrating olfactory ensheating cells can be a vehicle for the entrance of ZIKV in the embryonic brain.

009 - DE NOVO MUTATIONS IN A SCHIZOPHRENIA FAMILY CASE BY EXOME SEQUENCING

Golbert D.C.F.[1]*, Mota N.B.[1]*, Kroll J.E. [1,3], Copelli M. [2], de Souza S.J. [1,3]#, Ribeiro S.[1]#

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Inherited alleles account for most of the genetic risk for schizophrenia (SCZ), exceeding 60% in two national family studies [1,2] and 80% in twin studies [3]. However, de novo single nucleotide variants occur in a small fraction of cases and could be implicated with the cognitive measures of genetic risk in schizophrenia. Genetic studies of this genetic disorder have appeared in recent years with the application of next-generation DNA sequencing technologies in genome wide association studies, which have revealed the complexity of its genetic architecture. High-throughput DNA sequencing of SCZ families and exome studies have provided direct evidence that affected offspring have an excess of de novo mutations [4-13]. In identical twins, schizophrenia develops in both subjects in almost 50% of cases [14]. Since identical or monozygotic twins share a common DNA sequence, their study represents an ideal design for investigating the contribution of de novo mutations and epigenetic factors to disease etiology. Specifically, the family case explored in this study has peculiar traits of two schizophrenic monozygotic twins. Both were diagnosed at the same time and one of them clinically evolved, in a stronger fashion, the negative symptoms and impairments of cognitive functions. Furthermore, their mother had a psychotic break after 50 years old, a

rare age of the onset. Other family members are not clinically diagnosed with any mental illness. We have previously shown a strong correlation of negative and cognitive symptoms in schizophrenia with speech connectedness measured by graph theoretical tools [15]. We performed an exome sequencing analysis of DNA on peripheral blood DNA samples obtained from a unique sample of both parents and the two twins, using the Illumina NextSeq500 platform. We also characterized negative/cognitive symptoms with psychometric scales and memory reports (to quantify speech connectedness). The initial approach has been conducted on the basis of functional classification of the de novo mutations, neutral versus deleterious sequences, trying to identify selected risk alleles (gene sets or pathways) present just in specific individual. Interestingly, when comparing unique variations of twins, we identified one Zinc finger gene with nonsense alteration that we intend to test its action through pharmacological approaches using induced pluripotent stem cells from urine expanded cell culture. This approach is going to be applied to explore other pointed important variations. We intend to align our findings with other exome data to explore whether genes affected by mutations in schizophrenia overlap with those mutated in autism and intellectual disability, trying to understand the cognitive pathophysiology shared with other neurodevelopmental disorders. In conclusion, we produced a significant amount of data that is under analysis using a variety of bioinformatics approaches and manual annotation. The analysis and possible identification of biomarkers is an advance in the early disease diagnosis together speech analysis.

010 - IDENTIFICATION OF CELLULAR GENERATORS AND MAINTAINERS OF TINNITUS

Thawann Malfatti, Richardson Leão, Katarina Leão

Tinnitus is a phantom sound perceived as ringing in the ears that still cannot be cured, most likely because its generation and maintenance mechanisms are not fully understood. This study will be focused on noise-induced tinnitus, known to cause chronic tinnitus perception in both humans and animal models. 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 will investigate the role of specific neuronal populations of the DCN in the generation and maintenance of tinnitus perception. Hearing thresholds of animals will be assessed by recording auditory brainstem responses (ABRs); noise-induced tinnitus will be induced using acoustic noise trauma (ANT); tinnitus-like perception will be assessed using gap prepulse inhibition of acoustic startle (GPIAS) tests; and control of neuronal excitability will be confirmed with in vivo unit recordings. In order to test if hyperactivity of DCN cells expressing calcium/calmodulin-dependent protein kinase type II alpha (CaMKIIa) is important for tinnitus generation and maintenance, animals will be divided in groups, and for each group, activity of CaMKIIa+ cells of the DCN will be manipulated to try to prevent tinnitus development; decrease tinnitus perception; and generate tinnitus by CNO application or blue light bursts stimulation. Preliminary data shows that there is a shift in animals hearing threshold after ANT, with recovery 2 weeks after. Also, preliminary analysis of GPIAS results shows that ANT can decrease gap detection performance, suggesting that our ANT protocol is generating tinnitus in exposed animals. Secondly, we will manipulate T-stellate cells of the antero-ventral cochlear nucleus, using a transgenic animal, to decrease input from sound pathways during and following ANT, and examine the degree of tinnitus perception in this research model.

011 - CALLOSAL INPUT DOES NOT AFFECT OCULAR DOMINANCE IN CATS

Sergio A. Conde-Ocazionez, Christiane Peiker, Thomas Wunderle, David Eriksson and Kerstin E. Schmidt

Due to their localization in the brain's topography, visual callosal connections (VCCs) act in the central binocular visual field of frontal-eyed animals. Chiasm section in cats indicated that VCCs provide the ipsilateral eye part of binocular receptive fields (RFs) at the vertical meridian (Berlucchi and Rizzolatti, 1968). VCCs were also reported to contribute critically to binocular responses in this area, a finding not confirmed in later studies. Whereas recent studies attribute the majority of binocularity (and its plasticity) in rodents to VCC, their functional contribution to binocular responses in carnivores remains controversial.
In order to investigate this issue quantitatively in chiasm intact cats we studied monocular and binocular neuronal responses in the receiving 17/18 transition zone (TZ) and adjacent parts of areas 17 and 18 during reversible deactivation of the sending hemisphere. On average, we observe only tiny shrinkage of RFs in area 18 and TZ driven through the ipsilateral eye, and of RFs in area 17 only when driven binocularly. Overall, ipsilateral eye responses benefit more from intact VCC than contralateral eye responses. Thereby, surprisingly, VCC removal did not affect ocular dominance distribution or contralateral bias of the receiving areas. We conclude that binocular RFs across the VM as such are established in vertical (thalamo-cortical) rather than in horizontal circuits and that the VCC influence is more modulating.

012 - DIFFERENCES IN X- AND Y CELL INPUT TO CALLOSALLY PROJECTING NEURONS?

Luã C. de Souza, Sergio A. Conde-Ocazionez, Dardo N. Ferreiro and Kerstin E. Schmidt

Neurons in cat primary visual cortex (area 17 and 18) do not only respond selectively to the same eye and to contours of the same orientation or movement direction, but also to certain spatial frequencies (SF). Differences in SF preference in area 17 and 18 are thought to emerge from the distinct distribution of retino-geniculo-cortical afferents of X (high SF channel) and Y cells (low SF channel). The transition zone (TZ) between areas 17 and 18, which exhibits a SF preference intermediate to the two adjacent areas, receives also dense visual callosal connections (VCC). While early recordings from VCC concluded that interhemispheric transfer benefits low SFs (Berardi et al. 1986), a recent imaging study limits its influence to passive reinforcement of SF responses already defined by retino-geniculo-cortical input (Ribot et al., 2011). Although VCC act within the very central, binocular visual field, responses driven by different eyes have never been examined separately. In order to investigate the functional contribution of VCC to spatial frequency selectivity of eye-selective responses within the TZ, we recorded monocular and binocular spiking activity to gratings of different SFs. During reversible thermal deactivation of the VCC, responses to low SFs decreased much more than responses to high SFs. Interestingly, this selective influence was significant for stimulation through the ipsilateral eye only but ceased with binocular stimulation, and get almost reversed for stimulation through the contralateral eye. Our findings speak against passive reinforcement of retino-geniculo-cortical input by VCC. They rather confirm a selective callosal influence on low SF responses in the TZ, especially for ipsilateral eye, and most likely on high SFs for contralateral eye stimulation. This might explain the incongruence of previous results obtained with binocular stimulation only and possibly reflects different contributions of the eye-specific X and Y afferents to callosally projecting neurons.

013 - DIFFERENTIAL FIRING OF NEURONS RECORDED IN THE HIPPOCAMPUS AND RELATED CORTICAL STRUCTURES DURING NATURALLY SLEEP-WAKE CYCLE

Koike, B. D. V.[1]*; Almeida-Filho, D.G.[1]*; Billwiller, F.[2]*; Farias, K. S.[1]*; Blanco W.F. [1]; Libourel, P.A.[2]; Ribeiro, S.[1]; Luppi, P.-H.[2]; Queiroz, C. M.[1]

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It is well accepted that during rapid eye movement sleep (REM sleep also called paradoxical sleep, PS), the cortical activity is closer to that occurring during waking (WK) than during Non-REM sleep (NREM sleep or slow wave sleep). Indeed, spectral analysis of EEG recordings revealed that both REM sleep and WK are characterized by the presence of theta and fast gamma oscillations in contrast to NREM sleep during which sigma (spindles) and slow delta oscillations predominate. Unit recordings confirmed that the discharge rate of neocortical neurons is higher both during REM sleep and WK than during NREM sleep. However, a number of studies indicate that cortical activity and the subcortical pathways at its origin are not strictly identical during WK and REM sleep. Indeed, a significant increase in cerebral blood flow has been found in humans in specific brain areas including thalamic nuclei, limbic and paralimbic areas, and posterior cortices during REM sleep compared to quiet WK. In contrast, the inferior and dorsolateral prefrontal cortices were found deactivated. In that context, it seemed essential to determine which populations of cortical neurons are activated during REM sleep. We recently found in rats that, during REM sleep hypersomnia compared to control and REM sleep deprivation, the dentate gyrus, the claustrum, the cortical amygdaloid nucleus, the medial entorhinal and retrosplenial cortices are the only structures containing neurons with an increased expression of Bdnf, FOS and ARC, known markers of activation and/or synaptic plasticity. However, it is crucial to demonstrate whether neurons in those structures are indeed more active during REM sleep in comparison with other behavioral states and, more importantly, what is their relation to the main brain oscillations. To answer these questions, we used customized movable electrode arrays chronically implanted in freely moving rats to determine unit activity of neurons during naturally occurring sleep-waking cycle in two cingulate cortices, the retrosplenial (RSC) cortex, because of the increased expression of activity-related genes, and the anterior cingulate area (ACA) as a negative control. We show that the mean firing rate is higher during REM sleep when compared with SWS in both structures. In the RSC, the mean firing rate during REM is even higher than during waking. Also, we show that 43.5% and 68.6% of ACA and RSC neurons, respectively, are more active during REM sleep than during any other state. Interestingly, electrodes with unit activity showed strong cross-frequency coupling between hippocampal theta (4-12 Hz) phase and the amplitude of high-frequency oscillations in the cortex (ACA: 80-120 Hz and RSC: 120-160 Hz) during REM, but not during active WK, despite similar theta oscillation in both states. As cingulate cortices (ACA and RSC) are known to be related to recent and remote memory retrieval and REM sleep theta oscillation is known to be related to context memory consolidation, these results may contribute to elucidate the mechanisms of cingulate cortices involvement in memory.

014 - Ih IN CA1 PYRAMIDAL CELL DISTAL DENDRITES CONTRIBUTE TO THETA OSCILLATION IN VITRO

Margareth Nogueira and Richardson Leão

The 4-12 Hz brain oscillation known as theta oscillation have been associated with movement when generated in the dorsal hippocampus and anxiety like behaviours in the ventral

hippocampus. We have previously shown that in horizontal hippocampus slices(from the ventral/intermediate hippocampus), OLM interneurons targeting distal dendritic compartments of CA1 pyramidal cells (PC) can modulate theta oscillations. In this work, we investigated the pyramidal cell membrane properties that facilitate theta generation by dendritic targeting interneurons. We first found that high density of Ih in distal apical dendrites of PCs produced rebound dendritic action potentials following OLM inhibition. Using pressure ejection of ZD7288 to block distal Ih, we found that OLM interneuron stimulation can no longer generate theta oscillations in slices. Taken together, our data show that an interplay between OLM interneurons and PC is crucial to theta generation. Also, we show that Ih in distal dendrites is crucial to theta rhythmogenesis.

015 - SALICYLATE GENERATES ANXIETY-LIKE BEHAVIOR AND TYPE 2 THETA OSCILLATION IN THE VENTRAL HIPPOCAMPUS OF MICE

Rafael Frazon

Salicylate, the main compound of many medications as Aspirin, is known to cause tinnitus if consumed in high doses or in a chronic way (for the treatment of osteoporosis, for example). Tinnitus is the hearing or perception of a sound when no physical stimulus is present. Tinnitus is not a disease itself, but a symptom present in some diseases, and is associated with anxiety and other mood disorders. Despite being directly related with auditory system, tinnitus is not generated from one specific region of the brain. Additionally, some studies showed that salicylate affects various brain regions besides the auditory system, as the striatum, amygdala and the hippocampus. Early studies have ascribed a unitary function to the hippocampus: declarative memory processing. However, more recent studies showed that the hippocampus not only has other functions, as emotional processing, but also can be divided into ventral and dorsal, and the ventral part plays an essential role in emotional processing. The most studied oscillation of the brain is the theta rhythm, and it can be found in the entire hippocampus. Two types of theta can be distinguished: the type 1, that is atropine resistant, has a higher frequency (7 to 10 Hz) and is related with motor pattern behaviors; and the type 2 theta, that is atropine sensitive, has a lower frequency (5 to 7 Hz) and occur during anesthesia, alert immobility and high arousal situations. The present study investigated the electrophysiological effects of salicylate in the ventral hippocampus of behaving mice. Through salicylate injection we generated type 2 theta in the ventral hippocampus. We also found that salicylate led to anxiety-like behavior.

POSTER SESSION 2 (TUESDAY)

016 - INVESTIGATING THE EFFECTS OF 5-METHOXY-N,N-DIMETHYLTRYPTAMINE TO NEUROGENESIS IN THE NEIL3-KO MICE DENTATE GYRUS

Rafael Vitor Lima da Cruz, Richardson Naves Leão

Adult neurogenesis occurs in all vertebrate taxa. However, birds and mammals have a limited adult neurogenesis capacity. In mammals, newborn cells are restricted to two small areas of the brain, the sub ventricular zone (SVZ) and the sub granular zone (SGZ) of the dentate gyrus in the hippocampus. Adult neurogenesis in the hippocampus was experimentally shown to increase the learn ability of rodents in memorizing tasks. In the last two decades, the number of publications in this field has growing up pointing to many clinical applications of an increase in the neurogenesis, as prevent Alzheimer's disease, precise aging and treat

depression, in fact many classical antidepressants are thought to act by increasing generation and survivability of adult developed Granule Cells.
The 5-Meo-DMT is a naturally psychedelic compound use by many syncretic churches in the South America as part of a ritual and it is believed to aid in several human illnesses including depression. Using 5-ethynyl-2'-deoxyuridine (EdU) a modified thymidine analogue which can incorporate into newborn cells synthetizing new DNA strands, the incorporated EdU can be detected through a reaction between ethynyl group of EdU and a fluorescent azide in a copper-catalyzed [3+2] cycloaddition, without any previous treatment to expose DNA and consequent damaging tissue. In this project we will assess the effect of a intracerebroventricular injection in a single dose of this non-selective serotonin receptor agonist to the neurogenesis in the dentate gyrus of wild type mice and Neil3-KO (Neil 3 is a DNA oxidative damage base repair protein, this animals has naturally a normal disruption in the neurogenesis and can be a reliable model to investigate clinical neurogenic boosters potentials compounds). These results will through light on the antidepressant effect of DMT and the possibility of using this compound in the pharmacopeia of mood disorders.

017 - IMPLEMENTATION OF PLACE CELL RECORDINGS USING MOVABLE TETRODES IN RATS

Rafael Pedrosa

The formation of new declarative memories depends on the hippocampus and associated structures. Electrophysiological activity in CA1 codifies spatial representations by the firing rate of place cells and by oscillations of local field potentials. The aim of the present project is to record well-isolated CA1 neurons in the dorsal hippocampus while rats run for water reward on both ends of a linear track. We will perform stereotaxic surgeries to chronically implant a new prototype microdrive with 8 movable tetrodes that allows progressive positioning of the electrodes at the targeted pyramidal cellular layer. If succeeded, this project will provide the first place cell data ever registered in Brazil and should serve as ground for future studies aiming to understand the formation of spatial memories through electrophysiological correlates.

018 - INTRAHIPPOCAMPAL ADMINISTRATION OF PILOCARPINE IN MICE AS A NEW MODEL OF TEMPORAL LOBE EPILEPSY

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Animal models have contributed significantly to our understanding of the pathophysiology of temporal lobe epilepsy (TLE). In most preparations, the "epileptic condition" is obtained after a long-lasting status epilepticus (SE) induced by systemic administration of chemoconvulsants. It has been recently suggested that SE-induced by systemic administration of pilocarpine or kainic acid may lead to multiple epileptic foci which add variability in the observations regarding seizure statistics. Also, systemic pilocarpine administration has been associated with high mortality rate while local application of kainic acid yields generalized cell death and low (if any) prevalence of spontaneous seizures. Interestingly, few studies have evaluated the effects of local application of pilocarpine, especially in the mouse. Here, we describe the behavioral effects of local application of pilocarpine (4 doses of 700 μg/μL solution: 100, 350, 570 and 1000 nL) in the mouse hippocampus during isoflurane anesthesia. Pilocarpine caused a long-lasting and dose-

dependent SE (animals with SE: 100 nL, N = 3/6; 350 nL, N = 4/4; 570 nL, N = 5/5; 1000 nL, N = 8/8). Mice receiving high doses of pilocarpine (570 and 1000 nL; N = 5-6) showed reduced latency to movement after termination of isoflurane anesthesia in comparison with saline-treated mice (12.5 ± 1.1 and 26.0 ± 1.5 min, respectively; $p < 0.05$, Mann-Whitney U-test). Similarly, animals treated with high doses of pilocarpine (570 and 1000 nL) presented decreased seizure latency (12.2 ± 0.7 and 13.0 ± 1.5 min, respectively) and increased seizure severity (Racine class: 5 - 100%) in comparison with animals treated with low doses (100 and 300 nL; 33.2 ± 6.3 and 23.3 ± 5.0 min, respectively; $p < 0.05$, Mann-Whitney U-test). Animals receiving saline did not display behavioral SE or seizures. However, all animals lost weight after the surgical procedure for local administration (including saline-treated animals), but again, the weight loss was dose-dependent. Interestingly, none of the animals treated with pilocarpine (N = 23) presented tonic seizures and the death rate was lower in comparison with systemically treated animals. Together, these data suggest that intrahippocampal administration of pilocarpine in mice can be a good and reliable experimental model of TLE. The advantages include (i) the easiness of the experimental procedure, (ii) reduced mortality, (iii) localized epileptic focus and (iv) reduced variability. We are now conducting electrophysiological recordings to test whether the genesis and spread of epileptiform activity are also dose-dependent. In conclusion, we believe this model will contribute in bringing new insights about the pathophysiology of TLE.

019 - SEIZURE DETECTION AND ANALYSIS: A SVD-BASED ALGORITHM

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Understanding how epileptic seizures affect different regions of the brain and finding ways to avoid its occurrence are major areas of interest in neuroscience. For these purposes, quantitative descriptions of synchronous activity based on EEG/LFP recordings are important tools in the characterization of the spatio- temporal dynamics of the epileptic process. In this work we combine SVD-based methods and synchrony indicators on a data set with 19 seizures from 4 mices to explore the degree of synchronization during preictal, ictal and postictal states in a Temporal Lobe Epilepsy model. In particular, for most of the seizures, we have found low and high synchronization in the beginning and in the end of the ictal periods, respectively. This result is remarkable from the seizure's detection point of view. Analysing also the synchrony indicators out of the seizure, we discovered higher synchronous activity during postictal with respect to preictal periods, highlighting the influence of postictal depression on the brain activity.

020 - DYNAMICS OF STATUS EPILEPTICUS TWO MODELS OF TEMPORAL LOBE EPILEPSY

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Temporal lobe epilepsy (TLE) is characterized by a progressive occurrence of epileptic seizures originating particularly in the hippocampal formation (mesial TLE). The administration of kainic acid (KA) or pilocarpine (PILO) can induce a prolonged convulsive state (status epilepticus, SE) that can lead to spontaneous seizures. Systemic injections and the lack of

electrophysiological monitoring during SE lead to high mortality rates, widespread cell death and high behavioral variability during the chronic phase of epilepsy. This project aimed to induce SE by intra-hippocampal injections of KA or PILO, and analyze their behavioral and electrographic progression. We implanted two bundles of microelectrodes in the hippocampus bilaterally, one bundle in the medial prefrontal cortex and a cannula above the intermediate hippocampus for KA or PILO infusion. Following SE induction, we analyzed the behavioral and electrophysiological evolution of KA and PILO animals. SE was blocked after 2h by the injection of an anti-convulsant cocktail and the animals were continuously monitored by video-EEG for up to 72h. Seven days after SE, animals had the brains removed for histological localization of cannula and electrodes. Video and EEG recordings were analyzed by visual inspection and spectral decomposition. Our results showed that PILO animals had less wet-dog shake behaviors, shorter latency for first behavioral seizure and SE onset than KA rats. Electrophysiologically, we observed that high frequency oscillations (>150 Hz) occurred short after the injection of both drugs (15-40min before SE onset). Finally, we have identified a distinct modular organization of paroxystic activity during the SE in each group, which consisted of blocks of nested rhythms. These findings suggest that PILO is more epileptogenic that KA and produces distinct SE dynamics. Our data emphasizes the importance to conduct electrophysiological recordings during SE induction in order to reduce variability during epileptogenesis and produce a more homogeneous model of chronic epilepsy.

021 - TOWARDS EEG-CLAMP: REDUCED EEG SPECTRAL ENTROPY THROUGH VISUAL NEGATIVE FEEDBACK

Ernesto Soares and Sidarta Ribeiro

Electroencephalography (EEG)-based neural control is an active field of research with major scientific and therapeutic potential applications, both acute (e.g. delivering temporally precise stimulation to disrupt epileptic seizures or parkinsonian tremor), and chronic (e.g. effecting brain connectivity changes through synaptic plasticity triggered by the reliable and repetitive precise timing of endo- and exogenous events). Distinct control strategies studied so far differ in such parameters as the type of EEG data used (e.g. instantaneous EEG phase or power), and in the feedback stimulation method used: Invasive, such as electrical Deep-Brain Stimulation (DBS) or non-invasive, such as Transcranial Magnetic Stimulation (TMS). In this regard, the use in EEG control of natural sensory pathways (e.g. visual, auditory and somatosensory) remains uncharted. Here we describe research towards a naturalistic visual-based EEG neural control technique ("EEG-clamp"). We used intermittent periodic visual stimulation, which causes the increase of EEG power at the stimulation frequency and its harmonics over occipital visual regions (the Steady-State Visual Evoked Potential, SSVEP), as feedback signals in a novel type of non-invasive Brain-Machine Interface, called Sensory Brain-Machine Oscillator (SBMO). Based on occipital EEG power calculated near real-time (delay <150ms), the SBMO continuously alternates between two visual stimuli delivered to the subject through a computer screen, either an inverting (20Hz) monochromatic radial checkerboard (ON state) or a homogeneous gray screen (OFF state). ON and OFF states where triggered when occipital EEG power (20 and 40 Hz, during the latest 500ms of data), or its derivative, crossed below or above, respectively, a predetermined threshold. We tested 3 distinct types of negative feedback (controllers) in 8 subjects. For each controller, a 3 min closed-loop trial was performed, when all stimuli were calculated in real-time, followed by a 3 min open-loop trial, when the stimuli were an exact repetition of the closed-loop trial. We found slow (~1.1Hz) and reliable closed-loop SBMO-induced occipital EEG power oscillations

that are spectrally less entropic, and therefore less random, than corresponding open-loop-induced oscillations. To our knowledge these results show for the first time that the operation of closed-loop SBMOs drives EEG activity into regimes that are inaccessible through conventional open-loop experimental designs.

022 - ACUTE AYAHUASCA EFFECTS ON EVENT-RELATED POTENTIAL RESPONSE TO VISUAL PERCEPTION AND IMAGERY

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Ayahuasca is a psychedelic beverage composed essentially by the serotoninergic agonist, N,N-dimethyltryptamine (DMT), and monoamine oxidase inhibitors (MAOi). Ayahuasca ingestion causes profound sensory, cognitive and affective changes. It's been also associated with a strong impact in the visual system, with increased brightness and sharpness of objects, vibrations of the visual field and vivid mental imagery, sometimes referred to as "seeings". The main goal of this study is to use electroencephalography (EEG) to evaluate neural changes between perceived and imagined stimuli during the effects of Ayahuasca. Frequent Ayahuasca users filled out the Vividness of Visual Imagery Questionnaire (VVIQ) and performed a visual adaptation protocol before and after Ayahuasca or placebo ingestion. This protocol is capable of evaluating neuronal activity of a test stimulus that is preceded by adaptor stimuli. If the adaptor produces similar effects on the test stimulus, the underlying neural representation of both stimuli is similar. Hence, we used face and object adaptors, either perceived or imagined, on test stimuli and analyzed the N170/VPP complex, typically much larger for faces than for other object categories. The Hallucinogen Rating Scale (HRS) was also applied after the experiment to evaluate the psychological effects of the substance. Our results showed that perceived and imagined adaptors affected the N170/VPP complex. Perceived adaptors suppressed the amplitude of the N170/VPP, whereas imagined adaptors increased it. Ayahuasca seems to decrease N170/VPP amplitude for adaptors and test images, regardless if they were adapted by an imagined or perceived image. Although the VVIQ score slightly increases after Ayahuasca ingestion, this increase did not reached significance. The four HRS factors scores (perception, somaesthesia, affect and cognition) were higher for the Ayahuasca group compared to placebo. Therefore, Ayahuasca not just modifies the psychological conscious state but also the visual perception and imagery processes as observed by EEG measurements.

023 - EFFECTS OF PRANAYAMA ON EMOTIONAL REGULATION

Morgana Menezes Novaes, Dráulio Barros de Araújo

Yoga is a practice originated in India, millennia ago, which has been associated with physical and mental well-being. The forth yoga limb, of the eight-limbed yoga system as presented by Patañjali in the Yoga Sutras, is called Pranayama. It is composed of a series of practices designed to gain aware-control of the breath, and has been used as an adjuvant treatment for the negative effects of stress and anxiety. This study aims to evaluate changes promoted by the practice of Bhastrika Pranayama, associated with anxiety and emotional regulation. This study is designed as a parallel arm randomized trial. Thirty young healthy adults were assessed by through two scales (IDATE and PANAS) and functional magnetic resonance imaging (fMRI) during an emotional regulation protocol. Subjects were randomly assigned

into two groups (control and pranayama). Both groups were evaluated before and after 30 days of training. One group practiced Bhastrika Pranayama, while the other played games, such as crossword, puzzle, domino, game cards and checkers, 3 times a week, for 4 weeks. Each intervention lasted 30 minutes. Data was analyzed with two-way ANOVA. Preliminary results showed decreased state anxiety (IDATE) ($F_{1,26}=4.30$; $p<0.05$; cohen's $d=-0.78$) and decreased negative affect (PANAS) ($F_{1,25}=8.56$; $p<0.01$; cohen's $d=-1.12$). fMRI revealed significant interaction (treatment x group) in left anterior insula ($F_{1,25}=4.94$; $p<0.05$; cohen's $d=0.85$) and right anterior insula ($F_{1,25}=8.68$, $p<0.01$; cohen's $d=1.13$) during negative stimuli observation. Reappraisal was associated with interaction in the right anterior cingulate cortex ($F_{1,25}=7.50$, $p<0.05$; cohen's $d=1.37$), right anterior insula ($F_{1,25}=8.94$; $p<0.01$; cohen's $d=-1.15$), and left dorsomedial prefrontal cortex ($F_{1,25}=5.20$, $p=0.03$; cohen's $d=0.87$).

024 - EEG CORRELATES OF THE ALTERED STATE OF CONSCIOUSNESS INDUCED BY AYAHUASCA

Jéssica A. Pessoa, Kátia C. Andrade, Dráulio Barros de Araujo

Ayahuasca is a beverage with psychedelic properties traditionally consumed by Amerindians, incorporated recently by some syncretic churches. Most frequently, Ayahuasca is prepared from the decoction of two plans, that contain the tryptamine N, N-dimethyltryptamine (N,N-DMT), and β-carbolines, such as monoamine oxidase inhibitors (MAOi). Ayahuasca leads to an altered state of consciousness, with intense perceptual and cognitive effects. The neural correlates of its acute effects have been investigated more recently by different neuroimaging techniques, such as electroencephalography (EEG). The most consistent finding is a decrease in alpha power. Other than spectral analysis, few studies have explored other EEG features that might help understanding the effects of Ayahuasca in the human brain. The first aim of this study is to identify other EEG correlates based on a deeper analysis of the alpha changes. For such, the following confirmatory and exploratory alternatives will be explored: (i) regional alpha power, frontal alpha asymmetry and structure of alpha wax and wane. 50 healthy volunteers took part in a randomized placebo-controlled parallel arm study. EEG data is composed of 4 repetitions of eyes open (20s) and eyes closed (40s) protocol. The same protocol was repeated at three different moments: baseline (~10 min before ingestion), 2 and 4 hours after the intake. All volunteers also filled out two questionnaires: the Hallucinogenic Rating Scale and the Amsterdam Resting-State Questionnaire. EEG data is currently being preprocessed and prepared to statistical analyses.

025 - THE EFFECT OF MULTISENSORY TRAINING AND POST-TRAINING NAPS IN BREAKING MIRROR INVARIANCE DURING ALPHABETIZATION

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Mirror invariance occurs when there is no discrimination between symmetrical images, such as a face from the left or right profile (Pegado et al., 2010). During alphabetization, mirror invariance hinders the students' ability to distinguish mirror letters (e.g. b and d), leading them to write letters with the reverse orientation (Duñabeitia et al., 2010). Research has shown that multisensory teaching strategies can improve literacy (Pegado et al., 2014). Laboratory studies have also shown that post-learning sleep benefits a variety of learning tasks (Diekelmann and Born, 2010). Children often sleep during the day, but it remains unclear how to best use sleep to improve school learning. Here we set out to verify whether

multisensory training and sleep can be used in the school setting to accelerate the breaking of mirror invariance in letter writing. To date we have investigated 32 children (5-7 years old) at the beginning of literacy acquisition. We implemented a specific protocol for daily multisensory training during 30 min, followed by 2h nap sessions along three weeks. The children were divided into 4 groups: training plus nap; training; nap and no nap no training. Subjects were tested on writing letters (either invariant or mirror) following training using different sensory modalities. Our preliminary results suggest that auditory training either alone (p= 0.0239) or followed by a nap (p= 0.05859) was associated with a better performance in writing mirror letters than that of subjects in the "no nap" or "no training groups". Similar results were obtained when training was proprioceptive (letters written by blindfolded subjects) for training only (p= 0.005993) or training plus nap (p= 0.004165). Ongoing experiments seek to determine whether post-training sleep contributes to long-lasting learning beyond the positive effects of training.

026 - GRAPHS PREDICTING COGNITION AND ACADEMIC PERFORMANCE IN ADOLESCENTS

Sasha Luísa de Azevedo Nunes; Natália Bezerra Mota, Sidarta Ribeiro, Francisco Ângelo Coutinho, Grace Schenatto Pereira Moraes

The analysis of speech graph attributes is a powerful tool to measure psychiatric and cognitive performance. As shown in oral reports, graph attributes vary with psychoses and predict cognitive deficits in patients. Furthermore, graphs reports with more nodes and more connections indicate better IQ and reading performance in infants of 6-8 years old. Here we set out to use graph analysis to quantify cognitive changes during an intervention project within the school setting. We specifically wanted to assess whether 1) the intervention would be sufficient to change graph attributes, and 2) the graph attributes could represent an indirect measure of school performance. Students in the age of 12-14 years were divided in two groups. The first had normal classes (n=18), and the second group had intervention classes (n=22), in which two distinct subjects (Portuguese and Science) were interdisciplinary taught. A pre-test was applied before the lecture to measure prior knowledge, and other questionnaires were applied after the lecture in order to assess intervention-related changes over time. Graph attributes did not change after the intervention, but rather maintained stability between pre-test and post-test, thus demonstrating that structural properties of the writing were stable across groups. Correlation between the average largest strongly connected component (LSC) and academic performance in Portuguese was significantly positive in both groups, suggesting that school learning is accompanied by increased written connectedness. In addition, the two groups showed a positive correlation between academic performance in Sciences and the average number of words, edges and largest connected component (LCC), but only the intervention class showed a positive correlation with LSC. The results indicate that speech graph analysis used to investigate oral reports can also be applied to written tests to indirectly assess cognitive performance in the school setting across a range of ages.

027 - SPEECH GRAPH ANALYSIS OF REM AND NON-REM DREAM REPORTS

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Despite a growing body of literature, it is unclear whether mentation recorded immediately after Rapid Eye Movement (REM) sleep is qualitatively different from that recorded after non-REM sleep. One way to explore potential disparities has been to investigate the linguistic differences in dream reports collected immediately after awakening from REM and non-REM sleep stages. Two potentially useful methods, yet to be applied in this regard, are Speech Graph Analysis (SGA) and Latent Semantic Analysis (LSA). SGA has been able to distinguish verbal reports of schizophrenics (Mota et al., 2012), and is particularly revealing of psychosis when analyzing dream reports (Mota et al., 2014). The present study aims to use SGA and LSA to investigate possible structural and semantic differences in dream reports from the three major sleep stages: N2, N3, and REM. To this end, 22 healthy participants slept in a laboratory and were awoken during a specific sleep stage. Participants were then asked to report any dream mentation, and to answer subjective rating scales relating to their dream content. Dream reports were transcribed and converted into word graphs using SGA software (http://neuro.ufrn.br/softwares/speechgraphs). The initial SGA results indicate that graphs from REM dream reports are larger and more connected than those from N3. They also suggest that N2 graphs represent an intermediate form between REM and N3 – smaller and less connected than REM graphs, but larger and more connected than N3 ones. There were significant correlations between SGA attributes and ratings of dream intensity, dream recall, auditory perception and emotionality. Altogether, these findings indicate a complex relationship between the graph structures of dream reports and the sleep stage from which they are obtained. Future analysis using LSA will probe for differences in sentence-sentence cohesion measures and potential semantic similarities among dream reports recorded after awakening from specific sleep stages.

028 - QUANTIFYING 'WORD SALAD': GRAPH ANALYSIS OF MEMORY REPORTS MEASURES COGNITIVE GAIN THROUGH EDUCATION AND COGNITIVE DEFICITS ON PSYCHOSIS

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Language is known to depend on age 1-3, education 4,5, and psychiatric state 6-10, but the development of normal and pathological linguistic structure, from infancy to adulthood, is yet to be quantitatively characterized. To this end, we began by investigating graph attributes calculated from memory reports of 200 healthy and psychotic subjects, ages 2-58. Lexical diversity, connectedness and graph size showed monotonic asymptotic increase across ages in healthy subjects, with a corresponding decrease in short range recurrence. These changes were explained by years of formal education, and were well fit by an exponential function with characteristic time of <1 year for recurrence and lexical diversity, and 11-13 years for graph size and connectedness. The same graph attributes showed little dependence on age or education in psychotic subjects, remaining structurally near random. The results point to structural randomness as an immature trace of language, and an important role of education to shape a structural language pattern through written language that influences the mature speech. This approach also suggests that it is possible to predict cognitive deficits and differential diagnosis of psychosis during the first episode psychosis, identifying psychotic subjects that would present negative and cognitive impairment through clinical evaluation and receive Schizophrenia diagnosis after 6 months follow-up. We applied the PANSS and collected memory reports from 21 patients undergoing first episode psychosis and 21 well-matched healthy controls. The patients were followed for 6 months to establish the diagnosis

according to DSM-IV. After all the data were collected, each report was represented as a graph, 3 connectedness attributes were extracted and calculated how similar they were from a random graph distribution. These attributes were then correlated with the PANSS negative subscale, combined to compose a single Fragmentation Index, and used to predict diagnosis and negative symptoms with machine learning. Random-like speech was more prevalent in the Schizophrenia group (64% x 5% in Control group, p=0.0002). Combined in one index, connectedness attributes explained most of the variance of the PANSS negative subscale (R^2=0.92, p=0.0001). The Fragmentation Index classified low versus high scoring of PANSS negative subscale with 93% accuracy (AUC=1), and predicted the Schizophrenia diagnosis with 89% accuracy (AUC=0.89). Speech graph connectedness measures the random-like symptom described as "word salad". The normal increase in speech connectedness observed during healthy development is disturbed on Schizophrenia, and the Fragmentation Index is sensitive to this early change, providing a precise marker of negative symptoms that predicts Schizophrenia diagnosis during first episode psychosis.

029 - SPEECHGRAPH ANALYSIS OF LITERARY TEXTS: INVESTIGATION OF PSYCHOTIC TRAITS

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Recent studies in computational psychiatry (Mota et al., 2012, 2014, 2016 - in preparation) indicate significant structural differences between the speech of psychotic and healthy subjects. Graph analysis of these subjects' autobiographic reports allows the quantification of psychotic speech symptoms, marked by poor, disconnected and repetitive speech. Based on a literal reevaluation of ancient texts, Julian Jaynes proposed that psychosis was socially prevalent until around 1,000 BC (Jaynes, 1976). This conjecture was corroborated for the first time by Diuk et al (2012), who used Latent Semantic Analysis to demonstrate that semantic similarity to the introspection concept increased over time in Judeo-Christian and Greco-Roman texts from the first millennium BC. Here we set out to test the hypothesis that ancient texts are structurally more similar to reports from psychotic subjects than to reports from healthy subjects. To that end we assessed graph attributes in 448 historical texts from 3,000 BC to 2,010 AC, comprising six different cultures of Afro-Eurasia (Syro-Mesopotamian, Egyptian, Hindu, Persian, Judeo-Christian, Greek-Roman) and three more recent literary categories (Medieval, Modern, and Contemporary). A total of 14 graph attributes was assessed, comprising lexical diversity (number of nodes), connectedness (edges, largest connected component, largest strongly connected component) and size (diameter, average shortest path), recurrence (repeated edges, parallel edges, loops of 1, 2 or 3 nodes), and global attributes (average total degree, density, clustering coefficient). The results revealed a clear pattern: While lexical diversity and connectivity increased asymptotically over time, recurrence decreased. These findings are compatible with the notion that psychosis is an early trait of our species.

030 - THE LEGEND OF "PISADEIRA" - A BRAZILIAN FOLKLORE ABOUT SLEEP PARALYSIS

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Sleep paralysis (SP) is a dissociative state that occurs mainly during awakening. SP is characterized by altered motor, perceptual, emotional and cognitive functions, such as inability to perform voluntary movements, visual hallucinations, feelings of chest pressure, delusions about a frightening presence and, in some cases, fear of impending death. Most people experience SP rarely, but typically when sleeping in supine position; however, SP is considered a disease (parasomnia) when recurrent and/or associated to emotional burden. Interestingly, throughout human history, different peoples interpreted SP under a supernatural view. For example, Canadian Eskimos attribute SP to spells of shamans, who hinder the ability to move, and provoke hallucinations of a shapeless presence. In the Japanese tradition, SP is due to a vengeful spirit who suffocates his enemies while sleeping. In Nigerian culture, a female demon attacks during dreaming and provokes paralysis. A modern manifestation of SP is the report of "alien abductions", experienced as inability to move during awakening associated with visual hallucinations of aliens. In all, SP is a significant example of how a specific biological phenomenon can be interpreted and shaped by different cultural contexts. In order to further explore the ethnopsychology of SP, here we present the "Pisadeira", a character of Brazilian folklore originated in the country's Southeast, but also found in other regions with variant names. Pisadeira is described as a crone with long fingernails who lurks on roofs at night and tramples on the chest of those who sleep on a full stomach with the belly up. This legend is mentioned in many anthropological accounts; however, we found no comprehensive reference on the Pisadeira from the perspective of sleep science. Here, we aim to fill this gap. We first review the neuropsychological aspects of SP, and then present the folk tale of the Pisadeira. Finally, we summarize the many historical and artistic manifestations of SP in different cultures, emphasizing the similarities and differences with the Pisadeira.

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