Sociedad Chilena de Neurociencia

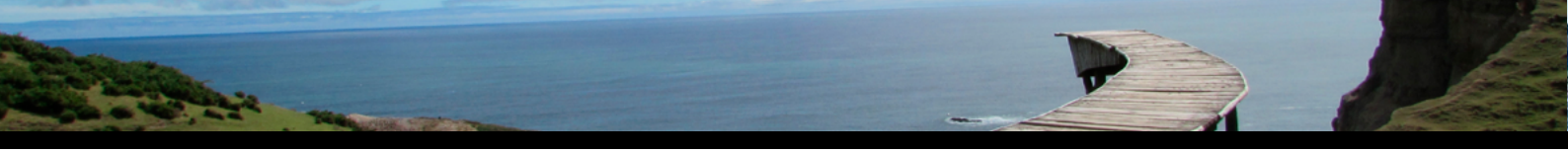
SOCIETY for NEUROSCIENCE

XIII Annual Meeting

Sociedad Chilena de Neurociencia

October 1-3, 2017

Hotel de la Isla. Castro - Chiloé



Message from the president

Welcome to the XIII annual meeting of the Sociedad Chilena de Neurociencia (SCN) in Castro, Chiloe, a place rich in folklore, architecture and biodiversity.

Since our origins, one of the aims of the SCN has been to bring science to society; this is the reason why we have organized outreach activities such as round tables and scientific talks at primary and secondary schools. Neuroscience is not only about research in our laboratories at molecular, cellular or cognitive aspects in normal and pathological conditions, also it has implications in our society: scientific help was needed in the recent episode of red tide in Chiloe which severely affect human and animal health as well as the local economy.

Red tide is caused by a bloom in dinoflagelates that produce toxins targeting the nervous system which can cause respiratory paralysis. Research on these gave the fundamental basis to develop new drugs to treat medical conditions as chronic pain, what would be unexpected 20 years ago.

This example reminds us that scientific knowledge might have profound implications to society.

For this annual meeting we have 10 symposiums, three plenary conferences, two oral communications and two poster session covering from molecular to cognitive aspects of neuroscience. One of these events is the Young Neuroscientist Symposium, an instance to potentiate the early career in science.

In this occasion our Society distinguishes the scientific work of Dr. Humberto Maturana, who has contributed into neuroscience with classical studies that have been followed for many scientist around the world. He has been a truly inspiration for new generations of researchers.

On behalf of the SCN Directory, organizers of this meeting, I would like to welcome and invite you to enjoy the meeting.

Patricio Rojas, PhD
President Sociedad Chilena de Neurociencia
October, 2017

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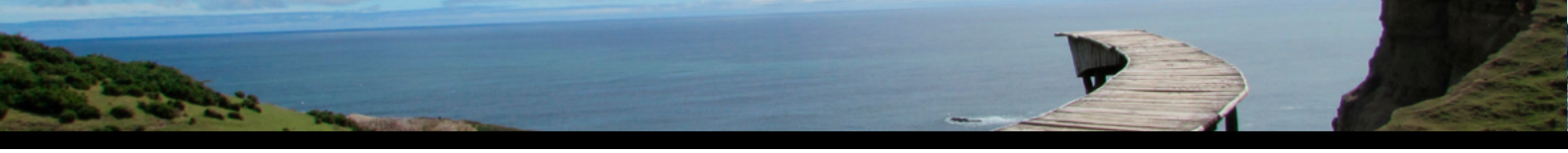


TABLA DEL PROGRAMA RESUMIDO

Time	Sunday, October 1nd	Time	Monday, October 2rd	Time	Tuesday, October 3rd
		08:30 10:30	**Symposium 3** **Symposium 4**	08:30 10:30	**Symposium 7** **Symposium 8**
		10:30 11:30	Coffee break	10:30 11:00	Coffee break
		11:30 12:30	**PLENARY LECTURE 2**	11:00 12:30	**Round Table**
		12:30 14:30	LUNCH	12:30 14:30	LUNCH
14:30 17:00	**Registration**	14:30 16:30	**Oral Presentations I and II**	14:30 16:30	**Young Investigators**
		16:30 17:00	**Coffee break**	16:30 17:00	Coffee break
17:00 19:00	**Symposium 1** **Symposium 2**	17:00 19:00	**Symposium 5** **Symposium 6**	17:00 19:00	**Symposium 9**
19:00 20:00	**Welcome LECTURE**	19:00 20:00	**Asamblea de Socios**	19:00 20:00	**SCN AWARD LECTURE**
20:00 23:00	**Poster Session I**	20:00 23:00	**Poster Sesion II**	20:00 23:00	**Dinner/Party**

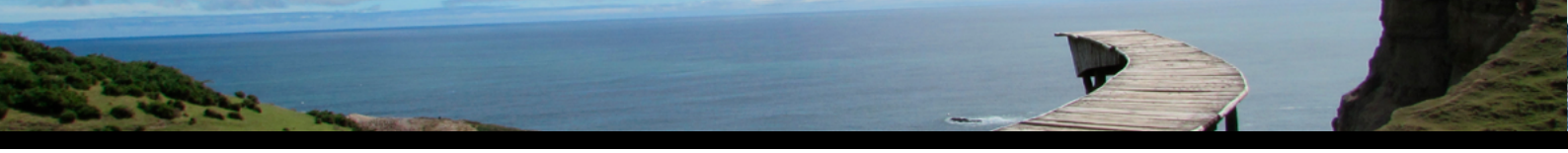
CONFERENCES

The Dynamic Basis of Rhythm Generation One Breath at a Time.

Ramirez J[1], [1]Neurological Surgery, Medicine, University of Washington.

The brain is a rhythm generator, and uses rhythmicity as a universal timing mechanism for learning and memory, sensory processing and the generation of rhythmic motor behaviors. Unraveling the mechanisms involved in rhythm generation provides important insights into how the nervous system processes and integrates complex information.
In this seminar I will focus on the neuronal control of the breathing rhythm, which may seem like a simple rhythmic motor behavior. But, every breath is stochastically assembled and reconfigured on a cycle-by-cycle manner to adapt and integrate breathing to our behavioral, metabolic, emotional, and artistic needs. Everyone experienced the complexity of breathing. When in love or when relieved, we turn a breath into a sigh; if we are talented we can turn a breath into an operatic experience; in hypoxia our breaths turn into gasps, and in panic we hyperventilate. The respiratory system never functions alone and is highly coordinated with the cardiac rhythm. Failure to coordinate these rhythms leads to dysautonomia and can end in sudden death.

At the basis of all these behaviors are excitatory microcircuits in the brainstem that function much like neocortical networks. These microcircuits are plastic and dynamically modulated, they depend on a variety of cellular mechanisms that include concurrent excitation and inhibition, bursting properties, glutamatergic synchronization, and neuro-glia interactions. These microcircuits are autorhythmic, and amenable to a rigorous cellular analysis in isolation and intact animals. Although, we are still far from understanding the many interesting emotional and cortical aspects of breathing, I hope that this lecture will nevertheless be inspiring to all of us. There is nobody that doesn´t depend on this rhythm of life: from the very first to the last breath.



Diversity and Evolution of Photoreception: From Circadian Light Sensors to Spatio-Temporal Vision.

Gomez M[1], [1]Biologia, Ciencias, Universidad Nacional de Colombia.

Sensory systems have attained an extraordinary performance, shaped by evolutionary pressures and by the physical constraints of the energy form that conveys the signal. Photoreception is possibly the most powerful means for obtaining detailed spatio-temporal information of our surroundings, partly because it exploits an external, abundantly available source of energy - sunlight - rather than relying on signals produced by objects, or self-generated by the subject, which are necessarily limited in scope and energetically costly. Photoreceptors probably evolved from pre-existing chemo-detectors which had already acquired G protein signaling cascades; in fact, opsins are GPCRs which associated covalently with a light-sensitive ligand. To improve photon capture, membrane specializations designed to pack large amounts of photopigment - such as cilia and microvilli - appeared since pre-bilateria, giving rise to the two canonical classes of photoreceptors; these are linked to distinctive opsin sub-types and cognate signaling pathways. These two lineages are largely segregated across the protostomia-deuterostomia divide, prompting suggestion of a bi-partite, parallel evolution of animal photoreceptors. However, recent evidence challenges such view, and indicates a wider diversity of light-signaling mechanisms than previously thought, but with a common, monophyetic origin. Clues have emerged from non-visual light dependent processes, like the entrainment of circadian rhythms and the control of the pupillary reflex; contrary to long-held beliefs, specialized light-receptors subserve these functions – a reasonable proposition, given that the requirements for monitoring general ambient illumination levels are quite different from those of spatial vision. Moreover, an unexpected kinship appeared between the 'circadian' receptors of vertebrates and visual receptors of invertebrates. A similarity between their respective photopigments was immediately evident, but the parallelism of downstream mechanisms emerged only slowly. The use of a non-model organism – amphioxus, the most basal extant chordate provided a boost, corroborating the light signal recruits the Gq/PLC/IP3/Ca cascade. In parallel, studies on photoreceptors that defy the traditional photoreceptor classification have revealed a diverging branch of visual pigments and a novel transduction cascade that engages a G-protein subtype that had never been implicated in sensory function; this seemingly occurs in mollusks, pre-chordates and echinoderms, pointing to a widespread distribution and ancient origin.

SIMPOSIUM

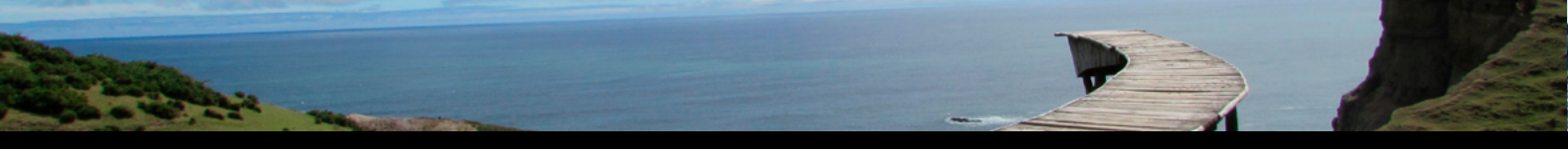
Brain Connectivity: Networks To Behaviour

Chair: Wael-El-Deredy

Properties of food representation and recognition.

Rumiati R[1], [1]Cognitive Neuroscience, Neuroscience, SISSA | Scuola Internazionale Superiore di Studi Avanzati.

Food is essential for our survival. It is therefore not surprising that the ability to discriminate what is edible from what is not, or the high-fat from low-fat food are fast occurring processes. We have attempted to answer several questions that have not been addressed to date, using mainly the neuropsychological approach with brain damaged patients, and EEG with neurologically intact individuals. First, are there other properties that can be discriminated equally early in visual food recognition, such as its level of processing? For instance, mice and non-human primates have been observed to prefer food that underwent some kind of processing, especially thermic, and cooked food has been argued to have made us human. Second, I will discuss whether recognition of natural and processed food mirrors, to some extent, the differences between living and non-living things. I will therefor present several studies in which we examined how the recognition of food and non food, and natural and processed food items eventually declines in normally ageing individuals and how such ability breaks down in brain-damaged individuals. An attempt to identify the atrophic areas that correlated with reduced accuracy has also been carried out in dementia patients. The main results are beginning to shape the domain specificity of food. First, our brain is able to detect as early as 120 milliseconds whether a food is natural or processed, everything else being equal. Second, food seems to be resilient to brain damage, especially if it is processed. Centenarians, however, are more accurate in recognizing natural food items that they report to have consumed more often in their long life. Lastly, I will provide evidence from two EEG studies about the electrical components of the recognition of the sensory/functional properties of food in three populations varying in body mass index, and of the natural/transformed properties.



Closed loop brain training: functional and structural connectivity changes due to learned brain self-regulation.

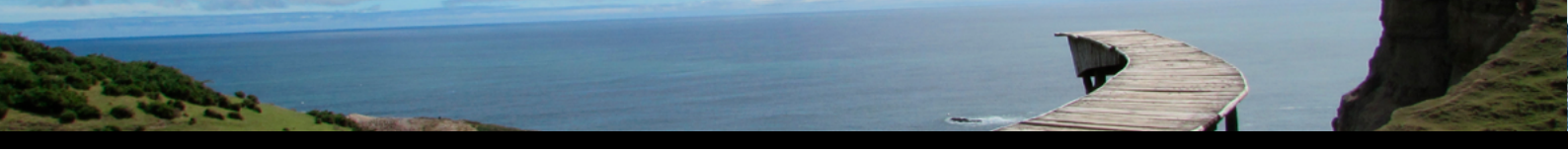
Sitaram R[1], [1]Institute for Biological and Medical Engineering, Medicine, Biology and Engineering, Pontificia Universidad Católica de Chile.

Brain-Computer Interfaces (BCIs) and Neurofeedback have emerged as technologies and methods for enabling the training of healthy individuals and patients to non-invasively self-regulate brain activity in circumscribed brain regions. However, current insights on several neural disorders state that brain dysfunction arises from a failed integration or “connectivity” between different areas, and not just by a dysfunction of single brain regions. This talk would enunciate recent developments in methodological and experimental work in the self-regulation of neural connectivity for investigating the relation between changes in functional connectivity, and neuroplastic and behavior.

Analyzing the influence of feedback, reward and instructions on brain self-regulation through dynamic mathematical modeling.

Bossonney K[1], Sitaram R[1], Sepulveda P[1], **Rodríguez-Fernández M[1]**, [1]Institute for Biological and Medical Engineering, Schools of Engineering, Medicine and Biological Sciences, Pontificia Universidad Católica de Chile.

The influence of feedback, motor imagery, reward and combinations of these factors in brain self-regulation was previously studied using real-time fMRI. Analysis of variance was used to compare self-regulation levels using mean blood oxygenation level-dependent (BOLD) signals across each run. The only group in which learning effect across training days was observed was the group that was given only contingent feedback. Although the group that was given both contingent feedback and monetary reward had the highest level of up-regulation early in training, it did not, however, show improvement with further training. This apparent lack of learning could also be due either to a ceiling effect (achievement of very high levels of performance very early in training), or to a late asymptotic performance that can only be seen perhaps with extended training. In order to further investigate these results, we studied the dynamics of the BOLD responses by means of mathematical modeling. Dose-response curves for the individual factors were fitted to logistic regression models and the obtained parameters used to predict combined responses by means of dose addition, response addition and integrated addition models. The models are able to fit the observed responses from the combination of factors and to discern between competing hypotheses.



Reduced Amygdala-Fusiform connectivity and maternal neglect.

EL-DEREDY W[1], Leon I[1], Rodrigo M J[1], [1]Ingenieria Biomedica, Ingenieria, Universidad de Valparaiso.

We used Dynamic Causal Modelling (DCM) to test for abnormal functional integration between two regions in the face processing network, amygdala and fusiform gyrus (FG), which would underlie neglectful mothers' insensitivity to crying infants. Maternal neglect, the most prevalent type of childhood maltreatment, involves a disregard of the infant's basic needs, usually conveyed by the distress signal of the crying face. We applied DCM to functional MRI data from 23 Neglectful and 20 Control mothers collected while they viewed 112 pictures of crying and neutral faces of infants and adults. We constructed intrinsic bidirectional fusiform (FG) ↔ amygdala models subtending to both infant and adult face processing. We added infant crying as a modulator to the top-down amygdala-FG link. There was significant difference between the two groups in the modulation of the top-down amygdala →FG connection by the context of infant crying only. Further, only in the neglectful mothers did infant crying have an inhibitory (negative) modulation on this connection. Disruption in the amygdala-FG connectivity may be related to poor attention to crying faces, and subsequently to the poor parenting behaviour in neglectful mothers.

GLIAL CELL-NEURON CROSSTALK IN HEALTH AND DISEASE

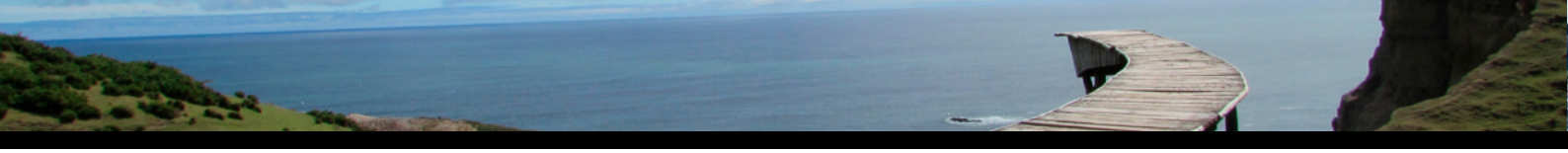
Chair: Rommy von Bernhardi

Multipronged control of astrocytic energy metabolism by neurons and the paradox of aerobic glycolysis.

Barros L F[1], San Martin A[1], Sotelo-Hitschfeld T[1], Lerchundi R[1], Fernandez-Moncada I[1,2], Baeza-Lehnert F[1,2], [1]Biología Centro de Estudios Científicos.[2]Escuela de Postgrado, Ciencias, Universidad Austral de Chile.

A neuron must go through innumerable cycles of activity through its prolonged life span, always on the verge of energy collapse, for neurons have no energy stores and the half times of their oxygen and ATP is measured in seconds. Genetically-encoded FRET nanosensors for metabolites are shedding new light on the mechanisms that ensure appropiate delivery of energy to neurons, a phenomenon termed neurometabolic coupling. Excitatory neuronal activity releases glutamate and K+. Within the first seconds, the rise in extracellular K+ depolarizes astrocytes and stimulates astrocytic glycolysis via the sodium-bicarbonate cotransporter NBCe1, while simultaneously triggering the release of lactate through a lactate-permeable 37 pS anion channel, the first of its kind. The astrocytic lactate channel is gated by depolarization and by lactate itself and conducts 1,000 times faster than the monocarboxylate transporters (MCTs) present in astrocytes and neurons. Acting in parallel fashion, K+, ammonium and nitric oxide inhibit the uptake of pyruvate and the consumption of oxygen by astrocytic mitochondria, thus increasing the availability of lactate and oxygen for neuronal use. Meantime neurons adapt to the workload by increasing their mitochondrial pyruvate consumption and their uptake of glucose. This activity-dependent astrocyte-to-neuron oxygen shunt provides a parsimonious explanation for the paradoxical phenomenon of brain aerobic glycolysis.

(Sponsored by Partly Funded By FONDECYT Grants 1160317 (LFB) And 11150930 (ASM). The Centro De Estudios Científicos (CECs) Is Supported By The Chilean Government Through The Centers Of Excellence Basal Financing Program Of CONICYT.)



Astrocytic D-serine is a new player in the chemosensory control of breathing.

Eugenín L. E. Lab. Sistemas Neurales, Facultad de Química y Biología, Universidad de Santiago de Chile.

Central chemoreception is essential for adjusting breathing to physiological demands and for brain CO_2/pH homeostasis. Failure in central chemoreception is a feature shared by life-threatening human conditions such as the Central Congenital Hypoventilation Syndrome and the Sudden Infant Death Syndrome. Glutamatergic neurotransmission is involved in respiratory rhythmogenesis and central chemoreception. However, the biological mechanisms by which glutamatergic contribution to central chemoreception is performed are still poorly understood. Here we show that caudal medullary brainstem astrocytes can synthetize and store D-serine, a high affinity endogenous agonist for the glycine-binding site of the N-methyl-D-aspartate glutamate receptor (NMDAR), which will be released together with L-glutamate in response to high levels of CO_2 (hypercapnia). Conversely, cortical astrocytes were unresponsive. D-serine activated the respiratory network in conscious mice and caudal medullary brainstem slices increasing the respiratory frequency (fR), whereas the NMDAR blockade abolished the increase in fR evoked by D-serine in slices. In conscious mice and caudal medullary brainstem slices, D-serine synthesis inhibition or D-serine enzymatic degradation decreased the hypercapnia-induced increase in fR and the basal fR revealing a D-serinergic tonic respiratory drive. The injection of D-serine into brainstem nuclei in slices revealed sensitive sites in the ventral respiratory column and the raphe nucleus. Our results demonstrate a novel role for D-serine as a mediator of the hypercapnia-induced respiratory response in caudal medullary chemosensory nuclei. We propose that D-serine released with glutamate from CO_2-sensitive astrocytes can account for the glutamatergic contribution to the central chemoreception.

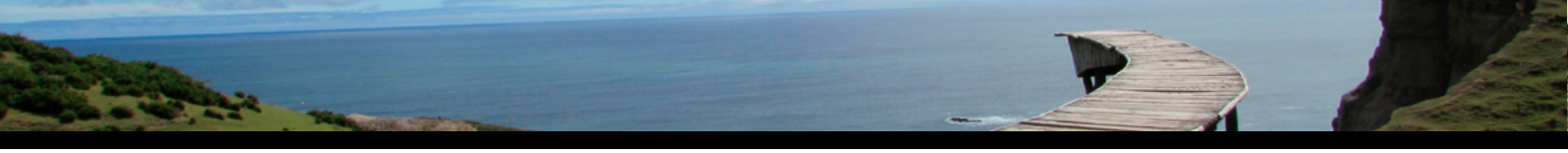
Supported by: FONDECYT 1171434

Neuron-glia communication by extracellular vesicles during regenerative programs.

Court F[1], [1]Center for Integrative Biology, Facultad de Ciencias, Universidad Mayor.

Nervous system function relies in the coordinated action of neurons and glial cells. In recent years, the importance of glial cells for several aspects of nervous system function has been underscored. Phenomena like synaptic activity, conduction of action potentials, neuronal growth and regeneration, to name a few, are fine tuned by glial cells. We have proposed a model in which the axon has certain autonomy from the neuronal cell body, and its associated glial cell is a major regulator of local axonal programs, including a regenerative program of axonal extension (Court and Alvarez, 2005), a destruction program activated by various stimuli (Barrientos et al., 2011; Villegas et al., 2014) and local protein synthesis in the axon (Court et al., 2008). Several intercellular mechanisms have been shown to operate on a local basis in the neuron-glia unit, including contact-mediated signaling and extracellular free ligands. Recently, another regulatory mechanism has emerged in which a cell releases vesicles containing RNAs and proteins, that are taken up by the recipient cell and the cargo is incorporated into the target cell (Simons and Raposo, 2009). Vesicular-mediated transfer of molecular cargoes between glial cells and neurons has been described in the nervous system (Lopez-Verrilli and Court, 2012; Lopez-Verrilli and Court, 2013). We have demonstrated vesicular mediated transfer of ribosomes from Schwann cells (SCs), the peripheral glial cell type, to axons in vivo after axonal damage as well as during axonal regeneration (Court et al., 2008; Court et al., 2011). Recently, we have found that exosomes secreted by SCs and selectively internalized by axons increase neurite growth substantially and greatly enhance axonal regeneration in vitro and in vivo (Lopez- Verrilli et al., 2013). We have now used a combination of next-generation sequencing, proteomics and bioinformatic analysis to identify RNAs and proteins present in SC- exosomes, and to search for candidates mediating the functional effect of SC-exosomes over axonal regeneration. This mode of interaction provides a new dimension to the understanding of the intercellular regulation at large, and we foresee that a number of phenomena of the nervous system still poorly understood will be studied under this new light.

Supported by grants from Geroscience Center for Brain Health and Metabolism (FONDAP-15150012), FONDECYT (No. 1070377), Millennium Nucleus RC120003 and Ring Initiative ACT1109.



Glial activation goes wrong as we age.

Von Bernhardi R[1], [1]Neurology, Medicine, Pontificia Universidad Católica de Chile.

Aging is the main risk factor for Alzheimer´s disease (AD). Its hallmarks are brain Aβ plaques formation, neurodegeneration and inflammatory activation of glia. Recent evidence from our lab and others, show that Aβ accumulation can be a consequence of glial cell dysregulation, which results in increased cytotoxicity, impaired Aβ clearance by glia, and neurodegenerative changes, all conditions that are observed in aged individuals. We found that in aging, there is an increased inflammatory activation of glial cells as well as an increased basal activation of Smad2/3/4, the canonical pathway of the regulatory cytokine TGFβ, whereas Smad3 activation in response to inflammatory stimuli is reduced in aged animals. Among the many molecules involved in the regulation of glial cell activation, scavenger receptor class A (SR-A), which participate both in Aβ phagocytosis and the inflammatory activation of glial cells, appears to be a potential target for AD. Here, we show by both *in vitro* and in *ex vivo* experiments that SR-A expression is decreased in aged individuals as well as through a Smad3-dependent mechanism after stimulation with TGFβ. Expression of SR-A was low already in young APP/PS1 mice compared with WT mice. Furthermore, lack of SRA was associated with increased Aβ accumulation as observed in the APP/PS1/SR-A$^{-/-}$ congenic mouse generated in our lab. Lack of functional SR-A was associated with dysregulation of glial cell activation, both at basal unstimulated conditions, with increased production of inflammatory cytokines and decreased levels of regulatory cytokines; and after inflammatory stimulation with LPS. Those conditions of increased inflammatory activation are able to potentiate neurotoxicity, potentiating neurodegenerative changes. APP/PS1/SR-A KO mice, showed increased plasma and hippocampal levels of inflammatory cytokines, and increased numbers of Aβ plaques in the hippocampus. Our results show that aging is associated with increased activation of the TGFβ pathway, which reduces SR-A expression by glial cells, promoting the accumulation of Aβ plaques, and favoring the cytotoxic activation of microglia and astrocytes, which appear to led to neurodegenerative changes and the behavioral impairment observed in Alzheimer´s disease.

INSIGHTS INTO HYPOTHALAMIC CONTROL OF ENERGY BALANCE AND FOOD INTAKE

Chair: Claudio Pérez-Leighton

Primary cilium and autophagy regulates inflammation and insulin sensitivity in hypothalamic neurons.

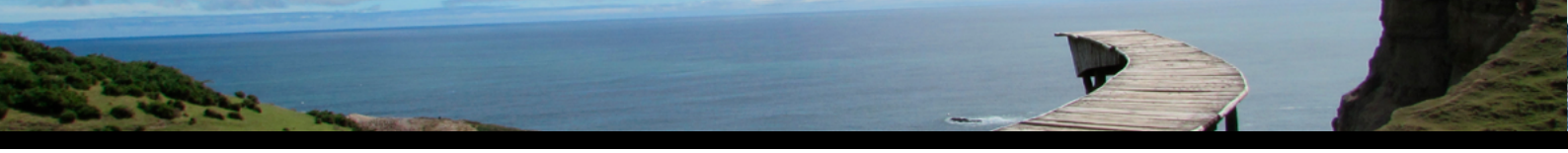
Ávalos Y[1], Morselli E[1], [1]Physiology, Biological Sciences, Pontificia Universidad Católica de Chile.

Introduction: Chile is the most obese country in South America, mostly due to the consumption of high fat diets (HFD). HFDs are rich in saturated fatty acids, such as palmitic acid (PA), which is significantly increased in the plasma of obese people and in the brain of mice following long-term HFD.
Autophagy, a process of lysosomal degradation of cytoplasmic material, acts as a quality control system that maintains cellular homeostasis. Chronic HFD inhibits hypothalamic autophagy and, conversely, the inhibition of hypothalamic autophagy promotes obesity, inflammation and insulin resistance in mice. Autophagy is required for the formation of an antenna-like structure named primary cilium (PC), which acts as a sensor of extracellular signals. Consumption of HFD decreases PC length in mice hypothalami and, in turns, PC depletion in hypothalamic neurons, triggers obesity and insulin resistance in mice. We propose that PA inhibits autophagy and causes PC dysfunction, promoting inflammation and reducing insulin sensitivity in hypothalamic neurons.

Methodology: N43/5 hypothalamic neurons were treated with pro-obesogenic concentrations of PA and autophagic flux was assessed by western blot (WB) and immunofluorescence (IF). Cilia length and the percentage of ciliated cells following PA treatment was observed by IF. The expression of pro-inflammatory cytokines induced by PA in autophagy-deficient and PC-depleted cells was evaluated by qPCR. Insulin-induced AKT phosphorylation was evaluated after autophagy inhibition or PC depletion by WB.

Results and conclusion: PA inhibits autophagic flux in N43/5 cells. Interestingly, both pharmacological inhibition of autophagy and PA treatment reduce the length and the percentage of ciliated cells. Inhibition of autophagy, as well as PC depletion, increases PA-induced expression of pro-inflammatory markers in N43/5 hypothalamic neurons. In addition, PA inhibits the phosphorylation of AKT induced by insulin. PC depletion attenuates the response to insulin in N43/5 cells. Altogether, these results suggest that PA inhibits autophagic flux and reduces ciliogenesis, which, in turns, promotes inflammation and reduces insulin sensitivity in hypothalamic neurons.

(Sponsored by This Work Is Supported By FONDECYT 1160820 And By The International Centre For Genetic Engineering And Biotechnology (ICGEB) CRP/CHL16-06.)



Sleep deprivation-induced obesity: role of orexin-mediated energy intake and expenditure.

Teske J[1], [1]Nutritional Sciences University of Arizona.

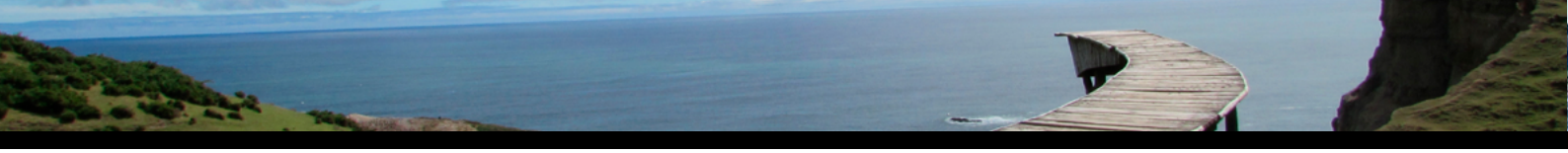
Inadequate sleep has emerged as a key contributor to obesity. Yet, brain mechanisms that promote positive energy balance through modulation of energy intake and expenditure remain unknown. We developed a rodent model of sleep deprivation-induced obesity in male and female rats that is ideal for identifying brain mechanisms underlying sleep deprivation induced weight gain. In this model, we show that acute and chronic exposure to pre-recorded environmental noise causes weight gain in noise-exposed male and female rodents relative to rats that sleep undisturbed. Moreover, weight gain in response to acute sleep deprivation was paralleled by reductions in physical activity and energy expenditure (EE, total and EE during sleep, rest, and movement) but not hyperphagia. In contrast, hyperphagia and reductions in EE contributed to weight gain in response to chronic sleep deprivation despite that chronic sleep deprivation had no effect on physical activity. Next, we investigated whether low orexin signaling in the ventrolateral preoptic area (VLPO), a known sleep center in the brain, contributed to weight gain due to inadequate sleep by reducing total EE and physical activity since elevated orexin signaling promotes negative energy balance. In contrast to the behavioral and EE response to orexin infusion in the VLPO before sleep deprivation, orexin in the VLPO was less effective at increasing EE and physical activity after acute sleep deprivation and completely ineffective after chronic sleep deprivation. These data suggest that sleep loss may reduce orexin signaling in the VLPO to in turn stimulate weight gain in response to sleep deprivation by reducing physical activity and the rate of energy expended during physical activity. These data have implications for reversing treating individuals who are have obesity and are sleep deprived.

Neuropeptides in the regulation of physical activity and food choice: orexin, dynorphins and GLP1.

Perez-Leighton C[2,1], [1]Food Science and Nutrition University of Minnesota.[2]Facultad de Medicina Universidad Andres Bello.

The hypothalamus integrates peripheral and brain information to regulate energy expenditure and food intake, thus affecting energy balance and body weight. Within the hypothalamus, several neuropeptides regulate different aspects of energy balance, and we have focused on three neuropeptides: The orexins, dynorphins and glucagon-like peptide 1 (GPL1). Our first line of research investigates the hypothalamic orexin/dynorphin neurons, which co-express and co-release the orexin and dynorphin (DYN) neuropeptides. The DYN peptides can be classified as opioid or non-opioid, depending on whether they bind to opioid receptors. We have been working towards understanding the role of the canonical non-opioid DYN peptide (DYN-A_{2-17}) on energy balance. Our data in mice show that DYN-A_{2-17} can acutely increase SPA, exercise, energy expenditure and food intake; and also potentiate the increase on food intake caused by orexin, but DYN-A_{2-17} does not have long-lasting effects on food intake and energy balance. Orexin and opioid DYN peptides can increase standard food intake, and together with non-opioid DYN peptides, we have started examining their individual role and interaction on palatable food choice and intake. Our preliminary data suggest that orexin, opioid and non-opioid DYN peptides have differential effects on food intake, depending on whether it is possible to choose between palatable and non-palatable foods. Our second line of research focuses on GLP1, a neuroendocrine peptide that can inhibit food intake and reward behavior. EX4 is an agonist of the GLP1 receptor that has been proposed as a potential anti-obesity therapy. However, whether the ability of EX4 to inhibit food intake and reward behavior is modulated by chronic intake of palatable foods and composition of the food environment remains unclear. Our data in mice fed cafeteria-style diet show that the types of foods offered relative to individual preference and experience with palatable foods modulate the anorectic effect of EX4 and its ability to block food reward behavior. Together, our studies contribute to understand how different neuropeptides regulate food intake and physical activity through the hypothalamus and their impact on regulation of body weight.

FONDECYT Regular 1150274, CONICYT PAI 82130017 and Universidad Andres Bello DI-523-14.



FROM NEURAL CONNECTIVITY TO NETWORK DYNAMICS

Chair: Patricio Orio

Mechanisms of spatial working memory in the prefrontal cortex.

Compte A[1], Barbosa J[1], Wimmer K[2], [1]Experimental and Clinical Neurosciences IDIBAPS.2Computational Neuroscience CRM.

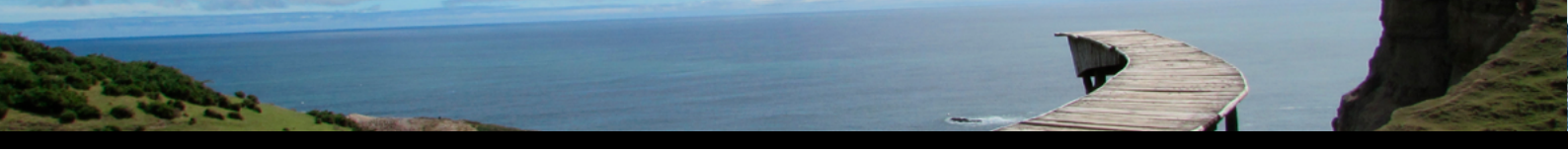
During oculomotor delayed response tasks, the activity of monkey prefrontal neurons is known to encode the parameters of memorized locations. Computational models have provided explicit hypotheses to test directly in neurophysiological data the mechanistic basis of this mnemonic representations. In this talk, I will present results that address the stability of the neuronal code during the memory delay, the architectural substrate that supports it, and evidence for temporal stabilizing mechanisms and their behavioral consequences. Our analyses and computational simulations show that sustained persistent activity of prefrontal neurons during the mnemonic period of spatial working memory tasks leave a trace of subthreshold memory imprints, possibly through synaptic plasticity mechanisms, that can be reignited into neural activity depending on task contingencies. By guiding the analysis of neurophysiological data with mechanistic cortical network models, and validating predictions with behavioral data, a consistent picture of prefrontal network dynamics underlying spatial working memory is emerging.

Functional connectivity in the retina.

Escobar M[1], Otero M[1], Reyes C[1], Herzog R[2], Araya J[2], Ibaceta C[2], Palacios A[3], [1]Departamento de Electrónica Universidad Técnica Federico Santa María.[2]Centro Interdisciplinario de Neurociencia de Valparaíso Universidad de Valparaíso.[3]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.

Mammalian retina contains a variety of retinal ganglion cell types differing in morphology, connecting different circuits and extracting different features from the outer visual world. Functional properties of retinal ganglion cells can be characterized in space and time through their receptive field estimation. This estimation gives the functional property of each ganglion cell, which depends on the specie and the location of the receptive field inside the visual scene. Additionally, for evoked and spontaneous activity, retinal ganglion cells present an orchestrated activation forming correlated activity in a small number or neurons, giving what we understand as functional connectivity. We have observed in the retina that this functional connectivity contains properties of neural assemblies, which are associated to neural encoding of different computations in the brain, such as memories or decision-making process. Along this talk we we will review functional properties of retinal ganglion cells found in a diurnal rodent for two different retinal regions, related to central and peripheral vision. Furthermore, we will describe how these different cell types interact to form neural assemblies, which could be mechanism used by the retina to encode the information contained in the input stimulus.

(Sponsored by CONICYT-FONDECYT 1140403 And 1150638, CONICYT-Basal Project FB0008, Millennium Institute ICM-P09-022-F, ECOS-CONICYT C13E06).



Irreversibility and Non-equilibrium Maximum Entropy Processes from Spike Trains.

Cofre. R[1], [1]CIMFAV, INGENIERIA, Valparaíso.

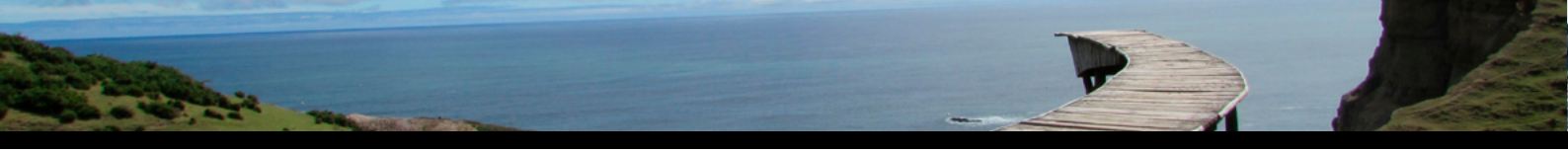
Experimental recordings of the collective activity of interacting spiking neurons exhibit random behavior and memory effects. Therefore, the stochastic process modeling this activity requires showing some degree of irreversibility. We use the thermodynamic formalism to build a framework, in the context of spike train statistics, to quantify the degree of irreversibility of any parametric maximum entropy measure under arbitrary constraints. We provide an explicit formula for the information entropy production and provide examples to illustrate our results. Additionally, we review large deviations techniques useful to accurately describe statistical properties in terms of sampling size and maximum entropy parameters. In particular, we focus on the fluctuation of average values of observables, irreversibility and the identifiability problem of maximum entropy Markov chains. We illustrate these applications using simple examples of relevance in this field.
ERC advanced grant ``Bridges', CONICYT-PAI Insercion 79160120

The interplay between Neural dynamics, Connectivity and Network Dynamics.

Orio P[1], Castro S[1], Xu K[1], Maidana J P[1], [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.

The dynamic of brain activity shows distinctive features that we believe are crucial for its functions of sensory processing, cognition and decision making. During the last years, there has been an increasing focus on multi-stability, mostly evidenced as the continuous itinerancy between different partially synchronized states in both fMRI and EEG recordings of task-free subjects. Multi-stability is thought to allow the system for the exploration of many state configurations thus enabling the efficient coding of the ever-changing surrounding environment. Our group is studying how different network characteristics can originate this dynamically rich behavior, using numerical simulations of biologically-inspired networks. Regarding topology, we have found that nodes connected with high degree shape the global connectivity conditions that permit multistability. On the other hand, we are looking at how the chaotic and/or stochastic nature of local (node) dynamics can influence global behavior. Our results show that chaos at the node level enhances the multi-stable dynamics, even though there are no visible effects on other global behavior such as synchrony transitions. This research will not only shed light on the origin of the dynamical richness of the brain, but only will serve as basis for an informed design of artificial intelligence systems that follow the design principles of the nervous system.

Funded by Basal Center AC3E (FB0008 CONICYT, Chile), the Millenium Institute CINV (P09-022F, MinEcon), and FONDECYT Grant 3170342 (to KX). SC holds a Ph.D. fellowship from CONICYT.



COGNITIVE NEUROSCIENCE AND AGEING: THE CONTRIBUTION OF CLINICAL RESEARCH

Chair: Andrea Slachevsky

Neuroimaging in Neurodegeneration.

Cruz de Souza L. Universidade Federal de Minas Gerias

Traditionally, the assessment of dementias requires neuroimaging investigation to rule out neurosurgical lesions that may account for the cognitive decline. Besides their value to exclude treatable causes of cognitive dysfunction (normal pressure hydrocephalus, subdural hematoma, e.g.), modern neuroimaging techniques extends beyond this classical role and are now employed to identify markers for the diagnosis of Alzheimer's disease (AD) and of other neurodegenerative diseases.

Structural (magnetic resonance imaging, e.g.) and functional (positron emission tomography [PET] with fluorodeoxyglucose and single-photon emission computed tomography, e.g.) methods provide topographical information about neural damage and enable the identification of specific lesional patterns that characterize AD and other dementias. These methods are also valuable tools to investigate the neural basis of cognitive and behavioral deficits that are commonly observed in neuropsychiatric disorders.

More recently, molecular brain imaging provides pathophysiological information regarding neurodegenerative disorders. Amyloid markers enable the assessment of amyloid load, while Tau markers tap in Tau-related lesions. The microglial activation may also be assessed, providing information regarding central neuroinflammation. These markers allow the *in vivo* identification of key pathophysiological features of degenerative disorders, like AD.
Taken together, modern neuroimaging methods opened a new window in the diagnosis and assessment of neurodegenerative disorders. Even though most of these techniques are actually restricted to research purposes, their application in clinical settings is expected to increase in the following years.

Cognitive consequences of hidden hearing loss.

Delano P[1,2], Leiva A[2], Martinez M[3], Soto A[3], Elespuru K[2], Delgado C[1,3], [1]Neurociencia, Medicina, Universidad de Chile.[2]Otorrinolaringología, Medicina, Universidad de Chile.[3]Neurologia y Neurocirugía, HCUCH, Universidad de Chile.

Epidemiological evidence shows an association between age-related hearing loss (presbycusis) and cognitive decline in elderly people. Presbycusis subjects with audiometric hearing thresholds worse than 40 dB are more likely to develop cognitive decline (Deal et al., 2017). The mechanisms that connect this epidemiological association are unknown. Here we propose that hidden hearing loss (HHL), that is the loss of synapses between inner hair cells and auditory nerve neurons without alterations in the audiometric thresholds, is an important factor linking presbycusis and cognitive decline. HHL can be assessed using supra-thresholds auditory brainstem responses (ABR) by measuring the amplitude ratio of ABR wave I/wave V.*Results:* 88 subjects from the ANDES (Auditory and Dementia study) study has been recruited in a prospective cohort of Chilean healthy hispano-mestizo elders ≥65 years, "cognitively" normal (MMSE>24) with different levels of age related hearing impairment.Audiometric thresholds correlates with perseverative errors in the Wisconsin card sorting task (executive function). Inferior colliculus ABR latencies (wave V) correlate with neuropsychological assessments (fluency and reverse digit span), while hidden hearing loss measures correlate with Trail-Making Test A time and errors (processing speed). These results suggest that different structures in the auditory pathway (auditory nerve, inferior colliculus) are related to the development of different cognitive impairments, showing that HHL is related to processing speed decline in healthy elders.

References

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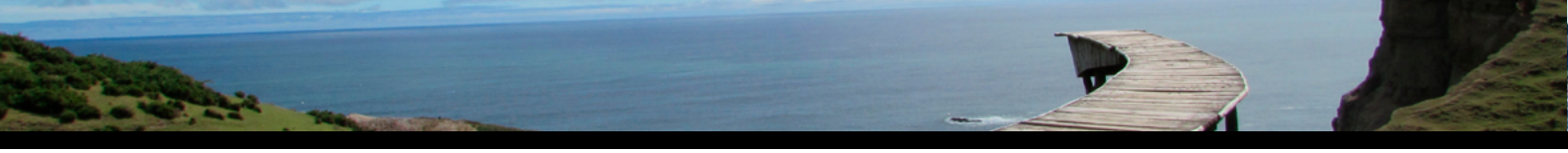
Funded by Proyecto Anillo ACT1403, FONDECYT 1161155 and Fundación Guillermo Puelma.



Functionality and dementia: A critical issue in dementia research.

Slachevsky, A. Associate Professor, ICBM and Neuroscience Department, Faculty of Medicine and Geroscience Center for Brain Health and Metabolism (GERO)), Chile; Universidad de Chile.

Dementia is defined as a clinical syndrome characterized by a progressive decline of cognitive abilities, severe enough to interfere with an individual's functionality in everyday life. Functional decline (FD) in dementia is defined as the difficulty or inability to perform activities of daily living (ADLs). The determination of FD is a key dividing line between predementia and dementia state. Everyday functioning is also a critical aspect in tracking disease progression in clinical contexts and treatment trials. ADL dependence has been correlated with poorer quality of life, increased healthcare costs, increased risk of mortality and institutionalization. However, despite its relevance, little attention has been paid to the characterization of FD in dementia. There are still important research gaps on FD in dementia. In this presentation, we will present our research on FD and discuss some of the key issue in the study of FD in dementia. First, current evidence suggest that FD need to be divided in different domain of activities, i.e. Instrumental Activities of Daily Living (IADLs), Basic Activities of Daily Living (BADLs), and Advanced ADL (a-ADLs). Second, cognitive impairment seems to be only one of the factors influencing FD. The contribution of non-cognitive symptoms, like neuropsychiatric and motor symptoms have emerged as critical contibutors to FD in dementia. Third, studies on the neural correlate of FD are still scarce. Study of the neural correlates of FD could contribute to a more comprehensive understanding of these underlying mechanisms. Finally, current instrument to assess FD in the clinical practice present several limitations. There is a room for new framework for asessment of FD, mainly considering current evidence about the benefits of timely diagnosis and tailored non pharmacologic intervention in dementia practice.

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Apathy and functionality in Alzheimer disease

Delgado, C[1,3], Vergara R[2], Martinez M[1], Soto A[1], Slachevsky A[5,3,4], [1]Neurología y Neurocirugía Hospital Clinico Universidad de Chile, Medicina, Universidad de Chile.[2]Biomedical Neuroscience Institute, Medicina, Universidad de Chile.[3] Neurociencia, Medicina, Universidad de Chile.[4]Ciencias Neurológicas Oriente, Medicina, Universidad de Chile.[5]Geroscience Institut, Medicina, Universidad de Chile.

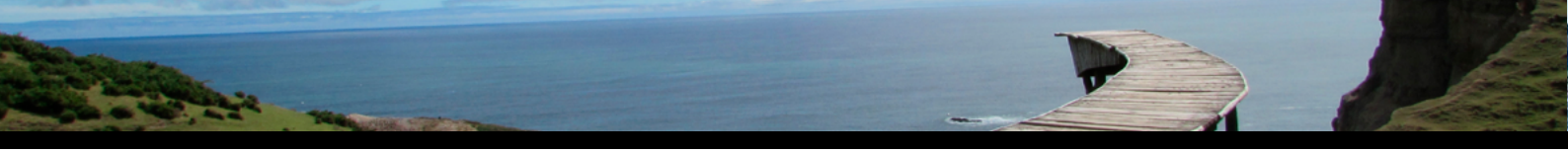
Background: Although memory impairment is the most frequent presenting symptom of Alzheimer disease (AD), neuropsychiatric symptoms (NPS) are usually contemporary, being cognitive impairment and NPS independent contributors to disability in AD. Apathy, defined as a deficit in self-initiated "goal directed behaviors" is the most frequent NPS in AD, and has been related with early functional impairment. Mechanistically has been divided in "cognitive", "behavioral" and "emotional" types (Robert 2010).

Objective: Study the cognitive and behavioral determinants of impairment in activities of daily living (ADL) in cognitively normal elders and AD patients. Methods: 145 subjects: 50 controls and 95 AD patients were graduated using the clinical dementia rating (CDR) in very mild dementia (CDR 0.5 n=38) and mild dementia due to AD (CDR 1&2, n=57). They were assessed with measures of cognitive performance; NPS and ADL impairment. The different subtypes of Apathy were determined using the Robert criteria. Lineal regression models were done to assess the better predictors for global and specific subtype of ADL impairment in every CDR status.

Results: Patients with AD were significantly older 74±7 than controls 71±6 (t=-2.47, p=0.014), without differences in education or gender proportion. At least one behavioral symptom was present in 93% of AD patients, compared with the 39% of the control group; apathy was present in 61 % of AD patients, with increasing proportion in relation with disease severity (CDR 0.5=44% CDR1&2=71%). The proportion of cognitive, behavioral and emotional types of apathy in AD patients were: 86%, 50%,30% respectively, being "cognitive apathy" present from the initial states, while "emotional apathy" only appeared in the CDR=1&2. The best predictors of ADL impairment in controls and CDR=0.5 were the severity of NPS (apathy and *Frontal-Psychotic* symptoms), while agitation-irritability symptoms and global cognition were the best predictors in mild dementia patients.

Conclusions: NPS were the best predictors of ADL impairment at any cognitive status. Apathy is mainly important in very mild states of AD, where it could affect complex ADL in different ways: from planning to emotional aspects.

(Sponsored by Anillo ACT 1403, FONDECYT 1140423).



NEUROL CONTROL OF THE CARDIORESPIRATORY FUNCTION: A VIEW FROM THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM

Chair: Julio Alcayaga.

Petrosal ganglion neuron modifications induced by chronic phenytoin treatment: implication in anticonvulsant treatment hypoventilation.

Alcayaga J[1], [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile.

Anticonvulsants, as phenytoin, are used in epilepsy and convulsion treatment in trauma patients in hospital emergency rooms. One of the major complications of its usage is the concomitant hypoventilation developed by some patients. Neurons of the petrosal ganglion, that innervate the carotid body and convey afferent innervation on blood gases, present a sodium persistent current that is blocked by phenytoin. Although largely used, the effects of phenytoin long lasting treatment on chemosensory afferences and ventilatory control are mostly unknown. Sprague-Dawley male rats were implanted with osmotic pumps delivering phenytoin (10 mg/day) or vehicle; ventilation and chemosensory activity recorded for up to 30 days. In normoxic conditions the afferent activity was unaffected by the treatment, and hyperoxic reduction of activity was similar than in control rats. Conversely, hypoxic responses were largely reduced by phenytoin treatment, especially when inspired O_2 fraction was below 15%. Recordings from identified petrosal chemosensory neurons showed that passive and most active properties were similar in both groups, but tonic responses were evoked in a significantly larger population of control than in phenytoin treated neurons. Additionally, the rheobase was increased by phenytoin treatment. Our ventilatory and cardiovascular recordings show that phenytoin treatment reduced ventilatory responses to hypoxia without significant modification of cardiovascular responses. The ventilatory responses to hypoxia were different in behaving and anesthetized rats, with a reduction of ventilatory frequency increases on the former and a reduction of tidal volume increases on the latter. Thus, chronic phenytoin treatment reduces chemosensory responses to acute hypoxia, with a concomitant reduction of petrosal chemosensory neurons tonic discharges and excitability. These modifications are accompanied by a reduction of ventilatory responses to acute hypoxia, suggesting that hypoventilation may result from the reduction in chemosensory afferent activity even in mild hypoxic conditions. However, because ventilatory responses in behaving and anesthetized rats relay on different aspects of the ventilatory response, a central effect of phenytoin is also present.

FONDECYT 1130177

Is there anything the brain can tell us about heart disease?.

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In heart failure with preserved ejection fraction (HFpEF) both cardiac autonomic imbalance and breathing disorders contribute to the progression of the disease. We hypothesized that sympathoexcitation and breathing disturbances are from a central origin in HFpEF. Then, we aimed to determine the effects of selective ablation of RVLM C1 neurons and RTN phox2b neurons on autonomic control, cardiac function, and breathing disturbances in rats with HFpEF. Sprague-Dawley rats underwent volume overload to induce HFpEF. Dopamine β Hydroxilase-saporin toxin (DβH) and Substance P-saporin toxin (SSP) were stereotaxically injected into the RVLM and RTN, respectively. Cardiac function was determined by pressure-volume loops and sympathetic drive was assessed by propranolol test. Whole body plethysmography was used to assess resting breathing patterns. The incidence of apneas and hypopneas (AHI) were score, as well as breath-to-breath interval variability. Compared to HFpEF vehicle treated rats, HFpEF+DβH rats display (HFpEF vs. HFpEF+DβH): reduced end diastolic pressure-volume relationship (EDPVR, 10.0±1.0 vs. 5±0.1 1/ml, P<.05) and reduced sympathetic tone (ΔHR, -98±12 vs. -52±8 bpm, P<.05). No effect of DβH on chemoreflex function was found. On the contrary, SSP-saporin normalizes chemoreflex drive in HFpEF. HFpEF+SSP rats showed reduced AHI (20±4 vs. 11±3 episodes/hr, HFpEF vs. HFpEF+SSP, respectively; P<.05) and breath-to-breath interval variability (SD1, 86±6 vs. 46±6 ms; SD2, 91±11 vs. 60±5, HFpEF vs. HFpEF-SSP, respectively; P<.05). Interestingly, we found that activation of central chemoreceptors in HFpEF rats result in a large increase in cardiac sympathetic outflow and worsens diastolic function by ~180%. Remarkably, ablation of RVLM C1 neurons blunted the cardiovascular effects of central chemoreceptor activation in HFpEF rats. Together our results showed that C1 neurons are critical for the maintenance of high cardiac sympathetic tone and contribute to cardiac function deterioration in HFpEF. In addition, phox2b chemoreceptor neurons are responsible for the heightened central chemoreflex drive and breathing disturbances observed in HFpEF. Importantly, the adverse hemodynamic response to central chemoreflex activation depends on C1 neurons.

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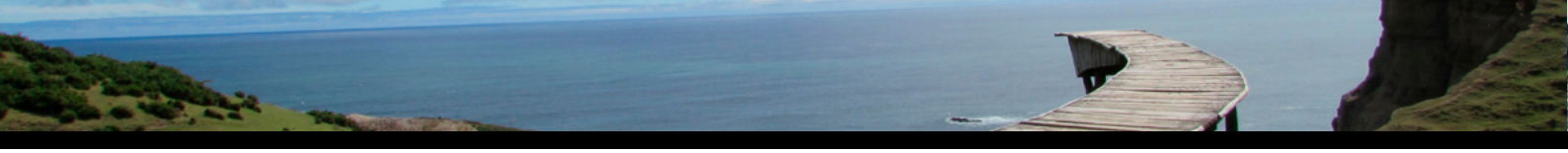


Carotid body chemoreceptor denervation in intermittent hypoxia mimiking obstructive sleep apnea.

Iturriaga R[1], Andrade D[1], Del Rio R[1], [1]Laboratorio de Neurobiologia, Ciencias Biologicas, Pontificia Universidad Católica de Chile.

Intermittent hypoxia, the main feature of obstructive sleep apnea, enhances carotid body (CB) chemosensory discharges, and induces autonomic alterations and hypertension. Accordingly, to assess the role played by the CB in the autonomic alterations and hypertension, we studied the effects of selective CB ablation in rats exposed to intermittent hypoxia. Male Sprague-Dawley rats (200 g) were exposed to 5% F_iO_2, 12 times/h, 8 h/day. After 21 days of intermittent hypoxia, under isoflurane anesthesia both CBs were cryogenically destroyed and rats were kept 7 more days in intermittent hypoxia. We studied the effects of CB ablation on arterial blood pressure (BP) measured by radio-telemetry (DSI, USA), ventilatory chemoreflex drive (whole body plethysmography), baroreflex sensitivity (BRS), heart rate variability (HRV), arrhythmia index and systemic oxidative stress (TBARS). After 21 days, rats showed systemic oxidative stress, hypertension (circa 10 mm Hg), enhanced CB-mediated chemoreflex evidence by the potentiation of the hypoxic ventilatory response, predominance of HRV low frequency band, a significant reduction in the BRS, and increased number of cardiac arrhythmic events. The CB ablation normalized the increased BP, reduced the enhanced hypoxic ventilatory response, normalized BRS and HRV, and markedly reduced the number of arrhythmic events. However, systemic oxidative stress was unaffected by CB ablation. Present results indicate that cardiorespiratory and autonomic alterations induced by intermittent hypoxia are critically dependent on the enhanced CB chemosensory discharge. The hypertension and autonomic alterations were abolished by the CB ablation despite that the continuous exposure to intermittent hypoxic stimulus maintains the systemic oxidative stress. Present results indicate that the CB plays a main role in the progression of the hypertension and autonomic imbalance.

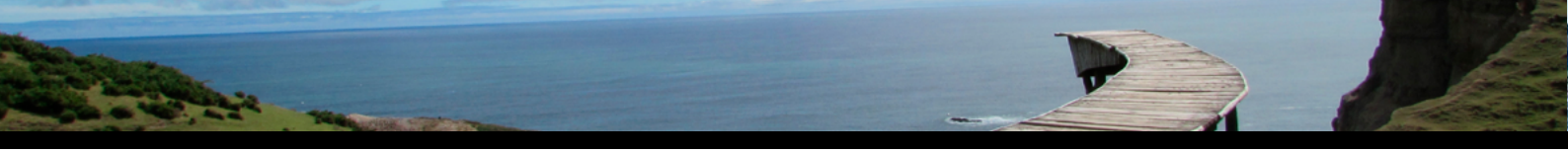
(Sponsored by FONDECYT 1150040)

Respiratory chemoreception´s neuroplasticity in a rat model of Parkinson´s disease.

Oliveira L[1], Tuppy M[1], Moreira T[2], **Takakura A[3]**, [1]Pharmacology University of Sao Paulo.[2]Physiology and Biophysics, Associate Professor, University of Sao Paulo.[3]Pharmacology, Assistance Professor, University of Sao Paulo.

Parkinson´s disease (PD) is a disorder characterized by loss of dopaminergic neurons in the substantia nigra (SN) and presents non-motor symptoms as breathing disorders. Previous study demonstrated that in 6-hydroxydopamine (6-OHDA)-model of PD there is a reduction in the number of Phox2b-neurons in the retrotrapezoid nucleus (RTN) and a decrease in the hypercapnic-ventilation (V_E) response 40 days after PD-induced. This functional deficiency is restored 60 days after 6-OHDA. Here we tested if A6 noradrenergic cells could be a candidate to restore this deficiency in this model. Hypercapnic-V_E response (7% CO_2) was assessed one day before and 60 days after bilateral 6-OHDA or vehicle injections into striatum and in the A6 in male Wistar rats. Bilateral injections of 6-OHDA decreased cathecolaminergic-neurons by 86% and 83% in the SN and A6, respectively. In those animals there is a reduction in the hypercapnic-V_E response 60 days after 6-OHDA (785 ± 18 vs. vehicle: 1417 ± 177 ml/kg/min). In another group 40 or 60 days after injections of 6-OHDA into striatum, the rats were exposed to hypercapnia and there was a reduction time-dependent in the number of hypercapnia-induced-Fos-ir cells in the RTN (40 days: 38 ± 3, 60 days: 8.5 ± 0.9 vs. vehicle 78 ± 3 cells) and an increase in the A6 (40 days: 46 ± 4, 60 days: 94 ± 22 vs. vehicle 1 ± 1 cells). Our data suggest that A6 noradrenergic neurons can be a candidate to assume the chemoreceptor function in a rat model of PD.

Fapesp, CNPq and CAPES



STRESS, MEMORY, ANXIETY AND FOOD INTAKE

Chair:Jimmy Stehberg.

In Vivo Recording in the Basolateral Amygdala During the Development of Anhedonic Behavior.

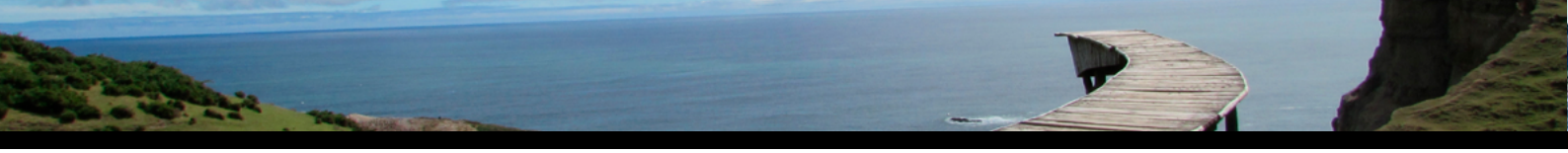
Dagnino-Subiabre A[1], Pérez C[1], [1]Laboratory of Stress Neurobiology, Center for Neurobiology of Brain Plasticity, Institute of Physiology, Faculty of Sciences, Universidad de Valparaíso. (Sponsored by This Work Was Funded By FONDECYT Grant 1141276 And Anillo De Ciencia Y Tecnología Grant ACT1403 To Alexies Dagnino-Subiabre)

Anhedonia or loss of pleasure is a cardinal symptom of the major depressive disorder and the basolateral amygdala (BLA) is a brain structure involve in the etiology of this disease. In line with this, chronic unpredictable stress (CUS) induces both dendritic hypertrophy and decreases of GABAergic neurotransmission in the rat BLA. Therefore, in this study we aimed to determine whether CUS affects in vivo the neuronal activity in BLA when rats develop the anhedonic behavior. Male adult Sprague-Dawley rats were implanted in BLA with a microelectrode array (Microprobe) and following the post-surgery period, implanted rats were separated in control and stress experimental groups. The local field potentials were recorded from BLA with a wireless recording system (Multichannel System), specifically when the rats drank water or sucrose solution during the sucrose preference test, a behavioral task to measure anhedonia. We found that sucrose solution intake in control animals was higher compare to water intake, while 2-4 Hz oscillations power in BLA was increased when rats drank sucrose solution compared to water. Conversely, after 21 days of CUS, chronically stressed rats had equivalent intake of sucrose solution and water but the 2-4 Hz oscillations power increased when stressed rats drank water respect to sucrose solution. Our results suggest that pleasure in the rats could be associated to the 2-4 Hz oscillations in BLA and the development of anhedonia is related to lower 2-4 Hz oscillations power in BLA. This study opens a new approach to understand the neurobiology of depressive-like behaviors.

Interaction between stress and fear memory: Implications for a traumatic memory?.

Molina V[1], [1]Instituto de Farmacología Experimental Universidad Nacional de Córdoba.

Stress promotes fear memory consolidation. Previous pharmacological, behavioral and electrophysiological findings from our laboratory suggested that prior stress attenuates inhibitory GABAergic control in the BLA, enhancing BLA excitability and promoting the induction of LTP in this brain area associated with the enhancement of contextual fear memory formation. Furthermore, using whole-cell patch clamp we observed no inhibitory postsynaptic current (IPSC) in stressed animals, suggesting that stress induced GABAergic disinhibition in BLA is due to attenuation or suppression of feedback inhibition. Additional findings showed that prior stress enhanced spine density in the Dorsal Hippocampus (DH) associated with contextual fear memory. Intra-BLA infusion of Midazolam (MDZ), prevented the facilitating influence of stress on hippocampal dendritic spine remodeling. In contrast, the blockade of GABA-A sites within the BLA induced structural remodeling in the DH, suggesting that GABAergic transmission in BLA modulates the structural plasticity in the DH associated to stress-induced promoting effect on fear memory. Consolidated memory can return to a labile state and become transiently malleable following reactivation. This instability is followed by a restabilization phase termed reconsolidation. The results revealed that prior stress resulted into a memory trace that was insensitive to the disrupting action of diverse drugs on fear memory reconsolidation. Prior stress prevented the reactivation-induced expression of Zif-268 and the GluN2B sites, two molecular markers of the labilization/reconsolidation process. In summary, prior stress limited both the occurrence of the reactivation-induced destabilization and restabilization. Further results showed that MDZ administered intra-BLA before stress prevented the induction of resistance to the interfering effect of drugs on reconsolidation, whereas the blockade of amygdalar GABA-A receptors by BIC before memory encoding induced resistance to interference. Overall, these results suggest that GABAergic signaling in the BLA, at the moment of memory encoding is determinant for the fate of the fear memory trace.



Impact of hypothalamic astroglial hemichannels on food intake and energy homeostasis.

Martin C[1], [1]Biologie Fonctionnelle et Adaptative Université Paris Diderot.

Neurons are embedded in a network of astrocytes, non-excitable glial cells that occupy a central position as they are inserted between neurons and blood vessels and are able to modulate neuronal activity. Although many studies gathered information on astrocyte physiology in vitro, few data have been collected in vivo. A key center for food intake and energy balance regulation in the brain is the hypothalamus. Hypothalamic astrocytes reside close to the circumventricular organs, such as median eminence, and express most receptors for energy-related signals (e.g., leptin, insulin). Therefore, they are exquisitely positioned to participate in the integration of circulating signal of hunger and satiety. Indeed, they show signs of inflammation in diet-induced obesity (Thaler et al., 2012). It has recently been shown that astrocytes, like neurons, are able to respond to circulating nutrients and hormones and thus participate with neurons in the regulation of body weight, energy expenditure and systemic metabolism (Garcia-Caceres et al., 2016).

Our objective is to examine the role of astrocyte in brain networks focusing on hemichannel-mediated gliotransmission. This way of communication between astrocytes and neurons has been shown to be necessary for NMDA receptor mediated synaptic plasticity (Henneberger et al., 2010) and fear memory consolidation (Stehberg et al., 2012). We infused an hemichannel blocker (TAT-L2) in awake behaving mice via a bilateral guide cannula implanted in the paraventricular nucleus (PVN) of the hypothalamus. We examined blood glucose, food intake and energy metabolism. The first results show that astrocytes manipulation by blocking hemichannels impact feeding behavior and metabolism.

The role of the Insular cortex in anxiety, and mediating the effects of stress hormones in anxiety.

Stehberg J[1], [1]Laboratorio de Neurobiología, Centro de Investigaciones Biomédicas, Universidad Andrés Bello.

The insular cortex, or just insula in humans, is a complex cortical area, buried deep within the temporal lobe. Imaging studies in humans show insular increase in activity in patients with various anxiety disorders, which appear to be proportional to their level of anxiety, and decreases with effective anxiolytic treatment. Notwithstanding, studies which evaluate systematically the role of the insula in anxiety using animal models are lacking. Our results show via intra-insular pharmacological manipulations, that the insula is involved in anxiety, with different regions having anxiolytic and anxiogenic roles. The insula also appears to mediate the anxiogenic effects of circulating adrenaline and arousal, via adrenergic activity at the insula, possibly affecting the activity of slow firing interneurons. Furthermore, the insula appears to mediate the effects of glucocorticoids (GCs) in anxiety. Interestingly, the microinjection of GCs into the insula can induce both anxiolytic and anxiogenic effects, depending on the dose injected, and in the level of the stress of the animal previous to the GC microinjection. The anxiogenic effects of GCs at the insula may be associated to a membrane-dependent signaling pathway, while their anxiolytic effects may be mediated by mineralocorticoid receptors. This role for the insula in anxiety is also observed in humans, as the stimulation of the insula using a special coil of deep Transcranial magnetic stimulation induces fast and strong decreases in anxiety in volunteers suffering from work stress. Our results show that the insula is critical for the regulation of anxiety levels, and for mediating the effects of stress hormones in anxiety.

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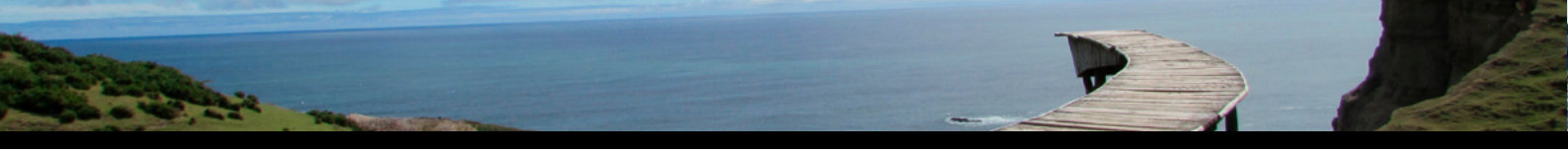


CELLULAR AND MOLECULAR APPROACHES TO UNDERSTAND NERVOUS SYSTEM FUNCTIONS

Chair: Christian González-Billault

Development, Evolution and Function of commissural systems.

Chedotal A[1], [1]Institut de la Vision Universite Pierre et Marie Curie.

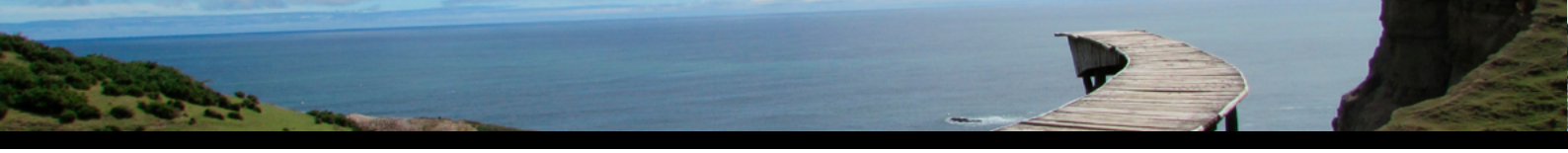
In most animal species including humans, commissural axons connect neurons on the left and right side of the nervous system. This communication between the two sides of the brain and spinal cord is necessary for a series of complex function, including binocular vision, coordinated locomotor movements, and sound direction localization. In humans, the balance of commissural and non-commissural axons is essential to CNS physiology and to the integration of sensory stimuli/inputs. Abnormal axon midline crossing during development causes a whole range of neurological disorders ranging from congenital mirror movements, horizontal gaze palsy, scoliosis or binocular vision deficits. Partial or complete corpus callosum agenesis are some of the most common brain malformations in children with variable neurological outcomes. I will discuss some of the genetic mechanisms underlying anomalies of midline crossing and present some of our most recent work that challenges the existing dogmas and suggest that commissural axon guidance mechanisms are more diverse across species than previously appreciated. To facilitate the analysis of the organization and evolution of commissural systems in vertebrates, we have developed a new imaging method which combines whole-mount immunostaining or commissural axon tracing, tissue clearing with organic solvents and 3D light-sheet microscopy. I will also present new applications of this method in the field of neuroscience.

Pre- and postsynaptic functions of the microtubule associated protein 1B.

Gonzalez-Billault C[1], [1]Biology, Sciences, Universidad de Chile.

Microtubule-associated protein 1B (MAP1B) is predominantly expressed during the early stages of neuronal development where it plays a pivotal role in neurite growth, and axon development. Later, its expression is down-regulated except in brain areas showing high plasticity that includes the hippocampus. We hypothesized that MAP1B can be found at pre- and post-synaptic compartments. Using Y2H approach we retrieved MAP1B interacting partners from adult brain. Here we described the interaction between MAP1B and Ube2L3 an E2-conjugase enzyme from the ubiquitin proteasome system (UPS) is important to regulate protein levels of the voltage gate calcium channel Cav2.2 at the presynaptic site. We evaluated changes in the pattern of pre-and post-synaptic puncta in neurons lacking MAP1B. An increase of “orphan” presynaptic puncta (lacking their postsynaptic counterparts) is verified in MAP1B KO neurons. Finally, ultrastructural studies revealed a decreased in both the number of synaptic contacts and the content of neurotransmitter vesicles in MAP1B KO neurons. On the other hand, we detected the presence of MAP1B in dendritic spines and synaptosomes fractions of wild type mice. Neurons derived from MAP1B-deficient mice showed decreased density of mature dendritic spines paralleled by increased immature filopodia-lile protrusions. In addition, MAP1B deficient neurons display a significant decrease of synaptic currents due to AMPA receptors. Altogether these results suggest that MAP1B may serve differential functions at the pre- and post-synaptic compartments, linking MAP1B functions with neurotransmission.

FONDECYT 1140325 and FONDAP 15150012



“The Integrated Stress Response in Neurodegeneration”.

Osorio L[1], Muñoz N[1], Jerez C[1], **Matus S[1]**, [1]Cell Biology Fundacion Ciencia & Vida.

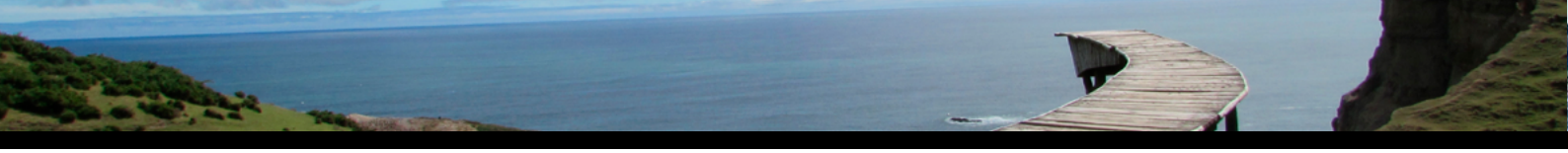
During life, every organism is exposed to diverse stress stimuli. The adaptation capacity is critical to maintain the homeostasis and ensure survival. Under stress conditions, eukaryotic cells activate a common adaptive pathway, termed the integrated stress response (ISR), to restore cellular homeostasis. We are focus in understand the contribution of this signaling pathway, which is driven by four kinases that phosphorylates the eukaryotic translation initiation factor 2 alpha (eIF2a), to neurodegenerative process and aging. Using *in vivo* and *in vitro* models, we study the consequences of targeting ISR components in pathological conditions, in particular, amyotrophic lateral sclerosis (ALS) to open new therapeutic strategies for treating neurodegenerative diseases.

This work was directly funded by FONDECYT 1161284, FONDAP program 15150012, Millennium Institute P09-015-F and PFB-16

iPSC-based disease modeling and therapy.

Zeng X[1], [1]California Buck Institute for Research on Aging.

I have focused my research on developing a model system to study human neural development using human pluripotent stem cells including embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC). Over the past decade we have demonstrated success by utilizing this system to study disease mechanisms of neurodegenerative disorders with a focus on Parkinson's disease (PD) and Alzheimer's disease (AD), and to identify key developmental regulators of the process of neural development, as well as to develop cell- and small moleculebased therapeutic targets for neurodegenerative disorders. I will discuss our recent advances in utilizing this approach for modeling PD and AD and cell replacement therapy.



FROM THE RETINA TO THE CNS: ROLE OF NEUROMODULATORY SYSTEMS

Chair: Oliver Schmachtenberg.

Tell me how you live, and I will tell you how your retina will be.

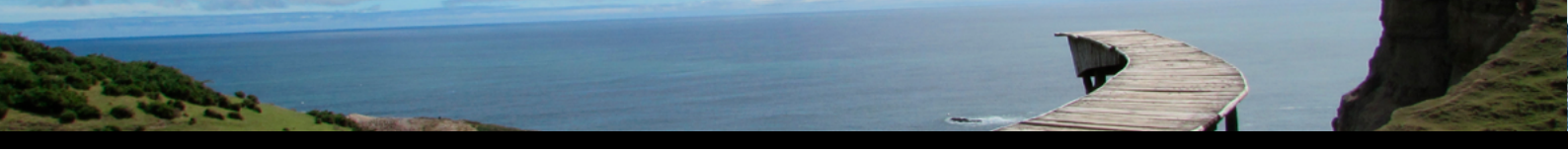
Rosenstein R[1], [1]Human Biochemistry, School of Medicine, University of Buenos Aires.

Environmental enrichment, a manipulation in which animals are exposed to complex conditions through adaptations in the physical and social environment, is composed by nesting materials, running wheels for voluntary exercise, tunnels, ladders, and toys with different textures, colors, shapes, and sizes, which are changed of place to stimulate novelty, and provide continuous opportunity for exploration and stimulating sensory, cognitive, and physical activity. Exposure to enriched environment (EE) induces changes in neuron morphology and synaptogenesis during development, adulthood and aging, supporting that brain neural plasticity in response to environmental experiences lasts throughout the lifespan. Retinal development is also responsive to EE. In contrast, the adult retina and optic nerve have long been considered “less plastic” than the brain cortex or hippocampus, the canonical sites of experience-dependent plasticity. I will show results demonstrating that EE housing, likely through the stimulation of the visual processing, protects retinal function and histology from acute ischemia/reperfusion injury, excitotoxicity and diabetic damage in adult rats. These data could open new perspectives for retinal diseases treatment and, if confirmed in the human condition, reinforce the holistic idea that lifestyles, directly having an impact on the central nervous system homeostasis, prevents and reduces the progression of visual diseases.

Physiological and pathological NO signaling in the retina.

Schmachtenberg O[1], Vielma A[1], [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaiso.

Nitric oxide (NO) is a freely diffusible signaling molecule involved in physiological and pathological processes in the retina. It exerts specific local actions depending on the cell and receptor type. In the outer retina, NO signaling via S-nitrosylation in photoreceptors was shown to enhance retinal sensitivity and be involved in dark adaptation. In the inner retina, NO is produced by subsets of amacrine and bipolar cells. Here, NO signaling via cGMP differentially modulates signal processing in the ON and OFF pathways. Light-dependent gap junction coupling and blood flow through retinal vessels are also mediated by NO. Under diabetic conditions, alterations of vascular NO synthesis, excessive NO synthesis by inducible NOS due to cellular inflammation and consequent free radical accumulation affect retinal signal processing early on and may lead to cellular injury and functional impairment.



Neuromodulation of synaptic transmission in the retina.

Chavez A[1], [1]Centro Interdisciplinario de Neurociencias, Instituto de Neurociencias, Facultad de Ciencias, Universidad de Valparaiso.

Changes in the synaptic efficacy of excitatory and inhibitory transmission can perturb the delicate balance of excitation and inhibition required for normal central nervous system function. Synaptic changes can occur by the action of several neuromodulatory systems, including dopamine, serotonin (5-HT) and endocannabinoids (eCB). The first step of vision, the transduction and encoding of physical light stimulus into a neuronal signals, occurs in the retina. In this neuronal circuitry, the eCB system which comprise two receptors, known as the cannabinoid type 1 and type 2 receptors (CB1R and CB2R), the endogenous ligands, the synthetic and degradative enzymes, and the transporters that regulate eCB levels are well positioned into the synaptic layers to affect synaptic efficacy in several species, including humans. However, how and under which circumstances eCBs and their receptors modulate retinal synaptic function remains unknown. It is also unclear how eCB signaling contributes to specific processes at the level of retinal circuitry to regulate visual responses. Here we will discuss *in vivo* and *in vitro* electrophysiological data suggesting that the eCB signaling and in particular, CB1R activation likely regulate both GABAergic and glycinergic synaptic efficacy onto bipolar and ganglion cells in the inner retina and thus might regulate the temporal properties of the visual response. By unmasking the role of this neuromodulatory system in the retinal circuitry, we expect to provide new insights into the cellular and molecular mechanisms underlying retinal function.

Supported by FONDECYT (1151091), Nucleo Milenio NuMIND (NC130011) and the Millenniun Institute CINV (P09-022F)
FONDECYT 1120513, 1171228 and the Millennium Institute CINV.

Selective NMDAR-dependent regulation of dendritic inhibition in the cortex.

Chiu, Ch. CINV-Max Planck Tandem Group Leader, Universidad de Valparaiso.

Although it is known that strong glutamatergic activity can modify the strength of GABAergic synaptic transmission, the underlying cellular mechanisms are not well understood. This question is complicated by the great diversity of GABAergic interneurons, which may exhibit heterogeneous rules for altering their synaptic weights. Here, we utilize cell type-specific optogenetic stimulation in mouse prefrontal cortical slices to study the capacity of GABAergic synapses formed by different interneuron subtypes to exhibit activity-dependent plasticity. We find that brief activation of NMDA-type glutamate receptors selectively increases inhibition mediated by somatostatin-expressing interneurons but not by interneurons expressing parvalbumin or vasoactive intestinal peptide. We investigate the molecular differences between subpopulations of GABAergic synapses onto superficial pyramidal cells that confer this differential capacity for glutamatergic regulation in the neocortex.

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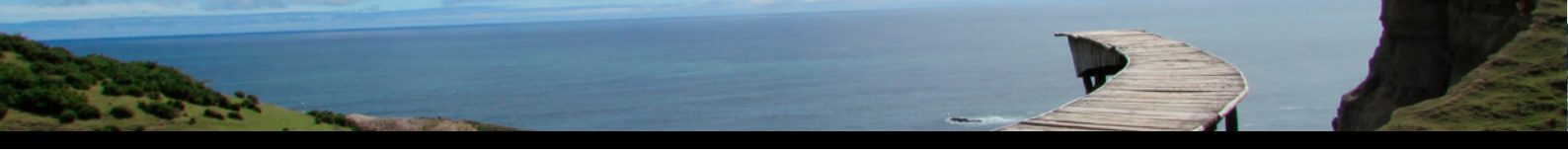


YOUNG NEUROSCIENTIST SYMPOSIUM

CHAIRS: Jorge Vera-Juan Bacigalupo.

Selective RVLM C1 neuron ablation improves cardiac sympathetic control in heart failure rats.

Andrade D[1], Toledo C[2], Lucero C[2], Díaz H[2], Arce-Alvarez A[2], Del Rio R[1], [1]Lab. Cardiorespiratory Control Pontificia Universidad Católica de Chile.[2]Center of Biomedical Research Universidad Autónoma de Chile.

Preserved ejection fraction heart failure (HFpEF) is characterized by enhanced sympathetic drive. Cathecholaminergic pre-sympathetic neurons from rostral ventrolateral medulla (C1 RVLM neurons) has been shown to be hyperactive which may be associated with increases in cardiac sympathoexcitation and progression of HFpEF. However, there is no causal link between RVLM C1 neurons and the enhanced sympathetic drive observed in HFpEF. Therefore, we hypothesized that selective ablation of RVLM C1 neurons will reduce cardiac sympathetic drive and improve cardiac function in HFpEF rats. Male Sprague-Dawley rats (~250g) underwent volume overload to induce HF. Selective ablation of C1 RVLM neurons was performed by bilateral injections of an anti-dopamine-beta hydroxylase (DβH)–saporin (SAP) toxin (7.5 ng/150nl) into the RVLM (AP= 12.36; ML= 2.3; and DV= 8.5mm from bregma). The degree of HF was estimated by echocardiography. Cardiac function was assessed by intraventricular pressure-volume loops. Autonomic control was assessed by propranolol (1 mg/kg i.p.) and atropine (1 mg/kg i.p.) and time-varying analysis. The incidence of cardiac arrhythmias was also scored. DβH–SAP toxin injections results in ~50% elimination of C1 neurons. We found that HF rats treated with DβH–SAP toxin ($p<0.05$, HF+Veh vs. HF+DβH-SAP, respectively) display: improve the fractional shortening (45.1±1.3 vs. 51.1±4.8%) decrease cardiac sympathetic drive (-98.0±12.1 vs. -52.2±7.9ΔHR), improve diastolic (0.009±0.001 vs. 0.004±0.001 mmHg/µl) and systolic cardiac function (0.2±0.01 vs. 0.5±0.1mmHg/µl), and decrease arrhythmogenesis (91.0±20.5 vs. 48.3±14.6events/hour). In addition, we found that acute central chemoreflex (CC) activation have no longer effect on autonomic control in HF rats that underwent DβH–SAP toxin treatment (Δ97.3±17.3 vs. Δ45.7±16.2% A.U.). We showed that RVLM C1 neurons play a critical role on the progression of autonomic imbalance, arrhythmogenesis and cardiac deterioration in HFpEF. In addition, we found that sympathoexcitation following acute CC activation is mediated by RVLM C1neurons. Together, our results suggest that central chemoreceptor neurons and RVLM C1 neurons may interact to induce respiratory-sympathetic coupling in HFpEF.

(Sponsored by Supported FONDECYT #1140275).

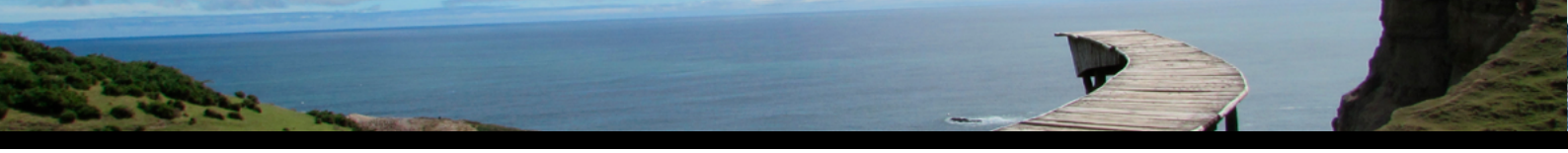
Wnt5a stabilizes AMPA receptors in hippocampal neurons, causing neuroprotection against Aβ oligomers.

Montecinos-Oliva C[2,1], Choquet D[1], Inestrosa N[2], [1]Laboratory of Dynamic of the Synapse, Interdisciplinary Institute for Neuroscience (IINS), Université de Bordeaux.[2]Department of Cellular and Molecular Biology, Faculty of Biological Sciences, Pontificia Universidad Católica de Chile.

AMPA receptors are responsible for most of the fast excitatory transmission in hippocampal neurons. They are among the most dynamic receptors and this accounts for the fine-tunning of synaptic response. Wnt5a is a ligand that, acting through the non-canonical pathway, has been linked to several roles in mature hippocampal neurons; dendritic spine density and maintenance of dendritic branching, increase number of PSD95 clusters and glutamatergic currents. This leads to suggest a key role of Wnt5a in the architecture of excitatory synapses *in-vitro* and *in-vivo*. Glutamatergic synapses are affected by $A\beta_{42}$ oligomers causing AMPA receptor endocytosis, diminished dendritic spine density and causing overall failures in synaptic excitatory transmission. On the contrary, it has been shown that Wnt5a protects neurons against $A\beta_{42}$ oligomers synaptotoxicity. We studied the mechanism through which Wnt5a protects from $A\beta_{42}$ oligomers. By using super-resolution microscopy in live and fixed hippocampal neurons (14-16 DIV), we found that Wnt5a modulates the dynamic and localization of AMPA receptors. Specifically, Wnt5a immobilizes AMPA receptors in synaptic and extrasynaptic sites. This correlates with an increase in co-localization and interaction between GluA2 and PSD95 in dendritic spines, as measured by immunofluorescence and co-immunoprecipitation. Interestingly, pre-incubation of Wnt5a prevents toxicity of $A\beta_{42}$ oligomers and maintains basal AMPA receptors dynamics.

Our data suggests that Wnt5a acts rapidly, as a regulator of synaptic architecture, and prevents and compensates $A\beta_{42}$ oligomers effects by immobilizing AMPA receptors in synaptic sites.

Work supported by the fundings of PFB12/2007 to NCI and a Claude Gay scholarship from the French Embassy as a CONICYT pre-doctoral fellowship to CMO.



The axonal trans-Golgi network controls membrane availability of cold-sensitive TRPM8 ion channels in peripheral nerve endings.

Cornejo V H[1], Carolina G[1], Matias C[2], Maria P[2], Rodolfo M[2], Andrés C[1], [1]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.[2]Departamento de Biología, Facultad de Química y Biología, Universidad de Santiago de Chile.

Cold thermoreceptor neurons (CTNs) are the primary sensors detecting cold environmental temperatures, and the thermo-TRP channel TRPM8 is the main molecular entity responsible for cold transduction in these neurons. The fine-tuning of cold sensitivity is determined by the activity and availability of this channel at the plasma membrane of peripheral nerve endings. However, the contributions of anterograde trafficking and the secretory pathway to the regulation of membrane channel availability in axons remain for the most part unknown.

To begin addressing this question, we disrupted endoplasmic reticulum to Golgi trafficking withGolgicide A (GCA), a pharmacological inhibitor of the ARF1-exchange factor GBF1, or via a dominant negative GBF1 mutant, E794K. Co-localization of TRPM8 channels with the *trans*-Golgi network (TGN) and endosomal components were analyzed in HEK293 cells and *ex vivo* after electroporation of dorsal root ganglia (DRG) using confocal microscopy. In addition, nerve terminal impulses (NTI) of corneal CTNs were recorded using a mouse eye preparation.

In HEK293 cells, GCA as well as the GBF1 E794K dominant negative increased the co-distribution of TRPM8 with TGN38, whereas they decreased the co-localization with endosomal components, such as LAMP1. More importantly, TRPM8 robustly co-distributed with TGN38 and pGolt, a marker of Golgi satellites, in axons of electroporated DRG neurons, and after treatment of sciatic nerve explants with GCA, accumulation of TRPM8 in TGN satellite was observed. Accordingly, in isolated nerve endings of CTNs in the mouse cornea, basal NTI activity, cooling threshold, maximal cold- and menthol-induced responses of CTNs were markedly, rapidly and reversibly reduced by GBF1 inhibition.

Our results support a novel, autonomous and GBF1-dependent trafficking mechanism to control the availability of TRPM8 channels in nerve endings of CTNs.

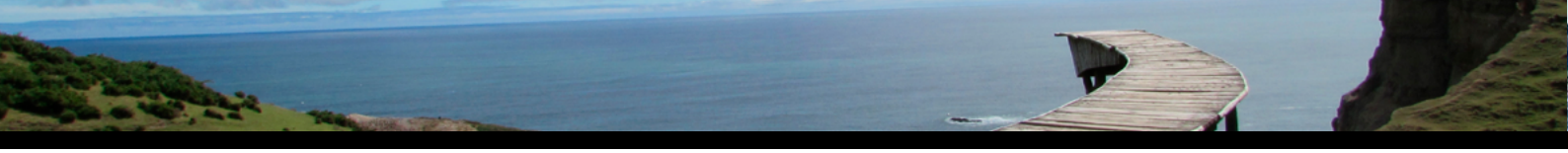
(Sponsored by FONDECYT #3160725 (VH), #3160666 (CG), #1161733 (RM, MP), #1170307 (AC) And ICM P09-015-F).

Axonal degeneration is regulated by lipid metabolism in Drosophila.

Sanhueza M[2,1], Court F[2,1], [1] Geroscience Center for Brain Health and Metabolism FONDAP.[2]Center for Integrative Biology, Faculty of Sciences, Universidad Mayor.

Axonal degeneration is an evolutionary conserved process that occurs as a consequence of mechanical damage, aging and neurodegenerative diseases. In our group we aim to understand the molecular basis of selective destruction of axons, a mechanism that has not been yet completely elucidated. To unveil novel pathways linked to it, we performed a comparative proteomic study and analyzed differences between WT mice and models of delayed axonal degeneration. *In silico*, this data highlighted candidate proteins, which are likely to be involved in the degenerative process. To assess *in vivo* their ability to modulate neuronal stability, we turned to *Drosophila* and used an RNAi-based approach to genetically modulate the expression of these proteins in a model of axonal injury in the fly wing. Among the validated hits, we found proteins involved in lipid metabolism; more specifically, components of the β-oxidation pathway. One of these hits, a previously uncharacterized *Drosophila* gene, is able to significantly delay the axonal degeneration process when is down-regulated, phenotype confirmed with other genes from this pathway. Therefore, we are currently pinpointing the role of this novel gene in axonal stability, using models of chemical injury, reduction of caloric intake, and analyzing the effect at an organism level using motor performance assay and viability as read-outs. Furthermore, we are trying to understand potential alterations of these phenotypes with aging, and correlate the progression of axonal degeneration with the fly lifespan, to ultimately clarify the role of lipid metabolism in neurodegenerative diseases and aging.

This work was supported by a FONDECYT Postdoctoral fellowship Nº 3170577 (MS) and Geroscience Center for Brain Health and Metabolism (FONDAP-15150012).



ORAL COMUNICATIONS I

Bumetanide enhances the pharmacological effect of phenobarbital, on electroencephalographic and behavioral level, in an animal model of temporal lobe epilepsy.

Mantellero C[1,2], Amaro J[2], Borquez M[2], Ocampo A[2], Valdes J[2], Rojas P[1], [1]Biología, Química y Biología, Universidad de Santiago de Chile.[2] Fisiología y Biofísica, Medicina, Universidad de Chile.

Temporal lobe epilepsy (TLE) is the most common type of refractory epilepsy to drug treatment. In epileptic conditions neurons have an increased excitability due in part to a change in GABA from inhibitory to excitatory. This is due to a change in the direction of electrochemical gradient of Chloride, whose concentration is maintained by KCC2 and NKCC1. Models of acute seizures have shown that NKCC1 is highly expressed explaining the high intracellular chloride. In a model of neonatal seizures, Bumetanide, an specific NKCC1 inhibitor, in combination with Phenobarbital shows a significant improvement in seizure control.

The aim of this work is to study in an animal model of TLE the refractoriness to a GABAA agonist Phenobarbital, and if in combination therapy with Bumetanide enhances its pharmacological effect decreasing the number of seizures, and a behavioral level reversing cognitive impairment.

Male 7 weeks old Sprague Dawley rats were administrated with Pilocarpine to induce Status Epilepticus (SE), and after two weeks they have spontaneous seizures. Animals were administrated with Phenobarbitalto assess the refractoriness of this treatment. After 2 weeks the rats that do not respond to pharmacological treatment with phenobarbital are separated into 3 groups, 1 group continues the treatment with Phenobarbital, other group with Bumetanide , and other with both; bumetanide and Phenobarbital, during two weeks.

Electroencephalogram (EEG) recordings were performed before and after the treatment with Phenobarbital and after the last treatment in each group, to quantify alterations in epileptiform activity. The results show all pharmacological treatments decreases the number of seizures.

To determine the effect of these treatments on cognitive impairment, object recognition test were performed, to evaluate episodic memory. Open field was conducted to evaluate anxiety, and last, social interaction was studied to evaluated sign that suggesting depression. The results show that the combination therapy improves behavioral parameters.

These findings support the idea that NKCC1 participates in refractorines to drug treatment in TLE FONDECYT n° 1130904.

Relative clause concordance and the syntax complexity in spanish: An ERP study.

Alonso-Sánchez M F[1], Alfaro-Faccio P[2], Zepeda-Rivera L[1], Von Chrismar D[2], [1]Escuela de Fonoaudiolgía, Salud, Universidad Santo Tomás.[2]Instituto de literatura y ciencias del lenguaje Pontificia Universidad Católica de Valparaíso.

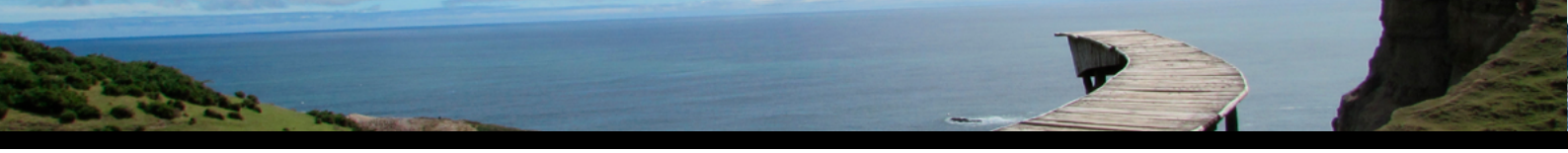
Human language is structurally organized from lower ranked units which when combined generate upper ranked units through a complex system of rules. This system of rules indicates not only the elements position, but also the relationship among them, from the phonological to the inter-clause level. Although these rules are not language independent —they are intimately related with the type of language— they as a whole form what Hauser, Chomsky, and Fitch (2002) denominate *faculty of language-narrow,* and place these rules in the center of the neurocognitive system which allows human language. However, the violation of these rules generates ungrammaticalities which are not only qualitatively detected by the speaker, but also they state an electrophysiological correlative. In fact, it has been extensively observed in the English language an early negative component (ELAN) close to the 200ms in morphological violations, and positivity at 600ms which is associated with the syntactic integration, an evident complex syntactic processing temporal marker, which involves the dorsal pathway starting from the superior temporal gyrus to the 44TH Brodmann area (Friederici, 2012). However, in Spanish, this component has been difficult to induce, probably due to the language's own features.

Under this context, the aim of the study was to establish an experimental paradigm which permits to distinguish between syntactic ungrammaticalities generated among clause components within the same hierarchy and clause components of different hierarchies. The electrophysiological correlative of the experimental paradigm should be highly differentiable.

Thereby, 240 sentences were introduced, word per word, for 450ms with a 200ms of interstimulus interval with a final yes or no question. They were organized in three different types: (1) copulative with endotaxial relative without concordance between subject and predicate, (2) copulative with endotaxial relative without concordance between subject and predicate as well as ambiguity in the attribute referent, and (3) well-formed sentences.

The ERPs were recorded with a 64 channel Biosemi EEG. A time window between 550 and 750ms post onset was analyzed in its amplitude with Analyzer Brain Vision, and the artefacts were removed with ICA. The results shown that the sentences whose ungrammaticalities produce gender and number concordance between linking verb + attribute and the relative sentence recall a higher amplitude in the P600 component, therefore, they distinguish an early morphological processing from a late and more complex processing.

FONDECYT 11160212.



Effects of age hearing loss on sub-cortical regions.

Belkhiria C[1], Delano P[2], Garrido C[3], Delgado C[3], [1] Departamento de Neurociencia, Facultad de Medicina , Universidad de Chile.[2]Departamento Otorrinolaringología, Facultad de Medicina, Universidad de Chile.[3]Departamento Neurología , Facultad de Medicina, Universidad de Chile. (Sponsored by This Project Is Funded By PIA-CONICYT Program: Anillo De Investigacion En Ciencia ACT1403).

Background: Age-related hearing loss (Presbycusis) is the third most common chronic health condition affecting adults over the age of 60. Several studies indicated that hearing impairment is the major modifiable a risk factor for dementia and Alzheimer disease which are the greatest global challenge for health and social care in the 21st century [1]. Although, the focus of research on age-related hearing impairment has expanded toward changes in the cerebral system [2-3], the mechanisms underlying Presbycusis and structural brain changes and cognitive decline remain unclear. The purpose of this study is to understand the neuroanatomical correlations between Presbycusis and the brain volume structure.

Methodology: As a part of the ANDES cohort, we have recruited 20 subjects > 65 years that were divided into Control (CG) mean age 71.8 ± 4 years and Presbycusis (PG) mean age 77.7 ± 3.9 years groups based on their audiometric thresholds (audiometric thresholds (> 20 and < dB in the best hearing ear). Comparison of Brain volume was done using magnetic resonance imaging voxel basedmorphometry.

Results: PG had larger volume of the cerebrospinal fluid, and showed bilateral significant ($P<0.05$) regional atrophy in frontal areas (BA 10 and 47), Superior temporal gyrus (B22), Inferior (BA 40) and Superior (BA7) parietal lobules in comparison with the CG. PG showed higher regional volume of left putamen and left caudate nucleus than the CG.
Discussion: The main novelty of this study refers to the higher volume of the left striatum in PG. Left caudate nucleos is related with executive functions and language functions and semantic processing. Larger caudate volumes were reported in early onset schizophrenia (EOS) [4], and were correlated with poorer verbal learning performance [5]. Therefore the caudate enlargement may be related with poor verbal comprehension or poor verbal memory in presbycusis patients, and may may reflect a “compensatory” structural plasticity which could be due to remodelling of neuronal processes.

Conclusion: This study will be extended through a larger number of participants (150) in order to explorethe mechanisms that related peripheral and central component of Presbycusis to cognitive impairment and brain volume structure.

This project is funded by PIA-CONICYT program: Anillo de Investigacion en Ciencia ACT1403.

Lombard effect and vocal hyperfunction: Biomechanical, acoustic and cortical changes in subjects with muscle tension dysphonia and normal voice.

Castro C[1], Prado P[2], Marfull D[1], Testart A[3], Weinstein A[4], Zepeda L[2], Zañartu M[2], [1]Fonoaudiología, Medicina, Universidad de Valparaíso.[2]Ingeniería Electrónica, Ingenieria Electrónica, Universidad Técnica Federico Santa María.[3]Fonoaudiología, Medicina, Universidad de Playa Ancha de Ciencias de La Educación.[4]Ingenieria Biomédica, Ingenieria, Universidad de Valparaíso.

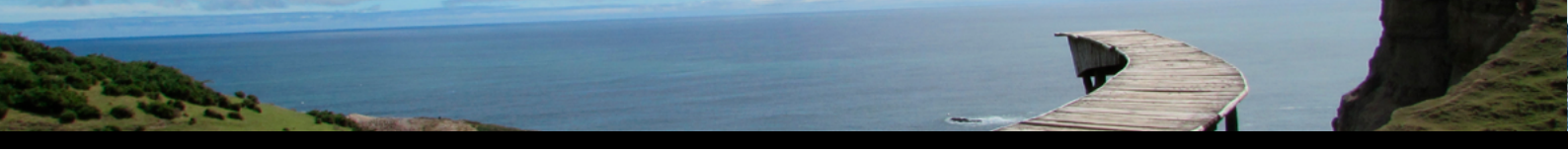
Background: One of the most common yet least understood hyperfunctional voice disorders is muscle tension dysphonia (MTD). MTD is described as poorly regulated activity of the intrinsic and extrinsic laryngeal muscles leading to high levels of stiffness and tension in the vocal folds.
The etiology of MTD remains unclear, but most MTD patients report having to produce an overly increased vocal effort under noisy environments. This an unconscious response, called the Lombard effect, where subjects increase the intensity and frequency.
We hypothesize that MTD patients may be more sensitive to the lombard effect, due to a possible dysfunction in the integration of auditory feedback.

Aims: To describe the acoustic, aerodynamic, biomechanical and neuronal cortical aspects of the Lombard effect in subjects with MTD and normal controls.

Methods:*Experiment 1: Physical component*
A group of 8 subjects with normal voice and 8 subjects with MTD was recruited. Subjects were asked to utter a series of vowels presented in images through a monitor. The images were presented during 5 seconds with a 5-second pause between stimuli. A total of 40 stimuli was distributed in 8 series of 5 images.
The complete sequence was performed under 3 conditions:
1. Baseline
2. In noise (speech noise at 75 dB HL)
3. In quiet after a 5-minute pause
For each condition, vocal function was assessed by high-speed videoendoscopy (VHS), aerodynamic measurements, neck surface accelerometer and acoustic measurements.

Experiment 2: Neurophysiological component
The cortical activity of 3 normal subjects was recorded using a 64-channel electroencephalograph (EEG). Each subject was asked to utter 16 series of 5 syllables with an 8-second pause between series and under 3 conditions described below. Acoustic and neck surface accelerometers signals were also obtained. To detect the events in the EEG recording, an onset detector is used to synchronize the events.
1. Baseline
2. In noise (speech noise at 85 dB HL)
3. In quiet after a 5-minute pause

Preliminary results: Preliminary results suggested that subjects with MTD might be more sensitive to the Lombard effect, since they generate a greater variation of SPL and have greater difficulties to return to baseline conditions when the noise is removed.
Regarding the biomechanical changes, all subjects presented an increase of the posterior closure during lombard effect, but the MTD patients exhibited greater vibratory asymmetry. Also in the aerodynamic measures this group show more changes in MFDR, RFE and H1-H2.
The EEG analysis is still underway and no results are reported at this time
This Work was supported by the Advanced Center for Electrical Engineering, AC3E, Basal Project FB0008, CONICYT.



Cortical and auditory efferent dynamics during selective attention to visual stimuli.

Dragicevic C[1], Navarrete M[2], Marcenaro B[3], Délano P[1,4], [1]Departamento de Neurociencia, Medicina, Universidad De Chile.[2]Programa de Magister en Ciencias Biológicas, mención Neurociencias, Ciencias, Universidad de Valparaíso.[3]Centro Interdisciplinario de Neurociencias, Medicina, Pontificia Universidad Católica de Chile.[4]Departamento de Otorrinolaringología, Medicina, Hospital Clínico de la Universidad de Chile.

In this project we study human cortico-cochlear modulations under selective attention to visual stimuli. Visual and auditory tasks were performed in alternating fashion by 14 subjects whose electroencephalogram and otoacoustic emmisions were recorded continuously and simultaneously. For simplicity, only the visual task was analyzed. By considering the auditory efferent system as part of the attentional networks that initiate and sustain modulations of cochlear sensibility, we transformed the raw microphone recording coming form the ear into a virtual channel containing only the amplitude of otoacoustic emissions (following two different approaches that yielded congruent results), and we treated it just like every other EEG channel, all subjected to the same analysis. Though we hypothesized that drops in cortical alpha waves during selective visual attention would serve as a mechanism that preceded the onset of a cochlear gain reduction, results showed that in our experiment, the visual task did not cause a net change in average otoacoustic emissions, from which it follows that average cochlear amplification remained essentially flat before and after visual attention. However, analysis in the frequency domain revealed novel low frequency (2-15 Hz) oscillations of cochlear amplification induced only during the visual attentional period, resembling EEG oscillatory activity in the same period. These oscillations were explored further through measures such as phase-locking to the attentional cue and cross-channel synchrony between otoacoustic emissions channel and every other EEG channel. In addition, we also incorporated the otoacoustic emissions channel into topographical projection maps of electroencephalographic activity mainly to illustrate the capabilities of our method. We end by speculating a yet to be demonstrated significant synchrony between otoacoustic emissions and electroencephalographic channels, as one way for establishing the functional coupling between cortex and the cochlea as demanded by attention.

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Corollary discharge associated to non-speech sounds is impaired in schizophrenia.

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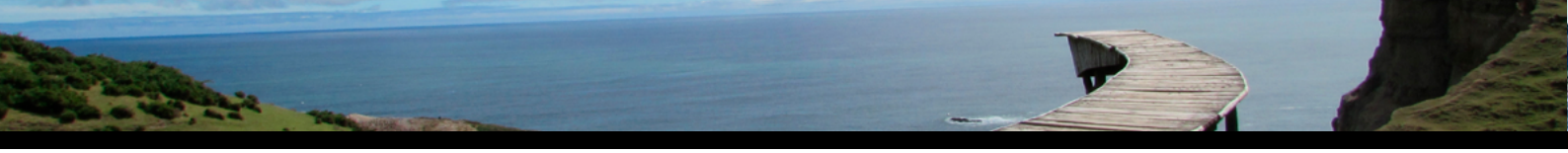
The corollary discharge (CD) is defined as the attenuation of a cortical response elicited by the sensory feedback of one's own actions. The CD associated with speech is impaired in schizophrenic patients and has been suggested as a possible mechanism underling auditory hallucinations. However, instead of been restricted to speech, this dysfunction might be part of a more general mechanism in which timing information of self-produced acoustic stimuli is altered. We tested this hypothesis by analyzing the CD associated to familiar non-speech sounds in schizophrenic patients (N=15) and age-matched healthy volunteers (N=19). In a training session preceding the electrophysiological study, beeps were presented binaurally to every participant at a constant rate of 0.556 Hz and the subjects were asked to learn pace of the acoustic stimuli. Following, participants were requested to reproduce the pace of the beep presentation by pressing a button (button-press-for-sound task). They received a visual feedback of their performance to reinforce the familiarity with the beep pattern. Event-related-potentials were recorded from 64 scalp-electrodes while (i) participants underwent the aforementioned button-press-for-sound task, without any feedback of their performance, (ii) they listened a playback of the sound pattern generated during the behavioral task, and (iii) a control motor task, in which they pressed at the same pace but without beep being generated. The subtraction between conditions (i) and (iii) was defined as active listening and the corollary discharge was defined as the amplitude difference of the N1-P2 complex between the passive and active listening conditions. Corollary discharge was evident in healthy control participants but was attenuated in schizophrenic patients. Furthermore, topography maps representing the scalp distribution of the N1-P2 complex significantly varied between groups. Main differences were the increased global field power observed in the temporal lobe and the shifted parietal activation of patients during the active listening condition as compared to those obtained in healthy volunteers. Cortical source localization analyses suggest an altered frontotemporal activation patterns in schizophrenic patients which may be anchored in a different connectivity pattern between these cortical regions.

This work was supported by CONICYT-Basal Project FB0008.



Network complexity of coherence patterns correlates with mean subjects´ reaction time.

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During the performance of a cognitive task, brain areas interact forming a transient network of brain activity. So far, the relation between activity network and cognition is poorly understood. Here, we use a reaction time (RT) task to show that the time course of the clustering coefficient, a measure of network connectivity, correlates with subject's mean RT. We proceeded by recording electroencephalography, computing the coherence index, and defining a network from the multigraph of coherence. Results show that the time of maximum clustering coefficient, computed from beta frequency coherence networks, significantly correlates with subjects' RT. We found no significant correlation between subject's RT and the peak of its event related potential, and a weak relation between the mean coherence in beta band and subjects' RT. Moreover, using a linear approximation, we estimated subjects mean RT based on the time evolution of the clustering coefficient. At the network level, the increment in clustering coefficient occurred on the parieto-occipital electrodes, our analyses suggest that it was related to an increment of the connectivity at right frontal electrodes. These results show that clustering coefficient correlates with changes in brains state, and can be used to estimate subject's performance, something that is not possible from direct measures of brain activity that don't reflect the complexity of neural interactions during cognitive tasks.

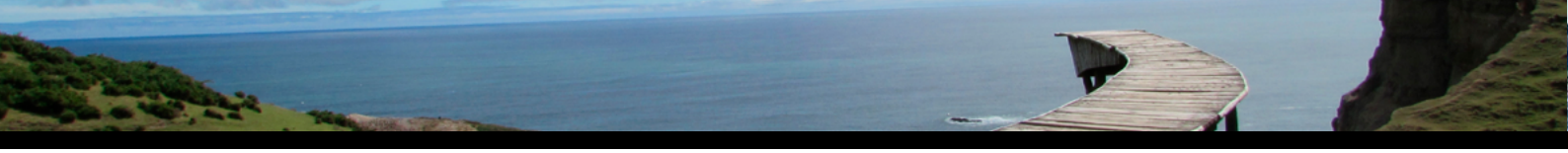
(Sponsored by This Work Was Made Possible In Part By A Grant From CONICYT, FONDECYT /Postdoctorado 3140306 To CD, And Iniciativa Cientifica Milenio ICM P10-001-F, P09-015-F, And Fundacion Guillermo Puelma.)

CONICYT, FONDECYT /Postdoctorado 3140306 to CD, and Iniciativa Cientifica Milenio ICM P10-001-F, P09-015-F, and Fundacion Guillermo Puelma.

Local topology of connectome as a parameter to stabilizes critical range in (a model of) global neural dynamics.

Castro S[1,2], Fernandez M[3], El-Deredy W[4], Orio P[1,5], [1]Centro Interdisciplinario de Neurociencia de Valparaiso, Facultad de Ciencias, Universidad de Valparaíso.[2]Facultad de Ciencias, Programa de Doctorado en Ciencias mención en Neurociencia, Universidad de Valparaíso.[3]Laboratorio de Electrónica Industrial, Control e Instrumentacion, Ingenieria, Universidad Nacional de La Plata.[4]Ingenieria Biomedica, Ingenieria, Universidad de Valparaíso.[5]Instituto de Neurociencias, Facultad de Ciencias, Universidad de Valparaíso. (Sponsored by SC Is Recipient Of A Ph.D. Fellowship From CONICYT. PO And WeD Are Partially Funded By The Advanced Center For Electronic Engineering (FB0008 CONICYT, Chile). The Centro Interdisciplinario De Neurociencia De Valparaíso (CINV) Is A Millennium Institute Sup).

The interplay between structural connectivity (SC) and neural dynamics is still not yet fully understood. Here we adopt a computational framework to study how SC is related to global neural dynamics. In a previous study, a model who integrates mean-field local dynamics to human SC found at least 2 global neural states, with either a high or low firing rate pattern. These 2 stable dynamics, or bistability, emerges in a range of the global coupling parameter G, limited by their critical values G- and G+. However. how the network topology shapes the critical G values has not been yet investigated. Our aim is to study if global or local topology are related to critical G values. We studied 4 different SCs: a cortical parcellation of human brain, a human binary equivalent, a Random Network (RN), and a Small-World (SW) equivalent. To depict global or local topology we use the k-core and the degree measure, respectively. We performed numerical simulations and calculated the critical G values. To analyze the effect of the topology in dynamics, we prune the edges of SCs in 3 specific ways: i) edges belonging to critical l-core/high degree nodes, ii)random edges, and iii) edges not belonging to critical k-core/low degree nodes. Our results shows bistability in all type of networks, showing this neural dynamics are related to structural topological principle. Second, the highest shifts in critical G values are achieved when the edges of highly connected nodes, as high degree or critical k-core, are pruned. Third, when we prune edges with low degree or from no critical k-core, the shifts in critical G values are small or null. Therefore, relevance of each connection to sustain the bistability can be analyzed with topology measures. Fourth, in all networks higher drifts in the critical value G+ are achieved when we prune edges based on degree rather than k-core. This evidences a difference when cut either the global or local topology. Fifth, when the degree distribution of networks pruned are shared, as in the binary human SC with the RNs, the shift in the critical G values are with same value. In conclusion, the degree distribution as a local connectivity feature, shapes the critical G points for bistability, and suggest it as a topological key parameter.



ORAL COMUNICATIONS II

Model quantification of direction selectivity in starburst amacrine cells in the mammalian retina.

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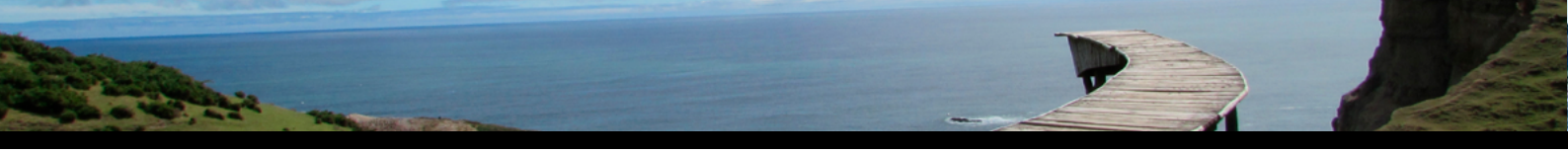
Detection of motion direction in the visual system of rodents is observed at processing stages as early as the retinal circuitry. Starburst amacrine cells (SAC), which are components of this circuit, appear to give rise to direction selectivity (DS), and for stimuli moving in a preferred direction, i.e., away from the soma, SAC dendrites release more GABA than for stimuli moving in the opposite direction. Several neural mechanisms have been shown to contribute to DS in SACs. However, the actual contribution of each mechanism to the phenomenon is yet to be determined. To quantify the contribution of intrinsic and network properties to DS, we implemented a simple, but biophysically plausible, model of 100 SACs including excitatory inputs from bipolar cells and inhibitory SAC-SAC interconnections. We validated the model reproducing published experimental data of dendritic Ca+2 and somatic currents during stimulation with bars, annuli, and gratings. We quantified DS using a DS index (DSI) for a range of stimulus widths, velocities, and intensities. DS was strong, i.e., DSI greater than 0.2, for velocities between 1 and 20 mm/s and medium range intensities, and increasing the distance between excitatory inputs shifted DS to stronger stimulus intensities. Restricting the bipolar inputs to the proximal 2/3 segments of the SAC dendrites dramatically expanded the number of stimulus parameters resulting in DS response, with an increase in the DSI. Finally, suppressing SAC-SAC inhibitory interactions greatly reduced the DSI for all stimulus parameters, except for a small range of weak and slow stimuli. Our results suggest that segregation of excitatory inputs to proximal dendrite segments is a major contributor to DS due to diminished response in the non-preferred dendrite. As well, lateral (SAC to SAC) inhibition appears to be necessary for displaying DS in a wider range of stimulus parameters. Our simplified model geometry sufficed to reproduce the genesis of DS response, and will allow to quantify the contribution of other possible mechanisms to DS.

Funded by Proyecto Basal AC3E (FB0008, CONICYT, Chile) and the Millenium Institute CINV (P09-022F, Iniciativa Científica Milenio, Ministerio de Economía, Chile).

Common signatures of physiological aging and aging by neurodegeneration in Drosophila models.

Tevy M F[1], Caris C[1], Maracaja-Coutinho V[1], Molina-Fernandez C[1], Capocefalo D[3], Lopez-Quilodran N[1], Martinez P[2], Mazza T[3], [1]Centro de Genómica y Bioinformática, de Ciencias, Universidad Mayor.[2]Biomedical Research Center Universidad Andrés Bello.[3]Mendel Institute Bioinformatics Unit, I.R.C.C.S. “Casa Sollievo della Sofferenza”. (Sponsored by FONDECYT N11130203)

A major challenge is to understand which cues contribute to the appearance of the hallmarks of aging.Transcriptional alterations constitute one primary hallmark of aging. To gain insights into this matter we used *Drosophila* because it allows whole organism time course transcriptomics of a collection of individuals raised synchronically in an identical environment. We used healthy aged and Alzheimer models to gain insights into the common signatures of physiological aging or aging by neurodegeneration. We performed bioinformatics approaches in the transcriptomes of these flies to discover common gene networks (GNs) acting during aging. We validated high through-put and *in silico* data with molecular tools, and we correlated these data to behavioral changes. To discover new interactions among the differentially expressed transcripts in both models of aging we obtained gene co-expression modules which reveal new age and sex specific genetic interactions during the aging process. Among the differentially expressed transcripts in aging, we discovered a set of long non-coding RNAs (lncRNAs). We mapped these lncRNAs to the modules and characterized its nearest coding gene to infer their putative function. LncRNAs common to both aging by neurodegeneration and physiological aging are positionally conserved to the human genome and their nearest coding RNA is enriched in brain tissue pointing to a role of lncRNAs in the aging brain. These data help elucidate the cues that lead to the appearance of the hallmarks of aging and thus contribute to the understanding of how a “healthy aged phenotype” is achieved.



Brain activity during active vision: an ecological approach to the study of neural dynamics.

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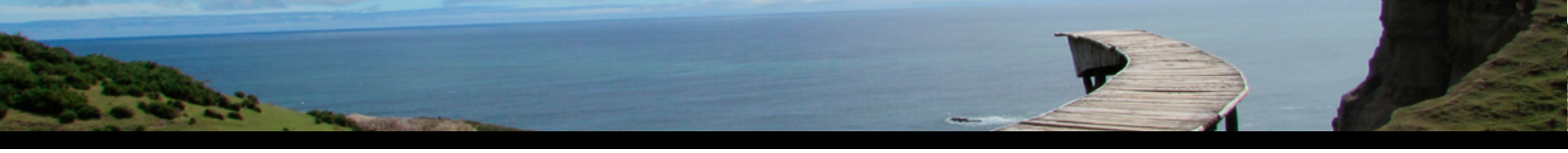
Most of our knowledge about neuronal mechanisms of visual perception comes from experiments where a stimulus is presented while the ensuing neuronal perturbation is analyzed. This scheme has brought us substantial knowledge about how the brain can respond to sudden changes in the environment. However, this experimental paradigm neglects a key fact about perception, which is that most of the time, the brain itself is the one that originates a sensory change by initiating motion of the sensory surfaces. This happens with eye movements in vision, hand movements in somatosensation, or sniffing in olfactory perception. In stark contrast to what happens during this passive processing, active sensing putatively enables the brain to process sensory stimulus at times precisely locked to the self-actions and thus engage modulatory mechanisms that exploit predictions about the nature and timing of the incoming stimuli. In this work, I am going to present electroencephalographic activity recorded while volunteers freely explored natural scenes. The analyses contrasted the image and fixation onset activity, as both represent the entrance of sensory information to the visual stream. Based on those results, we then compared the activity related to the onset (saccades) and the offset of the eye movement (fixation). These results demonstrated that during active vision, the nervous system engages a mechanism of sensory modulation that is precisely timed to the self-initiated stimulus changes. This mechanism could help coordinate neural activity across different cortical areas and, by extension, serve as a general mechanism for the global coordination of neural networks.

(Sponsored by Iniciativa Científica Milenio (ICM-P09-015F) And Fundación Puelma).
Iniciativa Científica Milenio (ICM-P09-015F) and Fundación Puelma.

Lithium control the topographic and temporal initiation of firing activity through a mechanism depending of β-catenin.

Oliva C[1], Tapia-Rojas C[1], Lindsay C[1], Inestrosa N[1], [1]Cellular and Molecular Biology, Ciencias Biológicas, Center for Aging and Regeneration CARE-UC and Pontificia Universidad Católica de Chile. (Sponsored by Supported By The Basal Centre Of Excellence In Science And Technology CONICYT-CARE (PFB 12/2007 To NCI), A FONDECYT (grant Number 1120156 To NCI). We Also Thank A Special Grant On ?Lithium In Health And Disease? From The Sociedad Química y Minera de Chile).

The anatomical connectivity to and from the hippocampus is segregated along its axis, suggesting that different memories could be allocated along its different circuits. Dorsal region is involved in spatial navigation whereas ventral region is involved in emotional events. Instead of being segregated, the gene expression has been allocated in discrete domains along the hippocampal axis. However, whether a topographically allocated function correlates with the activation of specific proteins along the circuit is still unknown. We measured the spontaneous firing activity of brain slices subdivided into ventral, intermediate and dorsal zones obtained along the entorhinal cortex (EC)-hippocampal septotemporal axis. Because the activation of Wnt signaling modulates the spontaneous firing activity in this circuit, we incubated the slices with lithium to inhibit the ubiquitous glycogen synthase kinase-3β (GSK-3β), to induce the accumulation of β-catenin and to examine whether this effect is functionally correlated with the changes in firing activity measured along the circuit. Our results indicate that lithium-induced changes in the spontaneous firing activity were inversely correlated with the intrinsic basal activity in each area. Lithium significantly increases neuronal activity both at the intermediate and dorsal hippocampus, where the basal activity was low, and less increase at ventral hippocampus, where the basal activity was high. This effect of lithium correlates with the initial inactivation of GSK-3β and the accumulation of β-catenin at intermediate and dorsal hippocampal zones. Simultaneous recordings at ventral and intermediate EC showed that, oppositely to hippocampus, lithium disrupts the high synchronous firing activity into low firing asynchronous activity, which in EC correlates with the reduction of β-catenin. In summary, lithium activates Wnt signaling protein components at the intermediate and dorsal hippocampus, reducing the activity in the rest of the circuit including in the EC, suggesting a correlation between β-catenin and neuronal activity. By this mechanism lithium could control the topographic and temporal initiation of firing activity, first in the spatial memory circuit and then in the emotion-related zones.



Improved remyelination by increasing neuronal activity in the freely moving mice.

Ortiz F[1], Habermacher C[2], Houry P Y[2], Graciarena M[3], Lopez C[1], Nait-Oumesmar B[3], Angulo M C[2], [1]Mechanisms on Myelin Formation and Repair Laboratory, Instituto Ciencias Biomedicas, Facultad de Ciencias de la Salud, Universidad Autónoma de Chile.[2]Physiology of NG2 Cells, U1128, Paris Descartes University.[3]u1127 Institut du Cerveau et de la Moelle épinière.

Oligodendrocytes precursor cells (OPCs) are the main source of remyelinating oligodendrocytes (OLs) in demyelinating diseases such as Multiple Sclerosis. These precursor cells receive glutamatergic synaptic inputs from callosal axons. It has been shown that neuronal activity regulates myelination; however whether activity from glutamatergic axons mediates remyelination has never been addressed. Using a model of lysolecithin (LPC)-induced demyelination, we have recently demonstrated that newly-generated OPCs inside a demyelinated lesion gain glutamatergic synapses during remyelination, suggesting a role of axon-OPC glutamatergic signal during the remyelination process (Sahel et al., 2015, Front Cell Neurosci). To investigate whether remyelination is an activity-dependent process, we are currently using an optogenetic approach in LPC-demyelinating lesions of Thy-1-ChR2-YFP transgenic mice. This strain expresses the light-activated channel channelrodhopsin 2 (ChR2) in a subset of callosal neurons allowing for the photostimulation of ChR2+ corpus callosum glutamatergic fibers. We are presently studying the effect of axonal photostimulation on remyelination in vivo. By using immunostainings against different celular types of the oligodendrogial lineage, our aim is to determine whether the proportion and density of proliferative OPCs and mature OLs change when axon activity in the lesion is increased in freely moving mice. Inmunostainings against myelin proteins along with electron microscopy analisis- both at different times after the onset of the LPC-induced demyelination-, are used to determine whether the time course of the remyelination process is modified by axonal photostimulation. Our results should shed light on the regulation of axon-OPC signaling during the remyelination process.

Supported by ARSEP, ANR, FONDECYT INICIACION 11160616

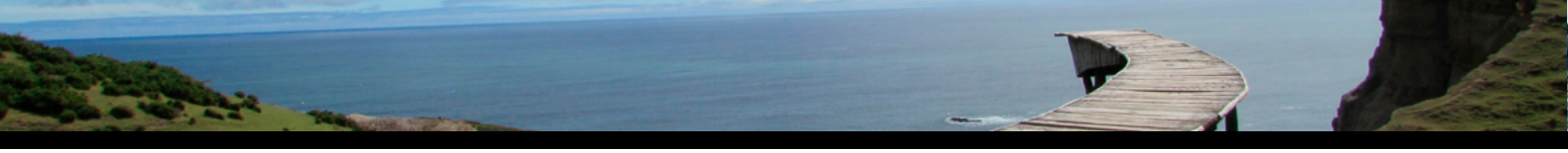
Ventro-dorsal hippocampal interaction controls context memory formation.

Fredes F[1], Silva M A[1], Shigemoto R[1], [1]Neuroscience Institute of Science and Technology (IST) Austria . (Sponsored by ERC AdG 694539 SINCHAIS).

Places and emotions are tightly linked in our memories. In mammals, this link is indispensable for avoiding harmful environments and remembering beneficial ones. Dentate granule cells (GCs) in the dorsal hippocampus fire very sparsely when an animal enters to a novel environment; the activation of this small set of neurons induces emotional responses linked with a specific context memory. The classical view assumes that GCs firing is mainly driven by the excitatory input from the entorhinal cortex. However, it has been shown that the entorhinal cortex exerts only a weak influence on GCs firing, and hence on acquisition of context memory. Thus, the precise mechanisms by which GCs fire in order to form contextual memories are still unknown.

We found that an intrahippocampal excitatory projection conveys a powerful drive over GCs in the dorsal dentate gyrus (DG). This projection, which originates from the mossy cells (MCs) located in the ventral portion of DG, targets the dendrites of dorsal GCs in the inner molecular layer. Electron microscopy confirmed that these terminals contact almost exclusively GCs spines. Using calcium imaging in freely behaving mice, we show that the activity of ventral MCs dramatically increases during novel environment exploration and decreases after familiarization. Local chemogenetic inhibition of ventral MCs terminals in the dorsal DG during the novel environment exploration significantly decreases the c-fos expression levels in dorsal GCs. Furthermore, the same manipulation in the acquisition phase of fear conditioning abolishes freezing during re-exposure to the same environment, whereas it has no effects on freezing levels in the retrieval phase.

Thus, our results suggest that a previously overlooked ventro-dorsal hippocampal interaction is required for the firing of dorsal GCs and consequently, context memory acquisition, challenging the classical view of the hippocampal contextual memory formation.



POSTER SESSION I

1) Analysis of the behavioral response to odorants in PINK1 -/- zebrafish larvae.

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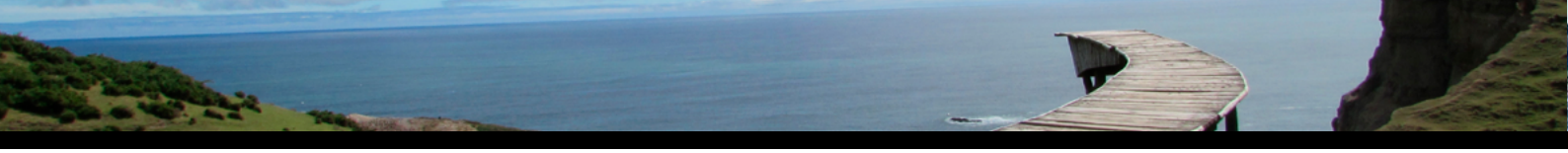
Olfactory dysfunction is a non-motor symptom of Parkinsonism present in almost 90% of sporadic cases. Although the link between olfactory dysfunction and genetic Parkinsonism is poorly understood, some studies indicate a relation between PINK1, a mitochondrial serine/threonine kinase, and olfactory dysfunction. However, possible alterations of olfactory neuronal circuits related to PINK1 have not been studied deeply.This work focused on the early olfactory dysfunction in a PINK1 loss-of-function zebrafish model. PINK1 mutant animals show a significant decrease of diencephalic dopaminergic neurons a few days after hatching, suggesting that olfactory dysfunction could appear at an early age. To address this possibility, we evaluated the behavioral responses of wild type and PINK1-/- mutant larvae to odorants that normally trigger aversive (cysteine) and attractive (alanine) responses. Stimulation with the odorant-free E3 medium, which resembles the mechanical component of the stimulus application, resulted in an increment of the distance travelled by PINK1-/- larvae at 3 and 4 dpf, when compared to the wild type response. When exposed to cysteine, 4 dpf PINK1-/- larvae showed a higher response than in the wild type, with an increase in the fastest swimming velocity (> 9mm/s). However, 3 dpf PINK1-/- larvae exposed to alanine did not show the increment in the total traveled distance and intermediate swimming velocity (3-9 mm/s) observed in wild type after E3 application. Together, these results suggest two different phenomena. As shown by alanine-induced responses, there is an early olfactory dysfunction in PINK1-/- larvae. However, when the stimulus is an alarm signal like cysteine, the observed increase in traveled distance and swimming speed suggests an anxiety-like phenotype.

ICM P-09-015-F, CONICYT PIA ACT1402, FONDAP 15150012.

3) Intranasal cotinine improves memory loss, depressive-like behavior, and GFAP+ cells loss induced by restraint stress in mice.

Alvarez Ricartes N[1], Perez Urrutia N[1], Oliveros Matus P[1], Echeverría Morán F[1], Iarkov A[1], Echeverría Morán V[1], [1]Tecnología Médica, Ciencias de la Salud, Universidad San Sebastián.

Posttraumatic stress disorder (PTSD) has been associated with a significant decrease in glial fibrillary acidic protein (GFAP) immunoreactivity (IR) in the hippocampus of rodents. GFAP is a family of proteins used as a marker of astrocytes and in less extent of immature brain cells. Astrocytes maintain brain homeostasis and support neuronal function. Astroglia dysfunction seems to be involved in the development of depression induced by stress. Cotinine, a positive modulator of the α7 nicotinic acetylcholine receptors (nAChRs), prevents memory impairment, depressive-like behavior, and synaptic loss when co-administered during restraint stress. In here, we studied the effects of post-treatment with intranasal cotinine on depressive behavior, visual recognition memory as well as the number and morphology of GFAP+ cells, in the hippocampus and frontal cortex of restrained mice. Mice between 2-3 months of age were restrained 6h/d for 21 days. After two weeks of treatments, with cotinine or vehicle, mice were tested for locomotor activity (Open Field Test), depressive-like behavior (Forced Swim test), and memory (Novel object recognition). After euthanasia, GFAP IR cells and their morphology were assessed using IHC. The results revealed that in addition to the depression and cognitive impairments, restraint stress induced a significant decrease in the number of GFAP+ cells and their arborization complexity. Cotinine prevented cognitive impairment and depressive behavior as well as restored GFAP+ cells morphology in both brain regions. The data obtained in this study suggest that cotinine effectively restores cognitive abilities as well as astrocyte function after chronic immobilization in mice.



5) Effect of musical expertise on the efficiency of attentional networks.

Barraza P[1], Medina D[2], [1]Centro de Investigación Avanzada en Educación (CIAE) Universidad De Chile.[2]Departamento de Música, Facultad de Artes y Educación Física, Universidad Metropolitana De Ciencias De La Educación. (Sponsored by This Research Was Supported By The Basal Funds For Centers Of Excellence, Project FB 0003 From The Associative Research Program Of CONICYT.).

The musical practice is one of the few human activity that can induce, in short period of training, both structural and functional changes in the brain. Despite numerous benefits of musical trainning on cognitive development, there is still no clear evidence of whether it has effects on extra-musical functions like attention. To elucidate this issue, we compared professional musicians (keyboard players) with a matched group of non-musician professional adults, while performing an attentional task that measures the efficiency of the alert, orientation and executive control networks. We found that musicians have a more efficient executive attentional control network than non-musicians. Differences in the efficiency of alert and orientation networks between groups were no found. In addition, it was found that the years of musical training strongly correlate with the efficiency of the executive attentional control network, that is, to more years of musical practice, greater efficiency of the executive control network. Taken together, our findings show that musical training has an effect on the efficiency of inhibitory control of intervening variables, which seems to be consistent with the type of skills that a professional musician should develop during the training period (eg. focus attention on musical performance, while controlling the effect of distracting environmental variables). Further research should be conducted to determine the neural dynamics underlying improvement in the efficiency of inhibitory control in adult musicians and the potential impact of musical training on attentional efficiency of school-age children.

This research was supported by the Basal Funds for Centers of Excellence, Project FB 0003 from the Associative Research Program of CONICYT.

7) Effect of chronic stress on prefrontal-hippocampal functional connectivity during acquisition of spatial reference memory.

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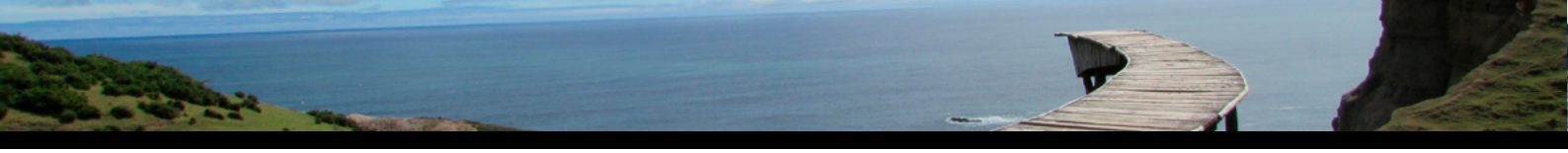
Learning and remembering the location of relevant places in the environment (i.e. spatial reference-memory) is crucial for survival. This cognitive function depend on the coordination of the prefrontal-hippocampal neural network supported by the emergence and synchronization of neural oscillatory patterns. We recently shown, though local-field potential (LFP) recordings in freely-moving mice, that spectral coherence, a measure of oscillatory synchronization, gradually increase in the prefrontal-hippocampal network throughout acquisition of spatial-reference memory. Also, we previously shown that chronic stress modifies prefrontal-hippocampal synchronization. However, it is unknown if chronic stress affects prefrontal-hippocampal synchronization *during* memory acquisition. To address this issue, C57BL/6 mice were chronically implanted with electrodes in the prefrontal cortex and hippocampus, and then subjected to restraint stress during seven consecutive days. Control mice were no subjected to stress. Mice of both groups were subjected to LFP recording during the acquisition of reference memory in the Barnes maze. Our preliminary results show that chronic stress affect both prefrontal-hippocampal oscillatory synchronization and path optimization during acquisition of spatial reference-memory. Altogether this project will help to understand the relationship between neural alterations and chronic stress induced impairment of cognitive functions.



9) Relations between explicit and implicit measurements of anxiety during an auditory working memory task in the elderly.

Espinoza M[1], Morales R[1], Delgado C[1,2], [1]Departamento de Neurociencia, Facultad de Medicina, Universidad De Chile.[2]Neurologia y Neurociencia, HCUCH, Universidad De Chile. (Sponsored by Funded By Anillo ACT 1403, Beca Puelma.).

Background: State-Trait Anxiety Inventory (STAI) is used to assess anxiety symptoms, it is divided in two parts: Trait anxiety (STAI-Y2) and State anxiety (STAI-Y1), STAI-Y2 indicates a personality dimension with anxious propensity and STAI-Y1 evaluates transient state. Also, there are implicit indicators of anxiety like the measurements of the autonomic nervous system (ANS) these include Heart Rate Variability (HRV) and Galvanic Skin Response (GSR). The Auditory Working Memory (WM) is a process of maintaining actively sounds or spoken language in memory over short periods of time. This capacity usually decrease with aging, may be related with hearing impairment. Therefore, it is interesting to study the influence of anxiety in the performance in WM in subjects with normal hearing or mild presbycusis. Objetives: To study the relation between the explicit anxiety measurements (STAI), implicit anxiety measurements (ANS) and the performance in an auditory working memory.

Methods: Subjects≥65 years, without Psychiatric or Dementia diagnoses, underwent an extensive Neuropsychological and auditory evaluation. Subjects completed the STAI-Y1 before and after the WM test. The ANS was registered using Biopac with measurements of the parasympathetic (PSN) and sympathetic (SNS) HRV and GSR in baseline and during WM task. We compared the ANS data between baseline and the different periods of the test using paired test and did correlations between implicit and explicit anxiety data.

Results: 15 individuals (mean [S.D.] 71,53 [5,705] years), answered the STAI-Y2 Scale (42,93 [10,85] score), STAI-Y1 before (35,07 [7,75] score) and after (40,53 [11,67] score) task, there was a significant increase in anxiety between both assessment ($t=-2.2$,$p=0.045$). STAI-Y2 was correlated with STAI Y-1 before ($r= 0,886$, $p<0,0005$) and after ($r=0,699$, $p<0,005$) task and STAI Y-1 before was correlated with STAI-Y1 after ($r=0,574$, $p<0,05$) task. The changes in SNS-HRV activity compared with baseline SNS-HRV increased significantly in three parts of the WM task ($t=3,6$,$p<0,05$), the PNS-HRV activity compared with baseline PNS-HRV activity decreased significantly in three parts of WM task ($t=3,6$,$p<0,05$) and GSR activity compared with baseline GSR activity increased significantly in the four parts of WM task ($t=-3,8$,$p<0,05$).

STAI Y1 before, was associated with baseline GSR records ($p<0,05$) and the STAI-Y1 after task, but was not associated with HRV- GSR measurements.

Conclusion: As expected explicit (STAI-Y1) and implicit (ANS) anxiety measurements increased during a difficult WM task in elderly. But it is still pending to analysis its relations with WM performance and hearing impairment.

11) Deep TMS for the treatment of Negative symptoms in Schizophrenia: not only an antidepressant effect.

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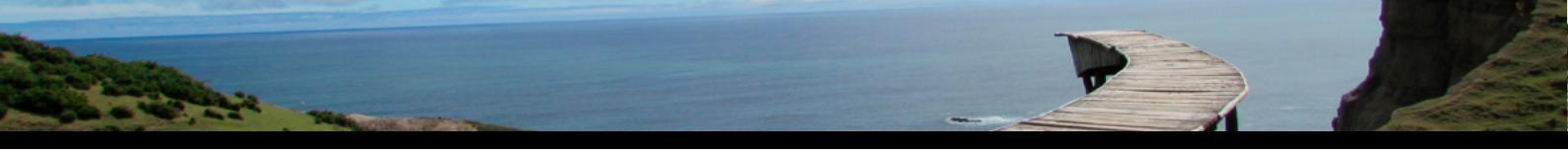
Negative symptoms of Schizophrenia show limited response to both typical and atypical antipsychotics. Further, reduced activity in the prefrontal cortex (PFC) in association with negative symptoms in Schizophrenia has been consistently reported. Therefore, repetitive transcranial magnetic stimulation (rTMS) applied over the prefrontal cortex (PFC) has been proposed as an adjuvant to pharmacological treatment, but whether the improvements obtained are specific to negative symptoms or attributable to antidepressant effects is still unclear. The aim of the present study is to determine to which extent the improvements in negative symptoms of Schizophrenia obtained after high frequency (18 Hz) bilateral stimulation applied over the lateral PFC symmetrically using deep repetitive TMS (dTMS) are attributable to antidepressant effects. This treatment was administered in a cohort of 16 patients with Schizophrenia under successful pharmacological control of positive symptoms, and predominant negative symptoms. We compared the effectiveness of dTMS on negative symptoms using the Scale for the Assessment of Negative Symptoms (SANS) and Positive and Negative Syndrome Scales (PANSS), and compared the improvement obtained in patients according to their depression severity before treatment using to the Calgary Depression Scale (CDS) . There were significant improvements in negative symptoms in response to treatment, which were similar, regardless of subjacent depression. Our data suggests that the beneficial effects of dTMS of the PFC cannot be attributed to potential antidepressant effects.



13) The role of sensory motor demand and immersion in attentional skills acquired by video gamers.

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During the past 15 years a great amount of work have shown how playing video game can improve visual attention. It has been even proposed as a possible therapy for people who had minor visual impairments. However, the mechanism explaining why this improvement take place is still unknown. Here we proposed that video games demand the optimization of at least one of two attentional mechanisms; maintaining attention while being strongly resistant to distractors (immersion), and fine tuning between attentional and motor systems (sensory-motor demand). In doing so, we developed a video game questionnaire asking questions depicting how strong was the immersion and sensory motor demand training in general population of video game players. Using more than a hundred people we validated the questionnaire using Factor Analysis and Cronbach's Alpha. We then invited subject to an in-lab procedure where they answered the validated questionnaire and performed an attentional flanker task. We then used the scores of the validated video game questionnaire scales (immersion and sensory-motor demand) to predict task performance and the amplitude of EEG evoked potential commonly analyzed for each of these tasks. Results obtained supports that early attentional P1 component are predicted by immersion score, while late frontal P3 was predicted by sensory-motor demand. Only sensory motor demand predicted behavioral results, suggesting longer reaction times for players with higher sensory demand scores. Our results support that the immersion and sensory motor demand needed during usual game play do modify classic attentional components, suggesting them as key mechanisms in this improvement. These findings represent the first step in understanding the neural mechanism which explain the attentional improvement produced by video games, giving hints of how an ad hoc game for therapy should be built.

15) Increased power of high-gamma oscillations in the rat nucleus accumbens during spontaneous social interaction.

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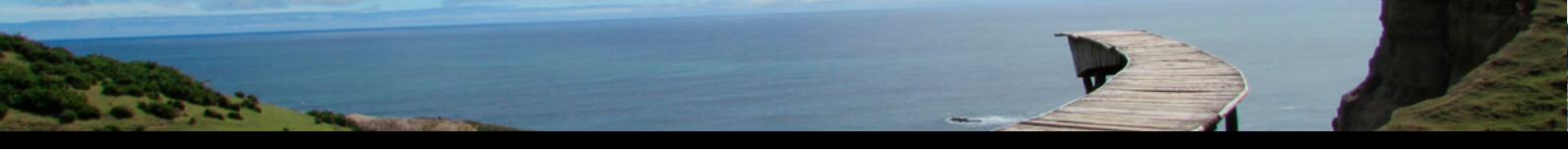
Positive social interactions are natural rewards and impairments in this domain characterize several psychiatric disorders. Empirical studies indicate that social reward is processed in the mesocorticolimbic network where nucleus accumbens (NAc) is a key region. Gamma oscillations in the NAc are involved in reward processing, but their specific correlation to social interaction remains unknown. In this context, we hypothesized that the power of gamma oscillations increases during social interaction in the rat NAc. Male *Sprague-Dawley* rats were implanted in the NAc and the local field potential (LFP) was recorded from this area using a wireless recording system. LFP was record during a spontaneous social interaction task where animals can freely move, touch and smell each other in a naturalistic manner. Then, we compared the power of gamma oscillations with a neutral non-social condition (open field test) in the same context previously used. We found an increase of high-gamma oscillations (80-100 Hz) power during spontaneous social interaction in comparison to the non-social condition. These findings suggest that high-gamma oscillations in the NAc are a key element for social reward processing. Further studies using animal models are needed to answer how alterations at this level could be related with the development of some neuropsychiatric disorders.

FONDECYT Grant N° 1141276, Anillo de Ciencia y Tecnología Grant Nº ACT1403 to Alexies Dagnino-Subiabre and Beca Doctorado Nacional CONICYT N°21150460.



17)The amplitude of otoacoustic emissions and olivocochlear reflex strength are associated with cognitive performance in elderly people.

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Increasing epidemiological evidence shows a relationship between age-related hearing loss or presbycusis and cognitive decline in elderly people. Hearing loss is one of the most important modifiable risk factors for dementia. The mechanisms that connect this epidemiological association are unknown. There are low or null literature that associates otoacoustic emissions with cognitive performance. The functionality of the inner ear, specifically of the outer hair cells, can be assessed by Distortion product otoacoustic emissions (DPOAEs) a higher amplitude means that the cochlea shows a high capacity as a low intensity sounds amplifier, likewise, the medial olivocochlear (MOC) function can be assessed by measuring the olivocochlear reflex (OCR) strength through DPOAEs amplitude changes induced by contralateral acoustic stimulation (CAS), Its activation causes a suppression of the cochlear response and consequently decreases the amplitude of otoacoustic emissions . Here, we recruited seventy-eight elderly subjects between 65 and 85 years, mean age 73.63, with normal hearing andpresbycusis. Subjects were evaluated with audiological and cognitive batteries. We correlated DPOAEs amplitudes and OCR strength with epidemiological data and cognitive performance. We found significant direct correlations between DPOAEs amplitudes of the right ear and the Mini-mental State Examination, Boston test (nomination) and reverse digit spam (working memory), and between the right ear OCR strength and Boston score and the percentage of impairment in Activities of Daily Living, and between OCR strength of the left ear and reverse digit spam. Our preliminary results suggest a relationship between inner ear function and OCR strength with cognitive performance in elderly people.

Funded by Proyecto Anillo ACT1403, FONDECYT 1161155, Proyecto REDES 150134 and Fundación Guillermo Puelma.

19) Virtual social rejection in persons with attention-deficit hyperactivity disorder.

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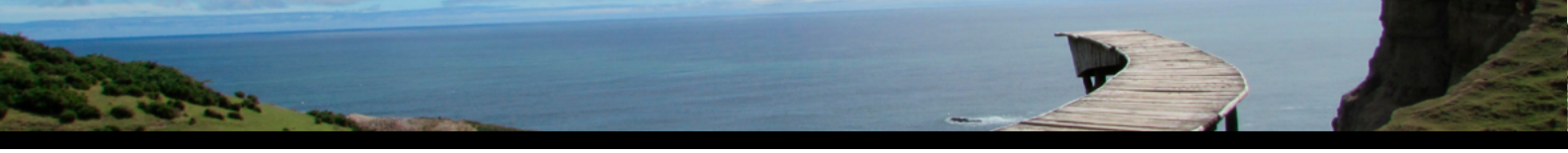
Brain processing of Social Rejection (SR) is not well understood, especially in atypical neurodevelopmental populations. For instance, people diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD) present difficulties processing communication cues, have less social acceptance, and more peers' rejections. Nowadays, a growing number of social interactions occur on social networks. We developed a social paradigm which emulates online acceptance and rejection by peers, allowing us to explore how the participants react to this social interaction messages. The study is focused on the way subjects with ADHD experience SR and whether they differ from Controls. To achieve this objective two groups of 20 participants were asked to perform a SR task in an experimental setting while recording the brain electrical activity (EEG).

Three databases of facial photos were created considering the potential age of participants (8 ± 1; 13 ± 1; 17 ± 1 years). The paradigm consisted of two stages: Selection and Guess. In Selection facial photos of age paired volunteers were presented to the participant in 6 screens with a 6x3 grid each (until a total of 100 images). The instruction was to request friendship to 50 peers. In Guess stage a single face was presented in the center of the screen in each trial. A sign representing the previous selection was present at the top left corner of the picture. Participant then guessed if they had been accepted/chosen or rejected, that response was added to the picture. Then a feedback sign appeared in the top right corner showing what actually happened. Feedback was manipulated granting the same number of acceptance and rejection trials. Finishing the experiment 5 consecutive acceptance trials are presented to compensate any rejection perception.

The average time of Selection phase is larger in ADHD group. Reaction times in both groups are larger when the guess is incongruent with the prior selection state. However, ADHD group showed this effect reduced when they guessed rejection to a previously selected person. These groups also presented electrophysiological differences: Feedback related negativity (FRN) is larger in ADHD than controls. They also exhibited an enhanced late positive potential (LPP) in right posterior parietal region. FRN difference suggests that ADHD group has greater sensitivity to negative social feedback while LPP has been related to difficulties in the integration of affective information.

These findings allow a preliminary characterization of SR processing in persons with ADHD, and can potentially help improve interventions to ameliorate socioaffective impairments in this condition which are often left aside.

FONDECYT Grant 1150241.



21) Visual saliency and free exploration in people affected with schizophrenia

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Schizophrenia (SCZ) is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. It has been reported that people affected with schizophrenia have restricted visual exploration characterized by a smaller number of fixations and saccades compared with healthy controls. However, it is unknown whether this restricted and unusual visual exploration is generated by processing mechanisms top-down, or if mechanisms bottom-up would influence exploration. We propose that the reduction of visual examination in affected people with schizophrenia is associated with a reduced visual evoked response attentional salience visual stimuli. To test the hypothesis we study the visual fixations in a group of people affected with schizophrenia (PAS) and healthy controls (HC). Both groups were presented four types of stimuli: 1) images with an area with a salient color, 2) luminance changing area flickering images 3) scenes containing faces and 4) unmodified control images. We found that the PAS group looks later at chromatic salient and face areas. Moreover, the time that PAS spend on the chromatic salient areas was greater than in HC. These results suggest that alterations in sensory processing are associated with a reduced visual evoked response attentional salience visual stimuli and this could contribute to the cognitive deficits that occur in SCZ. Moreover we study brain activity with a electeoencephalogram 64 channels and correlate eye movements with brain activity in a fixation event related potencial (fERP), we found that this potencial is diminished in PAS group in all conditions. This finding demonstrated that visual processing is affected in the PAS group and that reduced saliency response is a putative mechanism to understand restricted and altered visual exploration.

Iniciativa Científica Milenio ICM P10-001-F, P09-015-F, FONDECYT N 11140464 and Fundación Guillermo Puelma

23) Beta oscillations during visual exploratory behavior are timely lock to saccades in a content-dependent manner.

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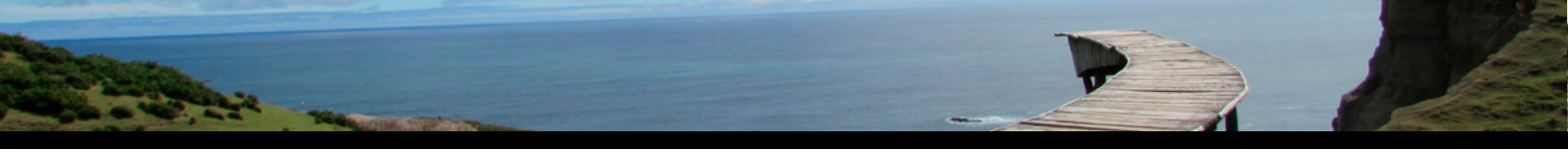
The Beta oscillation is a rhythmic neural activity that is widely present in the neocortex and has been linked to several cognitive processes, like working memory, motor planning, visual perception and memory formation. Recently, experimental evidence in the macaque visual system shows that while gamma activity is mainly involved in bottom-up communication, beta activity is related to top-down control, driving the sensory related gamma activity. Areas engaged in this top-down control have been related to movement and saccades execution. In natural vision, the V1 local field potential in the beta range appears to synchronize the action potentials of the visual neurons immediately after the saccades. This has been proposed as a necessary mechanism for active visual perception. Here, we explore the role of the beta oscillation of the EEG as a possible top-down mechanism in visual perception during active vision in humans. In this work, we recorded the electroencephalographic activity and the eye movement dynamics from 16 volunteers, while performing a free viewing visual exploration task. We analyzed the broad band signal in the frequency domain and the band limited signal in the time domain. We found evidence that the beta activity in the EEG increases immediately after a saccade, that this activity is highly synchronous, and it is modulated by the content of the image, dismissing the possibility of a motor contribution. These results suggest a dynamic role of the evoked beta activity during active vision in humans.

ICM P09-015-F y Fundacion Guillermo Puelma.



25) Neural oscillatory correlates of attentional deficit in visual perception of patients with schizophrenia and subjects with high-risk of developing psychosis.

Oyarzo P[1,2], Corral S[1,2], Mayol R[1,2], Aburto M[1,2], Castillo R[1,2], Abrigo C[1,2], González D[1,2], Silva H[3,2], Gaspar P[1,2,3], [1]Neurociencias, Medicina, Universidad de Chile.[2]Traslational Psychiatry Lab Biomedical Neuroscience Institute.[3]Psiquiatría, Medicina, Universidad de Chile.

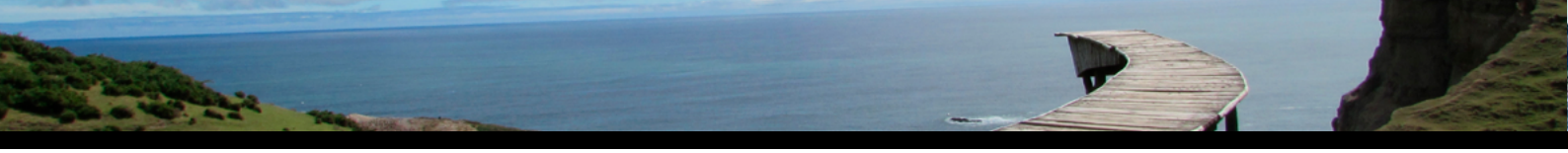
Functional impairments of visual processing in patients diagnosed with schizophrenia (SCZ) have been reported extensively. Specifically, in the evoked response to low spatial frequency (LSF) compared to high spatial frequency (HSF) visual stimuli. In addition, more recent findings have shown deficits in alpha band (7-14 hz) desynchronization after the stimulus presentation. It has been proposed that the modulation of these oscillations play a crucial role in selective attention processes. This alteration have been reported both for LSF and HSF stimuli, suggesting that stimulus-induced alpha modulation represents a separate domain of neurophysiological dysfunction from previously described impairments in sensory ERP generation in schizophrenia, with complementary contribution to visual information processing. Here, we assess the possibility that impaired spectral oscillations may also be present in the prodromal stages of the disease, accounting for more general dysfunctions that occur previous to the first psychotic episode. In order to answer this question we use a time-frequency approach to measure the unfolding of the power spectral density and modulations of ongoing oscillatory activity during a feature-based selective attention paradigm, comparing evoked electrophysiological activity between three groups of subjects: (1) diagnosed with SCZ, (2) with high-risk of developing SCZ (attenuated psychosis syndrome, APS), and (3) controls without psychopathological diagnoses. Specifically, we used a visual discrimination task based on the spatial frequency (SF) of stimuli. These were presented grouped in blocks according to two conditions in a random order: HSF and LSF. In each block target stimuli consisted of infrequent gratings having a slightly higher or lower SF than their respective standards. During the entire block, subjects were instructed to respond with a button press to the target gratings, which deviated slightly from the attended standard SF. Preliminary results show that the brain activity differed between the three groups in alpha and beta bands of the frequency spectrum. Specifically, patients showed diminished attention-related activity than the control subjects, but APS group exhibited enhanced activity compared to both controls and patients. These results confirm dysfunctions previously found in patients, and shed light over the affection of attentional processes during prodromal stages of the disease. Overall, these findings suggest that there could be different factors underlying visual impairment during early stages of SCZ and that the development of these symptoms may not simply a progressive degradation .

This work is supported by FONDECYT 11140464; Biomedical Neuroscience Institute (BNI); Department of Psychiatry, Clinical Hospital, University of Chile.

27) Psychosocial stress affects goal-directed attention: an integrative multilevel perspective.

Palacios I[1,2], Silva J[3], Bosman C[4], Rodriguez E[1,2], [1]Centro interdisciplinario de Neurociencia, Facultad de Medicina, Pontificia Universidad Catolica De Chile.[2]Laboratorio de Neurodinámica básica y aplicada, Facultad de Psicología, Pontificia Universidad Catolica De Chile.[3]Departamento de Psicologia Universidad del Desarrollo.[4]System and Cognitive Neuroscience University of Amsterdam. (Sponsored by None).

Attention is one of the most important cognitive function on driving cognition. It's being constantly reoriented by means of either top-down or bottom-up factors in a process that can be referred as attentional control. Some studies have suggested that stress-related states like anxiety can disturb the balance between those factors. However the neural mechanism underlying those changes and their potential relationship with the different components of the stress response has not been completely elucidated. Here we search for neural correlates of psychosocial stress during an attentional task and the possible differential influences of the stress components separately. Here we search for neural correlates of psychosocial stress during an attentional task and the possible differential influences of the stress components separately. 42 healthy participants were exposed to either an electroencephalogram-compatible version of the Trier Social Stress Test (TSST) or a control protocol. Additionally, immediately before and after those protocols, participants performed an attentional task. The induced stress response was verified by measuring changes on heart rate, salivary cortisol concentration and the score in the STAI scale (state version). As expected, psychosocial stress induced an increase of salivary cortisol, heart rate and self-reported anxiety. Interestingly, when correct trials between groups after both protocols were compared, correct trials in the control group were associated with an increase of gamma activity (30-65 Hz), usually involved in highly focalized performances. Conversely, correct trials of stress group correlated with an increase of beta activity (12-30 Hz), which is associated with continuous top-down monitoring. Finally, we found that beta activity correlates positively with anxiety and negatively with attentional accuracy. Our results suggest that both groups achieve correct trials by different ways, while participant of the control group were effortless, highly focused on the task, stress group was constantly self-regulating in order to maintain the goal-directed attention.



29) Changes on functional connectivity with neurofeedback based on real-time functional magnetic resonance in autism spectrum disorder.

Pereira J[2,1], Rana M[2,1], Tejos C[4,5,3], Sepulveda P[1,6], Torres R[1], Montalba C[5], Sitaram R[1,2,4], Ruiz S[1,2], [1]Department of Psychiatry Pontificia Universidad Católica De Chile.[2]Laboratory for BMI and Neuromodulation, Interdisciplinary Center for Neurosciences, Pontificia Universidad Católica De Chile.[3]Department of Electrical Engineering Pontificia Universidad Católica De Chile.[4]Institute for Biological and Medical Engineering, Schools of Engineering, Medicine and Biological Sciences, Pontificia Universidad Católica De Chile.[5]Biomedical Imaging Center Pontificia Universidad Católica De Chile.[6]Institute of Cognitive Neuroscience (ICN) University College London. (Sponsored by This Work Is Supported By Department Of Psychiatry And Medicine School, Pontificia Universidad Católica De Chile And CONICYT By Doctorado_ Nacional/2014-21140705, FONDECYT _Regular/1171313 & 1171320 And PIA/Project_ACT1416.)

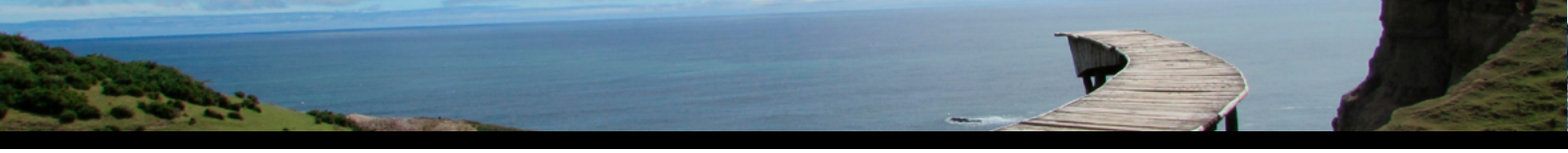
Neurofeedback based on fMRI (fMRI-NF) is a non-invasive approach that allows to achieve self-regulation of circumscribed brain regions, leading to behavioral changes[1]. Abnormal processing of human faces (FP) is associated with an abnormal activity of fusiform face area (FFA) in Autism (ASD)[2]. The aim is to evaluate changes on functional connectivity (FC) associated with tfMRI-NF in ASD. *Methods.* 5 volunteers with ASD (AG) (males; Age= M:16,5; SD:2,1) and 6 healthy adults (males, Age= M:32,3; SD:4,0) participated of 8 training runs of fMRI-NF on 2 training days (1.5 T. Scanner, Philips Achieva, Netherlands). Training run= 4 rest (REST) & 3 self-regulation blocks (UP) (block=30s). AG and 3 healthy volunteers (HG) received visual feedback contingent to the BOLD activity of their FFAs. The rest of the healthy volunteers (CG) received pseudorandomized information as "sham" feedback. *Offline analysis*. Self-regulation achievement was evaluated by rFFA [rFFA=((mean(BOLD_UP)-mean(BOLD_REST))/mean(BOLD_REST))*100]. FC (seed: fusiform cortex) was evaluated by. 1. FC mean of all training (zFC). 2. Slope of FC between both days (ΔzFC). *Results*. HG and AG achieved bilateral FFA self-regulation while CG could not achieve self-regulate FFAs [HG: L-rFFA= M:0.27; SD:0.15; p<0.001; R-rFFA= M:0.19; SD:0.09; p<0.001; AG: L-rFFA= M:0.37; SD:0.12; p<0.001; R-rFFA= M:0.28; SD:0.14; p<0.001]. *FC analysis:* 1. (zFC: P-FDR<0.01; two-sided): HG and AG showed FC with parahippocampal gyrus, inferior temporal gyrus and association visual areas through all training. In addition, HG showed FC with L-amygdala and R-insula. In contrast, CG showed only a FC with association visual areas. 2. (ΔzFC > 0.20): HG and AG showed an increment on FC with right hippocampus and a decrement with anterior cingulate cortex and association visual areas. In addition, HG showed an increment on FC with amygdala, but CG showed a decrement. *Discussion*. Volitional self-regulation of FFA with fMRI-NF is possible in patients with ASD and is associated with neural modulations related with FP. Is pending to study if fMRI-NF training of FFA is associated with an improving on FP in Autism. *References.* 1. Sitaram R, et al. Nat Rev Neurosci. 2017;18(2):86-100. 2. Nickl-Jockschat et al. Brain Struct Funct. May 2014.

31) Detection of ASSR as a function of neural habituation and averaging protocol.

Prado P[1], Martinez E[2], Weinstein A[3], El-Deredy W[3], Zañartu M[1], [1]AC3E Universidad Técnica Federico Santa María.[2]Neuroinformatics Department Cuban Neuroscience Center.[3]Biomedical Engineering Universidad de Valparaíso.

Detection of ASSR is affected by acquisition parameters such as length and the stopping criteria of the recordings. Due to the adaptation of the neural generators, estimation of ASSR also depends on the time at which averaging starts regarding the stimulus onset. The effect of habituation might be enhanced when the standard average of epoch of the raw data is replaced by weighted and sorting average procedures, since they normalize the amplitude and modify the temporal arrangement of the epochs to be averaged as a function of the background noise. We tested this hypothesis by analyzing the time course of the ASSR amplitude obtained with the three averaging protocols. ASSR were elicited in anesthetized adult rats by 8-kHz tones of 50 dB SPL, modulated in amplitude at 115 Hz. Due to the anesthetic, recordings only consisted of free-artifact epochs –i.e. peaks of electrical oscillations exceeding 50 mV were not obtained. Detection paradigms proposed for the clinical practice were implemented and the effect of the habituation on the detection rate of ASSR was analyzed as a function of the averaging protocol. Furthermore, a new acquisition protocol which prevent the ASSR-habituation was tested. Applying standard and weighted-averaging resulted in similar detection rates of ASSR. A lower rate was obtained by applying sorted-averaging when the analysis of the response started simultaneously with the stimulus presentation. Detection rates significantly improved when estimation of the response was performed by averaging only those epochs at which ASSR is not habituated. The greatest improvement was achieved by applying sorted-averaging. When continuous acoustic stimulation is delivered to elicited ASSR, an under-estimation of the ASSR-amplitude can result from applying sorted-averaging since this protocol neglects the habituation of the ASSR neural generators. Detection of ASSR can be remarkable improved by stimulation methods which prevent habituation. Since both weighted and sorted-averaging efficiently cancel artefactual activity, the detection of ASSR can be optimized using adequate combinations of averaging and stimulation protocols.

This work was supported by Advanced Center for Electrical and Electronic Engineering.



33) Electrophysiological correlates of visuospatial working memory: the effect of catecholaminergic imbalance.

Santander D[1], Wainstein G[1], Domic M[1], Valdés J[1], De La Parra A[2], Arias C[2], Brown E[3], Ossandón T[1], [1]Departamento de Psiquiatría, Facultad de Medicina, Pontificia Universidad Católica De Chile.[2]Instituto de Nutrición y Tecnología de Alimentos Universidad de Chile.[3]Neuroscience Statistics Research Lab Technological Institute of Massachusetts.

We have studied Attention-Deficit (AD) symptoms in a population with phenylketonuria (PKU), a metabolic genetic disorder. PKU subjects who have been correctly treated display mild deficits in cognitive functions like attention and working memory (WM) which emulate the symptoms observed in AD. In order to identify electrophysiological characteristics related to their catecholaminergic imbalance, and senses how the specific treatment in each PKU patient could be influencing their neurodevelopment, we studied a cohort of 20 PKU children; 20 children with AD, and 20 Controls. The subjects performed a Visual WM- task, composed by 180 trials coupled with Eye-Tracking (ET) and high-density Electroencephalographic (EEG) recording. In addition, we used the Expectation Maximization (EM) algorithm previously developed by Anne Smith and her co-workers, to establish a Learning Process (LP) in each subject during the WM task. With this, we could obtain the statistical definition of a Learning-Trial (LT), i.e. the specific trial during the subject develops an inherent LP and is sustained throughout the rest of the task. We are analyzing the neural dynamic on EEG and ET individually by subject, and between PKU, AD; and control groups, focusing on changes observed before, during, and after LT established, and comparing the results with the characteristics of their treatment. According to our first analysis, throughout the EM we could found 3 categories of subjects´ performance: A higher one, accompanied of an early LT; A lower performance without LT; and The highest performance without LT, outlining a LP and a strategy before the beginning of the task. In PKU subjects with higher performance and better treatment, these findings are coupled with a higher power in Beta bands in EEG during the presentation of trials with an emotional distractor, and a higher power in lower frequencies (delta, theta) during the trials with the presentation of neutral distractors. On the other hand, in PKU subjects with lower performance and without LT, a higher variability is observed both in EEG and pupillometric dynamics. So far, the first approach in AD and Control groups has confirmed the lower variability in parameters previously mentioned, comparing to the PKU children.

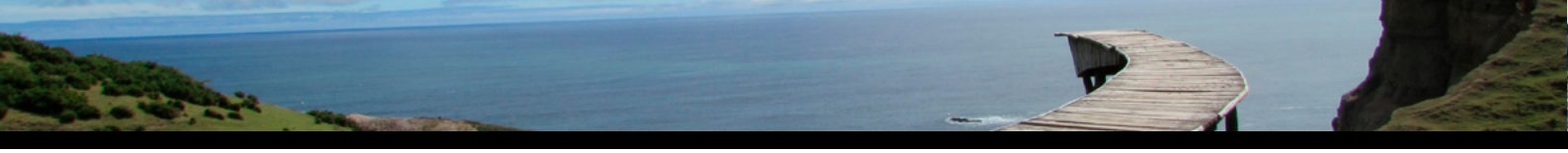
Research supported by Becas de Doctorado Nacional, año 2017 of CONICYT scholarship: 21150295 and FONDECYT regular: 1140996.

35) The changes in brain self-regulation due to reward observed through an fNIRS Brain-Machine Interface.

Thakkar I[1], Lagos W[2], Sulzer J[3], Torres R[4], Sitaram R[5], Ruiz S[6], Rana M[7], [1]Department of Neuroscience Pontificia Universidad Católica De Chile.[2]Department of Psychotherapy Pontificia Universidad Católica De Chile and Universidad de Chile.[3]Department of Mechanical Engineering University of Texas at Austin..[4]Department of Psychiatry, School of Medicine, , Pontificia Universidad Católica De Chile.[5]Department of Neuroscience and Department of Psychiatry, Faculties of Biology, Engineering and Medicine, Pontificia Universidad Católica De Chile.[6]Department of Neuroscience and Department of Psychiatry, School of Medicine, Pontificia Universidad Católica De Chile.[7]Department of Neuroscience and Department of Psychiatry Pontificia Universidad Católica De Chile.

Neurofeedback (NF) has been shown to typically work by pre-selecting a specific brain region or set of regions whose online signals are used as visual or other forms of feedback to train participants to control brain activity over several training sessions, often with specific instructions of mental strategies for control, and sometimes with additional reinforcements such as monetary reward based on concepts of instrumental conditioning. The learning process involved in achieving such brain self-regulation is presumed to be related to several factors such as type and contingency of feedback and reward, the use of mental imagery, duration of training, among others. Giving monetary reward proportional to performance is assumed to act as reinforcement for improving brain self-regulation. Prior work has shown that performance of a motor task improves with increasing incentives, while very high levels of incentives lead to the paradoxical consequence of worse performance. In the case of brain self-regulation, our recent data suggests that monetary reward enhances the magnitude of up-regulation of the activity in the Supplementary Motor Area (SMA) by NF training; however, this learned increase drops drastically when online feedback is removed. The above evidence raises an important question: whether there exists an optimal schedule or amount of reward that improves self-regulation learning, yet continues to maintain a level of control even after the feedback signal is retired. To answer the above question, we are conducting NF training in 3 groups of healthy participants, each group randomly assigned with 5 participants, to volitionally control brain activity in the SMA with 3 reward schedules: low, moderate and high reward. In the present study, we manipulate the level of reward rather than the frequency of reward presentation. The 3 groups are being trained with identical experimental instructions and real-time fNIRS-NF BMI (Brain-Machine Interface). Training effects in terms of brain and behavioral changes are tested by identical pre- and post-tests, namely, 2 transfer runs without feedback, and a self-paced finger-tapping task to assess motor response. During the first phase of the project, the fNIRS-NF system with different reward schedules (levels) has now been established and tested on volunteers (figure 1). The ongoing study is conducting the neurofeedback training in the 3 groups of participants. The results of this project will give insight into whether such an optimal reward does exist if it varies among individuals, and how it affects the learning curve and consequent changes in brain activity, in comparison with other reward schedules.

Department of Psychiatry and School of Medicine, PUC; FONDECYT Regular (Projects n° 1171313 & 1171320); Seed Fund: The Cockrell School of Engineering, UT Austin and PUC.



37) Aging alters performance in a visual attention task with auditory distractors in Alpha-9 Nicotinic Receptor Subunit Knock-Out Mice.

Vicencio S[1], Jorratt P[1], Terreros G[2], Delano P[1,3], [1]Neurociencias, Medicina, Universidad de Chile.[2]Instituto de Ciencias de la Salud Universidad de OHiggins.[3]Departamento de Otorrinolaringología Hospital Clínico de la Universidad de Chile.

The auditory efferent system in mammals is a network that originates in the auditory cortex and projects to the cochlear receptor through olivocochlear bundle, and it has been proposed to work as a top-down filter of peripheral auditory responses during attention to cross-modal stimuli. The synapses that medial olivocochlear neurons make with outer hair cells (OHC) are cholinergic and mediated by nicotinic receptors, that are constituted by α9 and α10 subunits. This is the final pathway from de central nervous system to the OHC and one of the physiological function of the α9 receptor is the suppression of auditory distractors during selective attention to visual stimuli. In this regard and in a recent study, we showed that selective attention to visual stimuli, in presence of auditory distractors, is altered in alpha-9 nicotinic receptor subunit (α9-nAChR) knock-out (KO) mice. In the current work, we decided to explore the effects of aging on the behavioral performance of α9-nAChR KO micein a two-choice visual discrimination task, in presence of auditory distractors (clicks and 15 kHz tones, and broad-band noise). We found that, in the presence of auditory distractors, one year old KO mice make fewer correct responses, omit a larger number of trials and make more perservative errors than younger KO mice (60-80 days). This type of errors reflect impulsive behaviors, which must be inhibited during attention. Thus, all of these results suggest that older KO mice have an increased impulsivity during decision making in the presence of auditory distractors.

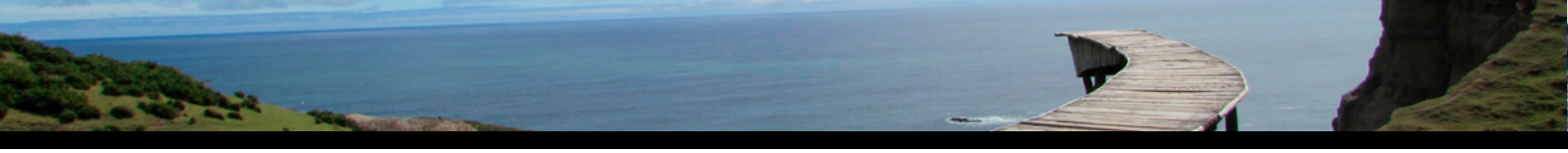
Funded by Proyecto Anillo ACT1403, Fundación Puelma.

39) Pupil diameter as a marker of Noradrenergic system dysfunction in ADHD during a working memory task.

Wainstein G[1], Rojas-Líbano D[2], Crossley N[1], Carrasco X[3], Aboitiz F[3], Ossandón T[3], [1]Psiquiatria, Medicina, Pontificia Universidad Católica De Chile.[2]Laboratorio de Neurociencia Cognitiva y Social, , Facultad de Psicología, Universidad Diego Portales,.[3]Servicio de Neurología y Psiquiatría, Facultad de Medicina, Universidad de Chile. (Sponsored by Our Research Was Supported By CONICYT, FONDECYT 1140996).

Attention deficit hyperactivity disorder (ADHD) is the most prevalent childhood neuropsychiatric disorder that has been linked to problems in selective attention and catecholaminergic systems. Therefore, first-line treatment for ADHD consists in norepinephrine-dopamine reuptake inhibitors (e.g. methylphenidate) which increase catecholamine availability at synapses. Despite its effectiveness, there is no objective diagnosis criteria. Nevertheless, a promising marker of cognitive states is pupil size. In fact, it correlates with task difficulty and arousal states. Moreover, findings suggest that pupil diameter (PD) dynamics reflect the activity of the locus-coeruleus norepinephrine (LC-NE) system which projects throughout the cerebral cortex, hippocampus and thalamus, among others. We hypothesized that changes in PD responses during an attentional task should reflect the differences observed in the system activity between ADHD patients, control subjects and the effect of methylphenidate. To evaluate this, we used a visuo-spatial working memory (VSWM) task, that tests the ability to retain information about the spatial arrangement of items presented visually to 50 children. 28 diagnosed with ADHD (aged: 10.71 ± 0.54); 22 belonged to a non-ADHD control group (aged: 11.58 ± 0.50); and a sub group of 17 ADHD patients (aged: 11.19 ±0.86) did the task twice, on and off methylphenidate. They performed a Sternberg-type delayed VSWM task. PD were recorded with an eye-tracker (Eye-link 1000, SR Research) at 1000 Hz. There were significant differences in the maximum PD amplitude between ADHD group to on-medication ADHD and Control group. Furthermore, the maximum PD value was inversely associated with the variability in the subject reaction time ($r = -0.726$, $p < 0.001$). Moreover, the maximum pupil diameter was directly associated with the subjects' performance in the task ($r = 0.659$, $p < 0.001$). Finally, performance was inversely associated with the variability in reaction time ($r = -0.725$, $p < 0.001$).For the first time, as far as we know, a direct and strong correlation between a marker of noradrenergic signaling and its direct relation to behavior in ADHD condition is shown. Additionally, we found a link between reaction time variability – the most reported marker of inattention in ADHD condition- and pupil diameter. Finally, this is the first evidence of a treatment modulation in ADHD's noradrenergic system during an attentional task, which could be used as a biomarker for further research, clinical and diagnostic applications.

Our research was supported by CONICYT, FONDECYT 1140996.



41) Lexical incongruence detection inschizophrenia.

Zepeda-Rivera L[1], Alonso-Sanchez M F[1], González J[1], Prado P[2], Aguilar M[1], [1]Escuela Fonoaudiología, Salud, Universidad Santo Tomás.[2]Centro avanzado de ingeniería eléctrica y electrónica , Ingeniería electrica , Universidad Técnica Federico Santa María.

The lexical processing in schizophrenia has been extensively studied, however a heterogeneous results has been observed. It has been argued that these differences are due to the experimental paradigm. In this line, it is necessary to evidence the performance of this group using an experimental paradigm that allows to compare the performance and the amplitude of the components in sentences that present incongruities inside and outside the lexical field. Due to this, the aim of this study was to detect and compare lexical processing in people diagnosed with schizophrenia and healthy controls, using event-related potentials (ERP) with elicitation N400 components. The study was carried out with three sentence conditions; Type 1 correct sentences “The child slept in his little crib”, type 2 incongruous sentences within the same semantic field “We make the bed with sheets and mattresses”, type 3 sentences incongruous with a word outside the lexical field “I played the piano from the Fifteen beetles “. The test was performed using a 64-channel EEG biosemi, the data were analyzed with the Brain Vision Analyzer program, the artifacts were removed with ICA (Independent Component Analysis). In the results we observed a greater amplitude of the N400 for type 2 sentences in the control group compared to the group with schizophrenia. These differences were not observed in type 3 sentences between subjects and controls. These results suggest that when inconsistencies are part of the same lexical field they are more difficult to identify by the schizophrenic group.

FONDECYT 11160212.

43) On the search of retinal Neural Ensembles.

Mora S[1], Herzog R[1], Palacios A[1], [1]CINV, Ciencias, Universidad de Valparaíso.

Neural ensembles are a strongly interconnected group of neurons activated by a sequential order of firing (Hebb 1949). However, even when this concept was proposed more than 60 years ago, only recently, the simultaneous recordings and analysis from hundreds of cells have turned out to be possible. Moreover, most of the effort to understand neuronal ensembles have been devoted, so far, to the cortex (Miller, 2014, Carrillo-Reid et al., 2015; Montijin et al., 2016). However, to the best of our knowledge at the time, little is known about their presence and function at the level of the retina –an accessible part of the central nervous system that communicates directly to the brain. Here we use both a multi-electrode array technique (USB-256 electrodes) for the recording of retinal ganglion cells (RGC) from a diurnal rodent and computational tools (e.g. Carrillo-Reid et al., 2015) to search for the presence and characteristics of retinal neural ensembles under different light conditions: I) spontaneous activity in the dark; II) full field light stimulation; III) white noise; IV) natural movie. After we validated our computational tools using synthetic data, we carried out a preliminary assessment to identify the occurrence of neural ensembles in the retina of Octodon degus, a diurnal rodent model for aging and neurodegeneration. A preliminary analysis from 270 recorded RGC under a repeated short natural movie (30s per trial) as stimulus suggests the presence of 10 different synchronic neural ensembles with significant synchronous activity ($P<0.01$). We found that the mean of neural ensembles in spontaneous and light evoked conditions doesn't differ significantly. These results are consistent with previous work in the mouse visual cortex V1, suggesting that the presence of retinal neural ensembles structures can be part of a mechanism of population coding. Nevertheless, the complete characterization and understanding of retinal neural ensembles need to be further established.

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ICM-P09-022-F Millennium Scientific Initiative of the Ministerio de Economía, Desarrollo y Turismo (Chile).
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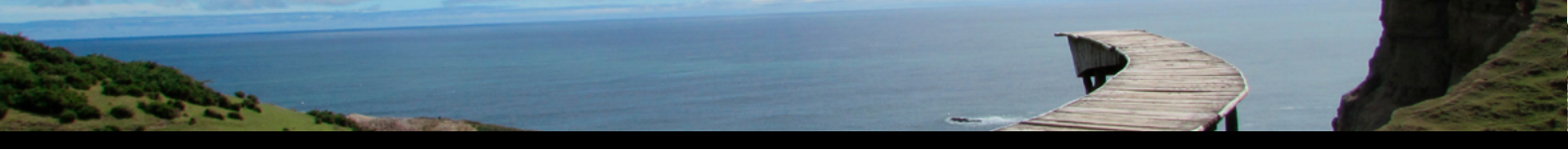


45) Light/dark cycles modulate asymmetric parapineal connectivity to the left habenula in zebrafish larvae.

Palma K[2,4,1,3], Meynard M[2,1], Cornejo V[2], Cerda M[4,1], Jara J[4,1], Härtel S[4,1], Concha M[2,1,3], [1]Biomedical Neuroscience Institute, Facultad de Medicina, Universidad de Chile.[2]Laboratory of Experimental Ontogeny, Departamento de Anatomía y Biología del Desarrollo, ICBM, Facultad de Medicina, Universidad de Chile.[3]Centro de Envejecimiento Salud Mental y Metabolismo Gero, departamento de biología, Facultad de Ciencias , Universidad de Chile.[4]SCIAN-Lab, Departamento de Anatomía y Biología del Desarrollo, ICBM, Facultad de Medicina, Universidad de Chile.

Introduction: Parapineal (PpO) neurons develop asymmetric connectivity to the left habenula (lHb) in the dorsal diencephalon of embryonic and larval zebrafish. Recent studies relate this asymmetric connectivity with sensory responses to light. However, the structural and functional bases of this behaviour are still unknown. To begin addressing this issue we investigated the axonal structural configuration and distribution of pre-synaptic proteins in PpO-lHb projections of zebrafish larvae searching for plastic changes modulated by light.

Material and Methods: PpO-lHb connectivity was visualised by confocal microscopy in dissected brains of *Tg(foxd3:GFP)* zebrafish larvae maintained under different Light (L) and Dark (D) conditions: (a) cycles of 14L and 10D hours [L:D], (b) continuous dark [D:D], and (c) continuous light [L:L]. After fixation, anti-GFP and anti-SNAP-25 inmunofluorescence were performed in peeled brains and confocal images acquired. 3D image analysis included manual/automatic segmentation, computing shape descriptors of PpO projections, and pre-synaptic puncta quantification.

Results: PpO projections show a characteristic morphology that undergo rhythmic changes in larvae subject to L:D cycles, particularly during the L-D and D-L transitions. Also, the number and composition of pre-synaptic protein expression in the PpO-lHb circuit show rhythmic remodelling two hours before the L-D and D-L transitions. This features were not found in the D:D and L:L conditions.

Discussion: These results suggest that the PpO-lHb circuit in zebrafish larvae responds to Light:Dark rhythmical changes through a mechanism of plasticity, generating structural and synaptic remodelling of PpO projections.

POSTDOCTORADO FONDECYT (3150540), FONDECYT (1151029, 1161274), FONDEQUIP (EQM140119, EQM130051) CORFO (16CTTS-66390), DAAD (57220037 & 57168868), FONDAP 15150012, CONICYT PIA ACT1402.

47) Epithalamic asymmetries: comparative approach of neurogenesis in zebrafish and medaka.

Ríos J[1,3,2,4], Signore I[1,3,2,4], Concha M[1,2,3,4], [1]Laboratory of Experimental Ontogeny, Faculty of Medicine, Universidad de Chile.[2]Instituto de Ciencias Biomédicas Universidad de Chile.[3]Biomedical Neuroscience Institute Universidad de Chile.[4]Center for Geroscience, Brain Health and Metabolism Universidad de Chile.

In this project we followed a comparative developmental approach of the epithalamic asymmetries of zebrafish (*D. rerio*) and medaka (*O. latipes*) to identify conserved and specie-specific ontogenic mechanisms between these teleosts.

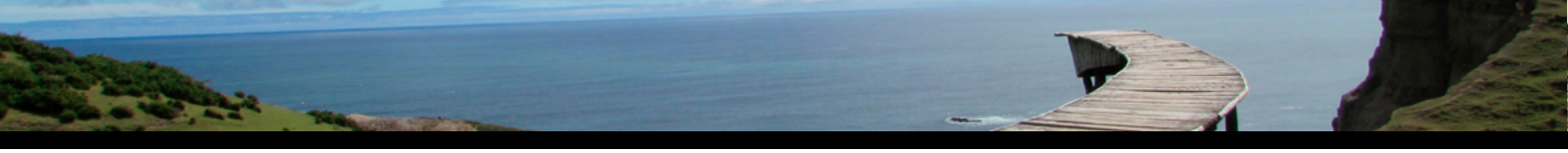
Both species show a conserved asymmetric morphological pattern in their epithalamus, characterized by (i) positioning of the parapineal organ (PpO) on the left side with efferent projections toward the ipsilateral habenular nucleus (Hb) and (ii) a left Hb that develops more neuropil than the right Hb.

Axonal projections from the PpO to the left Hb in both species show differences in their morpho-topological organization, which are described as heterotopic shifts. On the other hand, studies of the temporal dimension of epithalamic asymmetries using a method for time normalization based on the rate of somitogenesis reveal that PpO projections start earlier in medaka than in zebrafish, a phenomenon described as heterochronic shift.

Habenular neurogenesis starts first in the left habenula and this asymmetry is independent of the presence of PpO. On the other hand, proliferation of precursor cells starts in the left habenula and this is responsable of the generation of asymmetry in the ratio of lateral and medial subnuclei. These asymmetries are detectable by expression of genes like *lov* and *ron* and depend on the presence of the PpO.

In this study we found that *lov, ron* and other habenular markers show heterotopic changes while they conserve the onset of their temporal expression. We propose that if the PpO dependent and independent patterns of habenular asymmetry are conserved in both species, then habenular neurogenesis in medaka should initiate asymmetrically as is observed in zebrafish and at the same normalized time. On the other hand, considering the heterochronic projection of the PpO, the onset of asymmetric proliferation should be anticipated in medaka. However, we found that although the asymmetric pattern is conserved, habenular neurogenesis in medaka is anticipated compared to zebrafish and occurs before the onset of PpO projections to the left Hb. These results indicate a possible additional heterochronic shift in the development of the PpO-Hb circuit and/or the presence of a new ontogenetic relation between asymmetric neurogenesis in the Hb and PpO development.

FONDECYT (1161274), ICM P-09-015-F, CONICYT PIA ACT1402, FONDAP 15150012.



49) Activity of monomeric GTPases Rab5 and Rab11 is increased by BDNF stimulation in cortical neurons.

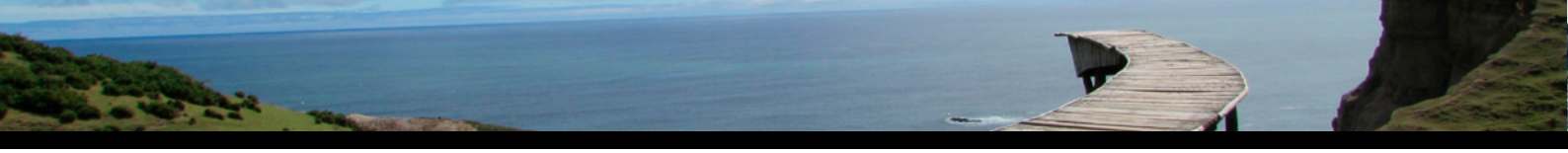
Stuardo N[1], Moya G[1], Bronfman F[1], [1]Departamento de Fisiología , Facultad de Ciencias Biológicas , Pontificia Universidad Católica De Chile.

Endocytosis and intracellular trafficking of the acquired cargo are highly regulated processes. In neurons, these processes are especially important in the transport of endocytosed neurotrophin receptors, such as TrkB. TrkB is the receptor that binds Brain Derived Neurotrophic Factor (BDNF), a trophic factor involved in neuronal differentiation, dendritic branching and growth. When BDNF binds its receptor, it is endocytosed, and its transported within the endocytic pathway. 2 important proteins that regulate the traffic within the endocytic pathway are Rab5, which regulates the transport in the early endocytic pathway, and Rab11, which regulates the recycling pathway. In order to be able to study the effect of BDNF over these 2 proteins, fusion GST proteins that recognize active Rab5 and Rab11 were produced and then used to detect said proteins by “in situ” fluorescence assay and pull down assay on 9 and 7 DIV neurons respectively. The results showed that stimulating with BDNF for 30 minutes increases the activity of Rab5 and Rab11, which suggests that BDNF should increase the early and recycling transport of TrkB within the neuron .We have also found that the activity of Rab5 is partially inhibited in a pull down assay by the use of K252a, a tyrosine-kinase receptor inhibitor. The use of this inhibitor also partially inhibited the formation of giant endosomes that is observed when stimulating with BDNF for 30 minutes in “in situ” detection assays. We are currently studying the effect of BDNF on Rab7, the GTPase in charge of transport within the endolysosomal pathway.

51) Effect of glucocorticoids acting at the insular cortex in anxiety

Bahamonde T[1], Tamburini G[1], Quintana D[1], Díaz R[1], Stehberg J[1], [1]Laboratorio de Neurobiología Universidad Andrés Bello. (Sponsored by FONDECYT 1160986).

Anxiety is one of the most prevalent symptoms among psychiatric and neurological disorders. Glucocorticoids (GCs) are steroid hormones released after stress that have a plethora of effects, including the modulation of anxiety levels, but the mechanisms by which GCs modulate anxiety have not been elucidated. To study the effects of GCs in anxiety, GCs were manipulated within the insular cortex, an area that has been recently found to modulate anxiety. To determine the effect of GCs microinjected into the insular cortex of rats in anxiety, corticosterone, corticosterone-BSA, as well as mineralocorticoid (MR) and glucocorticoid (GR) receptor antagonists were microinjected into the insular cortex, and anxiety levels were assessed using the elevated plus maze. Intra-insular administration of GCs produced both anxiolytic and anxiogenic effects depending on the amount of corticosterone injected. Intra-insular microinjection of corticosterone linked to BSA showed anxiogenic effects, while MR antagonist spironolactone induced anxiogenic effects. GR antagonist mifepristone had no effects on anxiety. Our results suggest that GCs in the insular cortex modulate anxiety, having both anxiogenic and anxiolytic effects depending on the amount of corticosterone injected. Furthermore, their anxiogenic effects may be mediated by a membrane-dependent mechanism, while their anxiolytic effects may be mediated by the activation of mineralocorticoid receptors.



53) Targeting astrocytes for antidepressants.

Cornejo F[1], Duarte Y[1], Méndez M[1], Quintana D[1], Olivares P[2], Stehberg J[1], [1]Laboratorio de Neurobiología Universidad Andrés Bello.[2]Laboratorio de Fisiopatologia Celular y Molecular Universidad Andrés Bello. (Sponsored by FONDECYT 1160986).

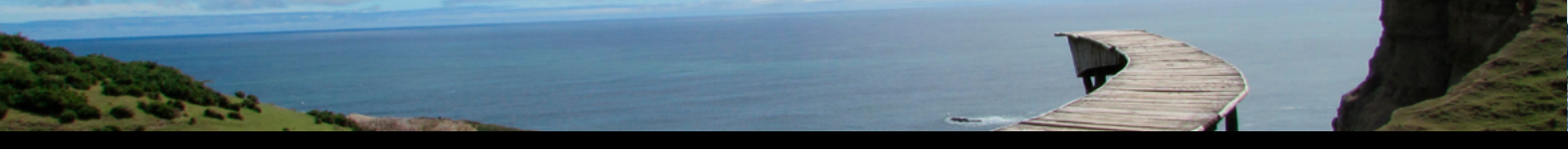
Astrocytes participate in synaptic communication by releasing “glio”-transmitters into synapses, via several mechanisms, which include connexin 43 (Cx43) hemichannels (HCs). Previous studies suggest that chronic restraint stress, a rodent model commonly used to induce depression-like symptoms, induces exacerbated astroglial Cx43 HC activity associated to increased glutamate and ATP release, in the hippocampus, a depression-relevant brain region. Hence, we decided to test whether astroglial Cx43 HCs could be targeted for the development of antidepressant molecules. First, we tested the potential antidepressant effects of TAT-Cx43L2 peptide, a mimetic peptide which blocks specifically Cx43 HCs, microinjected into the hippocampus. Incubation of hippocampal slices with TAT-Cx43L2 peptide induced decreased NMDA currents, which could be prevented by the addition of glutamate. Then, using molecular docking and structure-based virtual screening, we were able to identify one small molecule from public small molecule libraries, which was successful in blocking Cx43 HCs *in vitro*; Cacotheline. It significantly reduced Cx43 HCs activity in Cx43-transfected Hela cells, and it also showed antidepressant effects in a rat model of depression. Our results suggest that Cacotheline-derived molecules could be useful in the treatment for depression.

55) Individual differences on dorsolateral striatum single unit activity during amphetamine repeated administration.

Gatica R[2,1], Aguilar-Rivera M[3], Fuentealba J[2,1], [1]Centro Interdisciplinario de Neurociencia Pontificia Universidad Católica De Chile.[2]Laboratorio de Neuroquímica, Departamento de Farmacia, Facultad de Química, Pontificia Universidad Católica De Chile.[3]Department of Bioengineering University of California, San Diego. (Sponsored by Sponsored By FONDECYT N° 1141088, CONICYT-PCHA Doctorado Nacional 2016-21161366 And Concurso De Apoyo Para El Desarrollo De Tesis De Post-grado 2016 PMD-05/16.).

About a 15-17% of the subjects exposed to drugs of abuse progress to a chronic pathological use. In the behavioral sensitization model, a half of the animals develop and express locomotor sensitization after repeated drug administration. It has been observed that these individual differences in response to repeated exposure to drugs are associated with the persistence of neuroplastic changes in the nucleus accumbens only in addicted rats. The dorsolateral striatum (DLS) has a key role in habit acquisition. The increase of dopamine levels in the DLS after psychostimulant administration is correlated with the establishment of habitual drug seeking behavior. However, if DLS neuronal activity is modified is unknow. In this work, we studied the single unit activity of the DLS during amphetamine (AMPH) repeated administration. Rats were implanted with a custom made manipulator to control the positioning of an eight-tetrode array in the DLS. After surgery recovery, rats were once daily injected with AMPH 1,0 mg/kg i.p for five consecutive days. After four days of withdrawal, rats were injected with AMPH 1,0 mg/kg i.p to assess the expression of locomotor sensitization (day 10). DLS neural activity and rat locomotor activity were daily recorded before and after AMPH injection. A rat that at least doubled their locomotor activity in day 10 compared to day 1 was considered sensitized (if not, it was considered non-sensitized). The main findings are: 1) Basal firing rate and burst frequency of DLS neurons were significantly higher in the non-sensitized rats compared to sensitized rats, in all the recorded days; 2) Non-sensitized rats showed a decrease in the percentage of neurons that increased their firing rate after AMPH injection in day 2 compared to the other days on the same group and sensitized rats on day 2; 3) Non-sensitized rats have a higher percentage of neurons that did not change their firing rate after AMPH injection in day 2 and 10, compared to sensitized rats. These data suggest that an increased neural activity in the DLS is associated with a protective phenotype against AMPH sensitization, and also that protective neuroadaptations are observed early during amphetamine repeated administration.

Sponsored By FONDECYT N° 1141088, CONICYT-PCHA Doctorado Nacional 2016-21161366 and Concurso de Apoyo para el Desarrollo de Tesis de Post-grado 2016 PMD-05/16.



57) Palmitic acid induces hypothalamic inflammation through the activation of G-protein coupled receptor 40 (GPR40).

Hernández-Cáceres M[1], Morselli E[1], [1]Physiology, Biological Sciences, Pontificia Universidad Católica De Chile. (Sponsored by FONDECYT 1160820)

Introduction: Chile is the most obese country in South America, with a 27.8% prevalence of obesity. Chronic consumption of high fat diets, rich in saturated fatty acids (SFAs), is associated with obesity increase, which leads to chronic low-grade inflammation in the central nervous system (CNS). SFAs, such as palmitic acid (PA), accumulate into the CNS and activate an inflammatory response within the hypothalamus, the brain region that regulates food intake and energy balance. PA activates the G protein–coupled receptor 40 (GPR40), leading to intracellular Ca^{2+}mobilization, which might promotes inflammation and, in consequence, neuronal damage. However, whether GPR40 is involved in PA-induced hypothalamic inflammation is unknown. We **hypothesize** that *palmitic acid stimulates GPR40 promoting inflammation in hypothalamic neurons.*

Methods: Since neurons, astrocytes and microglia are implicated in diet-induced hypothalamic inflammation, we corroborated by immunofluorescence, in coronary brain sections of C57BL/6 male mice, the presence of GPR40 in these cells. In vitro, experiments were performed in the hypothalamic neuronal cell line N43/5 exposed to pro-obesigenic concentration of PA, in presence or absence of the GPR40 antagonist GW1100. To assess PA-mediated GPR40 activation, changes in intracellular Ca^{2+} levels were evaluated using Fura 2-AM. To confirm the functionality of the receptor, cells were stimulated with a GPR40 agonist GW9508. Inflammation was assessed by quantification of pro-inflammatory cytokines by qPCR. Statistical analyses were performed with ANOVA and post-test Bonferroni. **Results:** GPR40-positive cells were observed in the hypothalamus of chow mice, with GPR40 colocalized only with neuronal markers. The increase in intracellular Ca^{2+} induced by PA and GW9508 was abolished in cultures pre-incubated with the GPR40 antagonist, GW1100. PA induced an increase in pro-inflammatory cytokines (Il6 and Tnfa), which was partially reversed by GW1100.

Conclusions: These data suggest that PA-mediated GPR40 activation leads to enhanced inflammation, which can be directly related with dysregulated hypothalamic neuronal function and with the onset of obesity-associated diseases.

59)Sleep/wake disorders and the hypocretin/orexin system in a zebrafish model of Parkinson's Disease.

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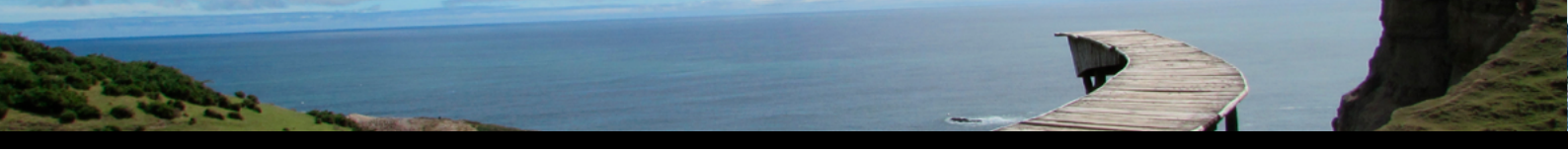
Introduction: Sleep/wake alterations are non-motor symptoms present in various neurological disorders including Parkinson's Disease (PD). Hypocretin/orexin, whose deficit is the main cause of narcolepsy, is involved in sleep/wake regulation. Since zebrafish is a suitable model for PD and sleep/wake behaviour, we evaluated the sleep/wake changes associated with alterations in the hypocretin (Hcrt) system in a PD zebrafish model.

Material and methods: We challenged 2 dpf zebrafish larvae with 6-hidroxidopamine (6-OHDA) during 72 hours using WT and *Tg(Hcrt:EGFP)* lines. Dopaminergic and Hcrt neurones were examined and quantified by anti-tyrosine hydroxylase (TH), anti-GFP immunostaining and confocal imaging. TH neurons were also observed by *in situ* hybridisation. Locomotor activity during day and night was measured with an automated tracking video system (TrackFish).

Results: The number of expressing TH (protein and mRNA) and Hcrt neurons decreased after 6-OHDA. The diencephalic 5-6-11 groups of aminergic cells, which resemble the mammalian substantia nigra, were sensitive to 6-OHDA. We found defects in zebrafish locomotor activity, i.e. distance travelled and swimming speed and sleep/wake pattern. Locomotion, but not number of TH neurons, improved after two-day recovery following 6-OHDA.

Discussion: Results suggest that 6-OHDA induces a behavioural disorder in zebrafish larvae. Alterations may arise from a reduced 5-6-11 dopaminergic population and/or be secondary to the reduced number and activity of Hcrt neurons.

POSTDOCTORADO FONDECYT (3150540), FONDECYT (1151029, 1161274), FONDEQUIP (EQM140119, EQM130051) CORFO (16CTTS-66390), FONDAP 15150012, CONICYT PIA ACT1402.



61) Characterization of a presymptomatic stage in a Drosophila Parkinson´s disease model: unveiling dopaminergic compensatory mechanisms

Molina-Mateo D[1], Fuenzalida-Uribe N[1], Hidalgo S[1], Molina-Fernandez C[1], Abarca J[1], Escandon M[2], Figueroa R[2], Tevy F[2], Campusano J[1], [1]celular biology, biological Sciences , Pontificia Universidad Católica De Chile.[2]Centro de Genómica y Bioinformática, Facultad de Ciencias, Universidad Mayor. (Sponsored by FONDECYT 1141233)

Parkinson disease (PD) is a neurodegenerative disorder characterized by several motor symptoms including shaking, rigidity, slowness of movement and difficult walking, which has been associated to the death of 70-80% nigro-striatal dopaminergic neurons. More than 90% of PD patients also present olfactory dysfunction in early stages. Although, the molecular mechanisms responsible for this disease are not clear, hereditary PD is linked to mutations in specific genes including, the PTEN-induced putative kinase 1 (PINK1) a mitochondrial protein. In this work we use single male flies to provide for the first time a thorough temporal description of the behavioral effects induced by a mutation in the PINK1 gene in adult *Drosophila*, a previously described animal model for PD. For doing this, we used a methodology previously reported (Colomb et al, 2012). Our data suggests that the motor deficits associated to PD are fully revealed only by the third week of age. However, olfactory dysfunction is detected as early as the first week of age. We also provide immunofluorescence and neurochemical data by using Fast-Scan Cyclic Voltammetry and HPLC that let us propose for the first time the idea that compensatory changes occur in this *Drosophila* model for PD. We found that these compensatory changes are associated to two specific components of the dopaminergic system: an overactive Dopa decarboxylase, the enzyme responsible for the last step in dopamine biosynthesis, and the increased expression of the plasma membrane Dopamine transporter, involved in maintaining the extracellular levels of dopamine in the synapse at physiologically relevant levels in early states of this animal model of PD. Thus, our behavioral, immunofluorescence and neurochemical data help define for the first time presymptomatic and symptomatic phases in this PD animal model, and that compensatory changes occur in the dopaminergic neurons in the presymptomatic stage.

63) Neuroprotective effect of Chronic Spinal Cord Stimulation (SCS) in an α -synuclein model of Parkinson's disease

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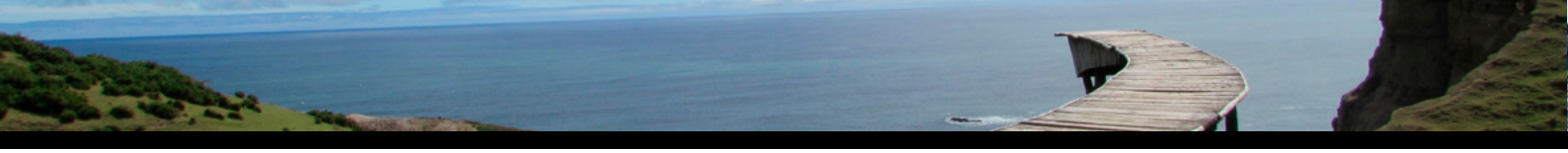
Parkinson's Disease (PD) is a neurodegenerative disorder characterized by the presence of inclusions in dopaminergic neurons from substantia nigra, known as Lewy bodies, and the progressive loss of these neurons. The protein α-Synuclein (α-syn) constitutes one of the main components of the Lewy bodies in sporadic cases of PD. Animal models overexpressing α-syn exhibit neuronal degeneration and abundant α-syn- positive inclusions, which recapitulates essential neuropathological features of PD. On the other hand, chronic Spinal Cord Stimulation (SCS), a neuromodulation technique consisting in the epidural delivery of electrical pulses in the dorsal portion of the spinal cord, has emerged as a potential treatment of PD. SCS showed to be very effective alleviating parkinsonian motor symptoms both in animal models and patients. Evidence collected in both the classical 6-OHDA neurotoxin and the α-syn animal models of PD, suggest that SCS could have long-term effects associated to neuroprotection. Neurotrophic factors, i.e. the Vascular Endothelial Growth Factor (VEGF), have been shown to support the survival of many neuronal populations both in culture and pre-clinical models of PD. Our research focuses in the study of the neuroprotective mechanisms that could be involved in the improvement of the motor performance of an α-syn animal model of PD submitted to chronic spinal cord stimulation. We used an α-syn animal model corresponding to Sprague Dawley male rats injected unilaterally in the substantia nigra with adenovirus AAV6-α-syn. Four weeks after the viral injection, rats were treated with high-frequency (300 Hz) SCS during five weeks, two sessions/week. Assays of immunohistochemistry showed that chronic SCS modulates the expression of vascular endothelial growth factor (VEGF) in the nigro-striatal pathway. This suggests that chronic SCS might exert neuroprotective effects through the regulation of VEGF, which is known for angiogenic and pro-survivalfunctions.

FONDECYT 1151478, NuMIND Millenium Nucleus NC130011 and BNI Millenium Institute P09-015-F



65) Interaction of neuropeptides DYN-A1-13 and orexin-A in the selection and intake of palatable foods.

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The hypothalamic orexin/dynorphin (ox/dyn) neurons regulate homeostatic and hedonic food intake. These neurons co-express and co-release the orexin and dynorphin (DYN) neuropeptides. Although orexin and opioid DYN peptides can independently increase food intake, whether their interaction is relevant for the control of homeostatic and hedonic food intake is unclear. The aim of these studies is to determine the role of the interaction between neuropeptides orexin and opioid DYN-A_{1-13} in the paraventricular nucleus (PVN) on food intake and choice. Balb/c mice cannulated aiming at PVN were injected with opioid DYN-A_{1-13} (0, 0.75 nmol), orexin-A (0, 0.25 nmol) and their combination when mice had access to chow or simultaneous access to palatable snacks and chow. The results show that when mice only had access to chow, DYN-A_{1-13} increased intake while orexin had no effect. However, when mice had simultaneous access to chow and palatable snacks, DYN-A_{1-13} selectively increased snack intake while orexin-A decreased snack and increased chow intake. The combination of both peptides did not have a significant effect on total food intake. These data suggest that these neuropeptides have differential effects on food selection and intake. Currently, we aredetermining the contribution of endogenous DYN signaling to the formation of snack preferences and the effects of orexin-A on food intake and choice. Together, these studies will illuminate how the orexin and opioid DYN peptides regulate food intake and choice. This research was supported by grant FONDECYT Regular 1150274 (CONICYT, Gobierno de Chile).

67) D-serine from medullary brainstem astrocytes is mediates the breathing response to hypercapnia.

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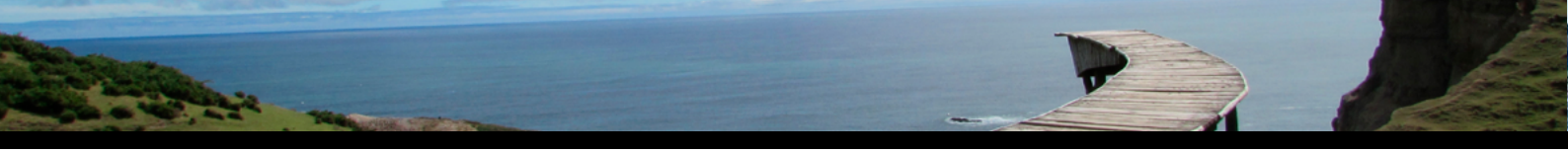
Previously, we show that D-serine (D-ser), an endogenous co-agonist for NMDAr in CNS, modulates fictive respiration in *in vitro* preparations from mouse neonates. Now, we have evaluated the effects of D-ser in breathing modulation i*n vivo* and the role of medullary brainstem astrocytes in hypercapnic response mediate by D-ser.

Modulation of respiratory rhythm by D-ser in unrestrained and awake CF1 adult mice was evaluated using whole-body plethysmography after a single intraperitoneal (i.p.) or after stereotaxic injection within raphe nucleus (RN) performed through a pre-implanted guide cannula. D-ser (250 mg/kg i.p.) increased the minute volume (V_E) and the respiratory frequency (fR) reaching up to 141.8 ± 14.0% and 124.8 ± 5.4%, respectively, 60 min post-injection. When 30-300 µM D-ser were applied directly into the RN, the increase in fR reached up 142.7 ± 12.5% of basal, two min after injection. The i.p injection of MET-phen (9 mg/Kg) reduce the basal fR, four-hour post injection (from 4.5 ± 0.1 Hz to 4.0 ± 0.1 Hz) and significant reduced the fR increase induced by hypercapnia, 2 (from 130.4 ± 2.6% to 111.9 ± 2.3%) and 4 hours (from 136.5 ± 4.2% to 118.2 ± 3.3%) after injection. To link astrocytes function with D-ser release during hypercapnia, we evaluate the hypercapnia response during impairment of astrocyte functions using fluoroacetate (FA) in glutamine-supplemented caudal medullary slices. The hypercapnia-induced respiratory response on glutamine-supplemented slices was similar to that observed in slices superfused with no-supplemented aCSF. In contrast, addition of 5 mM FA to glutamine-supplemented slices during 30 min impaired the respiratory response to hypercapnia (from 142.6% ± 8.8% to 111.7% ± 4.6%) and reduced the hypercapnia-dependent release of D-ser (from 168.8% ± 29.4 to 112.4% ± 15%). Interestingly, 50 M D-ser treatment restored the hypercapnia-induced respiratory response (149.3% ± 12.3%) in fluoroacetate treated slices.

Our results confirm the existence *in vivo* of a novel role for D-ser as that described *in vitro* where astrocytic release of D-ser induced by hypercapnia mediates the respiratory response in caudal medullary chemosensory nuclei.



69) Endoplasmic reticulum stress and neuroinflammation in heart failure: A novel link to sympathoexcitation.

Díaz H[1], Toledo C[1], Andrade D[1], Lucero C[1], Arce-Alvarez A[1], Del Rio R[1], [1]Departamento de Fisiología, Laboratory of Cardiorespiratory Control, Pontificia Universidad Católica De Chile.

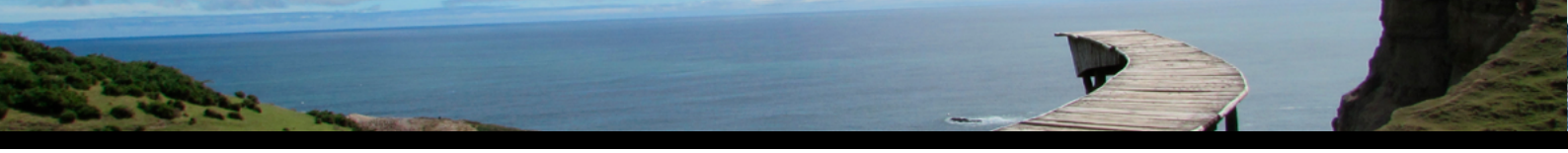
Heart failure with preserved ejection fraction (HFpEF) is characterized by increased sympathetic drive and decreased left ventricle compliance. We have shown that HFpEF rats display chronic neuronal activation in the rostral ventrolateral medulla (RVLM), a major region involved in the regulation of sympathetic outflow. Importantly, ROS, inflammation and angiotensin II (AngII) have been suggested to mediate sympathoexcitation in cardiovascular diseases. Recently, endoplasmic reticulum stress (ERS) has been proposed as key on AngII-mediated ROS production. Accordingly, we aimed to determine whether changes in ERS, ROS production, AngII AT1 receptor, NOX2, NF-κB and pro-inflammatory cytokine expression were associated with neuronal hyper-activation in the RVLM of HFpEF rats. Adult male Sprague-Dawley rats underwent volume overload to induce HFpEF. Cardiac function was determined by pressure-volume loops. RVLM micropunches were obtained from Sham and HFpEF rats to study neuronal activation as well as protein and mRNA expression using immunoblot and qRT-PCR. DHE staining was used to quantify O_2^- radical formation. Compared to Sham, HFpEF rats displayed increased end diastolic pressure (EDP) (5.6±0.1 vs. 3.8±0.3 mmHg, p<.05) and overt signs of cardiac hypertrophy (HW/BW 6.1±0.3 vs. 4.0±0.5 mg/g; p<.05). HFpEF rats displayed RVLM increased neuronal activation (FosB expression, 252±57 vs.100±4%, p<.05) and increased O_2^- production (12±2 vs. 4±1 au, P<.05). In addition, HFpEF rats showed augmented expression of AT1, p65-NF-κB and NOX2 (276±48, 280±48 and 136±19 vs. 100±9%, respectively p<.05). Furthermore, ERS markers CHOP and sXBP1 were 2- and 3-fold increased in HFpEF compared to Sham animals. Finally, we found an increased *de novo* synthesis of the proinflammatory cytokines TNF-α and IL-1βin the RVLM from HFpEF animals. Our data show for the first time that neuronal activation in the RVLM of HFpEF rats is associated with ERS. In addition, we found that AT1 and p65-NF-kB expression are both up-regulated in the RVLM of HFpEF rats suggesting that activation of the AngII signaling pathways and/or inflammatory signaling cascade in the RVLM may play a role in the maintenance of sympathetic neuron hyper-activation in HFpEF through an ERS-dependent mechanism.

Supported by FONDECYT # 1140275

71) Morphological and Neurochemical Characterization of the Neuronal Circuit Parapineal Organ-Habenula in Adult Zebrafish.

Meynard M[2,1,4], Palma K[2,4,1,3], Ibarra J[2], Concha M[2,4,1], [1]Center for Geroscience, Brain Health and Metabolism, Facultad de Ciencias, Universidad de Chile.[2]Laboratory of Experimental Ontogeny, Programa de Anatomía y Biología del Desarrollo, ICBM, Facultad de Medicina, Universidad de Chile.[3]SCIAN-Lab, Programa de Anatomía y Biología del Desarrollo, ICBM, Facultad de Medicina, Universidad de Chile.[4]Biomedical Neuroscience Institute, Facultad de Medicina, Universidad de Chile. (Sponsored by FONDECYT Posdoctorado 3160421, FONDECYT 1161274, ICM P-09-015-F, CONICYT PIA ACT1402, FONDAP 15150012)

Left-right asymmetry is a conserved feature of the nervous system of bilateria. In this regard one area of special interest for vertebrates is the epithalamus, a well conserved dorsal diencephalic brain region that serves as a link between the limbic and striatal forebrain and the monoaminergic system. The epithalamus is formed by the bilateral habenular nuclei (or Habenula, Hb) and the pineal complex. The Hb of many vertebrate species shows differences in size, cytoarchitecture, neurochemistry, connectivity, gene expression and neuronal activity between the left and right sides. The pineal complex is formed by the pineal organ and the parapineal organ (PpO). While the pineal is well conserved and morphologically symmetric among vertebrates, the PpO is only described in lampreys, teleost fish and lizards and shows pronounced asymmetries in efferent connectivity and in position. The PpO of teleost fish is located on the left side of the brain and projects only to the left Hb (lHb), giving rise to a unilateral circuit called PpO-lHb. The functional relevance of this circuit and their neuroanatomical asymmetry is still poorly understood. In zebrafish larvae, PpO efferents are widely distributed in the neuropil of the lHB, but there are no studies in adult animals. In this work we performed a neurochemical characterization of the PpO-lHb circuit in adult zebrafish by combining the use of the transgenic fish line Tg(*foxD3:GFP*), immunofluorescence for neurochemical markers, nuclear staining, immunohistochemistry, light microscopy and confocal microscopy. We found that, as in the larva, the PpO is positioned on the left side of the epithalamus in close proximity to the lHb. PpO efferents project to the neuropil of the lHb. The neurochemical characterization of the PpO-lHb circuit revealed the presence of classical neurotransmitters as well as neuropeptides. Our results provide novel insights into the anatomical organization and neurochemical identity of the PpO-lHb circuit in adult zebrafish.



73) Pannexin 1 modulates GluN2-subunit contribution to synaptic plasticity and spatial reversal learning in mice

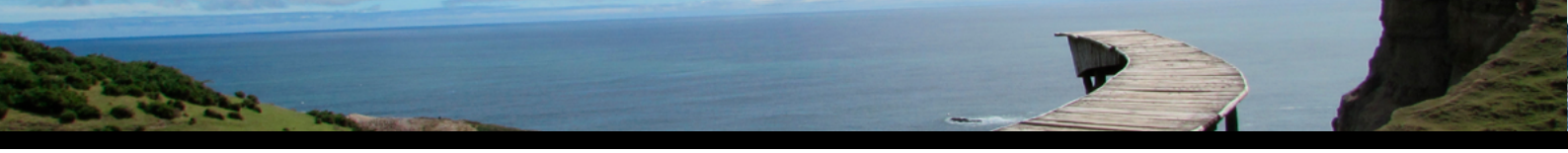
Gajardo I[1], Salazar C[2], Lopez-Espíndola D[3], Estay C[1], Flores-Muñoz C[2], Martínez A[2], Muñoz P[1,5,4], Ardiles Á[1], [1]Escuela de Medicina , Medicina, Universidad De Valparaíso.[2]Instituto Neurociencias, Ciencias, Universidad de Valparaíso.[3]Escuela Tecnología Médica, Medicina, Universidad de Valparaíso.[4]Interdisciplinary Center for Innovation in Health, Medicina, Universidad De Valparaíso.[5]Center for Applied Neurological Sciences, Medicina, Universidad De Valparaíso.

NMDA receptor-dependent long-term depression (LTD) is a form of synaptic plasticity that has received considerable support to be considered as a cellular model of the memory, where is essential for the refinement of neuronal connections during the acquisition and the storage of novel information in the brain. Pannexin 1 (Panx1) is an integral membrane protein that forms non-selective channels which have been shown to regulate the induction of hippocampal synaptic plasticity. In this regard, we previously demonstrated that the absence or the blockade of Panx1 channels precludes the induction of LTD and impairs object recognition and spatial memory. To evaluate if the absence of Panx1 affects the acquisition of new learned information during memory we trained Panx1 knockout (Panx1KO) mice and wild type (WT) littermates in a visual and hidden version of the Morris water maze. We found that Panx1KO mice find the hidden platform slightly more quickly than WT animals, nonetheless, when the hidden platform was located in the quadrant opposite to the previous learned location, Panx1KO mice spent significantly more time in the previous quadrant than in the new location indicating that the absence of Panx1 affects the reversion of a previously acquired spatial memory. Consistently, we observed that the absence of Panx1 modifies the contribution of GluN2 subunits of NMDARs to excitatory synaptic plasticity in the CA3-CA1 hippocampal synapsis of mice adults. Our findings contribute to the notion that Panx1 could modulate the induction of synaptic plasticity and related memory processes.

75) Assessment of retinal function in serotonin transporter (SERT) knockout mice

Alcaino A[1,3], Quiroz C[1,3], Vielma A[1], Olivares F[1], Cadiz B[1], Guajardo F[2], Ibaceta C[1], Sotomayor-Zárate R[2], Schmachtenberg O[1], Palacios A[1], Moya P[2,3], Chavez A[1,3], [1]Centro Interdisciplinario de Neurociencias, Instituto de Neurociencias, Ciencias, Universidad de Valparaiso.[2]Centro de Neurobiología y Plasticidad Cerebral, Instituto de Fisiologia, Ciencias, Universidad de Valparaiso.[3]Nucleo Milenio NuMIND, Ciencias, Universidad de Valparaiso. (Sponsored by Supported By FONDECYT 1151091 (A.E.C), 1160398 (RSZ), 1171228 (O.S.) And 1150638 (AGP), Núcleo Milenio Nu-MIND, NC 130011 (A.E.C And P.R.M) And The Millennium Institute CINV (P09-022F).)

The high affinity serotonin transporter (SERT) is essential for serotonin (5-HT) clearance and homeostasis at central synapses. While morphological analysis supports the expression of SERT in mouse retina, little is known about the role of normal and pathological 5-HT homeostasis in retinal visual function. Here, using high-performance liquid chromatography, immunocytochemistry, multi-electrode array and whole-cell voltage-clamp recording from retinal ganglion cells (RGCs), we evaluated the functional consequences of reduced SERT expression in the mammalian retina. Our results show a significant reduction in the total levels of 5-HT content in heterozygous ($SERT^{+/-}$) and homozygous ($SERT^{-/-}$) retinal neurons compared to wild-type (WT) littermates. These changes in 5-HT homeostasis are accompanied by alterations in the expression profile of 5-HT1a and 5-HT2c receptor subtypes. Remarkably, the 5-HT1a receptor subtype almost disappears from the outer plexiform layer, but increases its expression level at the RGC layer. In addition, we observed a decrease in global action potential firing rates of RGCs in $SERT^{-/-}$ compared to WT mice. At the single cell level, a decrease of the membrane potential and of spontaneous excitatory and inhibitory synaptic activity was observed in RGCs of $SERT^{-/-}$ micecomparedto WT littermates. Altogether, these results indicate that abnormal 5-HT homeostasis in the retinal circuitry alters global retinal function and RGC activity, suggesting that 5-HT plays an important role in regulating visual signal processing. Whether changes in the expression of the 5-HT1a receptor could account for the physiological alterations in retinal signal processing and RGC function is currently under investigation.



77) Light activation of the phototransduction cascade in membrane patches excised from the light-sensitive microvilli of Drosophila photoreceptors.

Bacigalupo J[1], Bacigalupo J, Delgado R[1], Delgado M G[1], [1]Biología, Ciencias, Universidad de Chile.

Phototransduction in the *Drosophila* compound eye takes place in 40,000 tightly packed specialized microvilli of the photoreceptor cells. Light activates rhodopsin that couples to G-protein (G-P), activating phospholipase-C (PLC). This enzyme hydrolyzes phosphatidylinositol 4,5-bisphosphate into 1,4,5-inositol trisphosphate, diacylglycerol (DAG) and a proton, mediating the opening of the light-activated channels, TRP and TRPL. TRP is highly Ca^{2+}-selective and carries 95% of the transduction current. Strong evidence supports DAG as the channels activator (Delgado et al J Neurosci 2014). Our aim was to study the phototransduction cascade in a system without the overwhelming complexity of the entire cell. We developed a procedure that allows to access the photosensitive microvilli and to excise inside-out patches where the phototransduction proteins, all membrane proteins, have their regulatory sites. In electrophysiological experiments using mutants and pharmacological compounds, we found that all the transduction proteins are retained and functional in the patches. The PLC activator M-3M3FBS lead to opening of the channels, but not in the PLC mutant *norpA*, revealing that PLC was present. The G-P activator GTP-γ-S GP also opened the channels, but not in *norpA* or under a PLC inhibitor (U73122), revealing that G-P was also there. Strikingly, the channels could be opened by light, in the presence of GTP (required by G-P), indicating that the entire cascade, including rhodopsin, was contained and functional in the patches. We also found DAG-kinase, which removes DAG by phosphorylation, as addition of ATP closed the channels and furthermore, we detected it in the microvilli by DAG-K fused to cherry fluorescent protein.

FONDECYT 1140520.

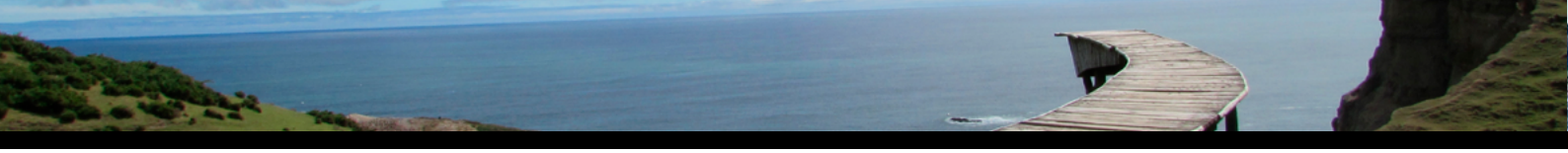
79) Patch clamp analysis of insulinergic and nitrergic modulation at first-order interneurons in Olfactory Bulb.

Calbiague V[1], Cadiz B[1], Vielma A[1], Bertea C[1], Schmachtenberg O[1], [1]CINV, Ciencias, Universidad de Valparaíso.

Retinal bipolar cells are visualinformation filters that connect the outer with the inner retina and receive input from both sides. In previouswork, we have shown that nitric oxide (NO) dose-dependently regulates the ERG b-wave and modulates theglutamate responses of specific types of bipolar cells. These antecedents suggest that theelectrophysiological profiles of retinal bipolar cells serve as sensitive early biomarkers forincipient neuronal damage caused by free radicals under chronic high glucose conditions.In the present study, organotypic rat retinal explant cultures are used to study the deleterious effects ofchronic high glucose concentrations on neuronal physiology. The glutamate responses and inhibitory feedback currents of bipolar cells will be analyzed by whole cell patchclamp recordings in rat retinal explants, cultured under normal and high glucose concentrations.

We aim to demonstrate rat retinal explants cultured under normoglycemic conditions, bipolar cells maintain the electrophysiological profiles they display in ex-vivo retinas for up to three weeks in culture.

FONDECYT REGULAR No. 1171228, and Millennium Institutive CINV.



81) Synapse-specific modulation of excitatory synaptic strength by TRPV1 channel in the hippocampus

Estay S[1,2], Lara I[1,2], Reyes C[1,2], Moya P[3,1,2], Chavez A[1,2], [1]Centro Interdisciplinario de Neurociencias, Instituto de Neurociencias, Facultad de Ciencias, Universidad de Valparaíso.[2]Nucleo Milenio NuMIND, Ciencias, Universidad de Valparaíso.[3]Centro de Neurobiología y Plasticidad Cerebral, Instituto de Fisiologia, Ciencias, Universidad de Valparaíso.

The transient receptor potential vanilloid 1 (TRPV1), is a nonselective ligand-gated cation channel predominantly expressed in afferents sensory neurons, where its activation can regulate synaptic transmission and neuronal function associated with pain sensation. Accumulating evidence indicates that TRPV1 channel is also expressed in several regions of the CNS, including the hippocampus, where its activation has been implicated in activity-dependent changes of synaptic efficacy. Indeed, TRPV1 channels retrogradely activated by the arachidonic acid derivative 12(S)-hydroperoxyeicosatetraenoic acid (12(*S*)-HPETE) regulate transmitter release at the excitatory CA3-interneuron synapse. Interestingly, 12(*S*)-HPETE mediated a type of mGluR-LTD at CA3-CA1 synapses, but whether this form of mGluR-LTD requires TRPV1 channels is unknown. Paradoxically, TRPV1 channels could be also clustered at postsynaptic terminals, raising the possibility that 12(S)-HPETE could act as intracellular messenger to activate TRPV1 and regulate synaptic function. However, the expression and functional role of TRPV1 in the hippocampus remains controversial. Here we used field and whole-cell recording techniques in acute mouse hippocampal brain slices to assessed the effect of 12(*S*)-HPETE and TRPV1 channels on excitatory postsynaptic responses at CA3-CA1 synapses. We found that application of 12(*S*)-HPETE to hippocampal slices induced depression of synaptic transmission and is required for the induction of mGluR-LTD. However, 12(*S*)-HPETE-induced effects were normally induced in TRPV1 knockout mice or when TRPV1 were pharmacologically blocked with capsazepine, strongly suggesting that TRPV1 channels might not be involved in the modulation of synaptic transmission mediated by 12(*S*)-HPETE at CA3-CA1 synapses. Remarkably, capsaicin, a well-known TRPV1 channel agonist, has no significant effect at the CA3-CA1 synapse, whereas in interleaved experiments capsaicin depressed extensively medial perforant path synapse in the dentate gyrus. Altogether these results indicate that TRPV1 channels are differentially expressed within the hippocampus regulating excitatory synaptic efficacy in the dentate gyrus, but not at CA3-CA1 synapses.

Supported by Nucleo Milenio (NC130011), Millenium Institute CINV (P09-022F), FONDECYT (1151091) and Proyectos para Estudiantes Convenio Desempeño (UVA 1315, 1401 y 1402).

83) Are there GABAergic neurons in the Ventral Tegmental area (VTA)? A long-range projection labeling and electrophysiological study.

Gonzalez C[1], Montero T[1], Henny P[1], [1]Anatomia Normal, Medicina, Pontificia Universidad Católica de Chile.

The ventral tegmental area (VTA) is a midbrain region implicated in behavior control, a function fulfilled by their extensive projections to striatal, cortical and limbic systems. This area contains intermingled cell populations of dopaminergic and GABAergic neurons with a lesser component of glutamatergic neurons. VTA dopamine neurons, by far the most studied population, are implicated in behavioral reinforcement and reward error prediction and their dysfunction has been implicated in several neuropsychiatric disorders and addictive behaviors. Less is known about VTA GABAergic neurons, though recent evidence has shown them to be a complex cell population with divergent projection patterns, heterogeneous intracellular electrophysiological profiles, as well as direct involvement in substance abuse/addiction. These evidences suggest the existence of functionally diverse subpopulations of VTA GABAergic neurons. In this work, we aim to identify and classify sub-populations of VTA GABAergic neurons according to their *in vivo* electrophysiological activity and projection targets. In urethane anesthetized mice, we identified individual GABAergic neurons with descending and/or ascending projections onto hindbrain, midbrain and thalamic structures (e.g. reticular formation, periaqueductal grey and posterior thalamus, respectively). These neurons were also classified by their spike duration and firing rate change as response to a hind paw pinch stimulus. These results evidence the heterogeneity of VTA GABAergic neurons in terms of their projection targets and electrophysiological properties. We also found that a large majority of these projection neurons also innervate the VTA locally by axon collateral terminals. By extending this analysis to a larger number of VTA neurons, we aim to characterize the VTA GABAergic efferences at the single cell level in order to better understand the multiple and parallel influences that the VTA may have on those various functions in which it is involved.

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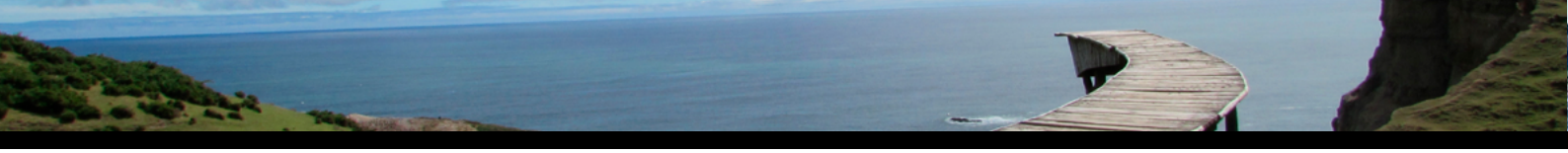
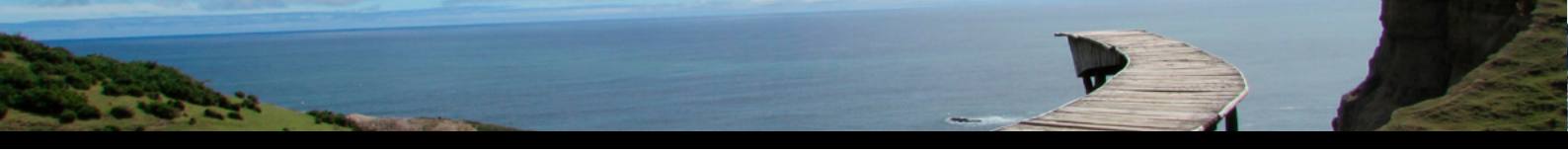


85) RETIRADO

87) Modulation of TRPM8 channels by basal phosphorylation.

Lavanderos B[1], Rivera B[1], Madrid R[1], Pertusa M[1], [1]Biología, Química y Biología, Universidad de Santiago de Chile.

TRPM8, a calcium-permeable cation channel activated by cold, menthol and voltage, is the main molecular entity responsible for detection of cold temperatures in the somatosensory system. It has been suggested that TRPM8 function could be regulated by several kinases that phosphorylate this channel in resting conditions, in both recombinant systems and cold thermoreceptor neurons. Nevertheless, the molecular bases of this modulation are still poorly understood. Our main goal is to explore in detail this regulation, identifying positions where the phosphorylation occurs, and evaluating the contribution of this posttranslational modification on TRPM8 channel function. To this aim, we have analyzed the phosphorylation state of immunoprecipitated TRPM8 channels with mass spectrometric analysis, and assessed channel function in HEK and F11 cell lines stably transfected with TRPM8-expressing plasmid using calcium imaging experiments. We found that TRPM8 is a phospho-protein in basal conditions, and we identified several residues within the N-terminal domain where this posttranslational modification takes place. Our functional results showed that the inhibition of the basal kinase activity using staurosporine enhances TRPM8 responses to cold and menthol, and causes a shift of 2°C in its temperature threshold to warmer temperatures in both cell lines, suggesting that the phosphorylation of TRPM8 produces a reduction in its response. Altogether, these results indicate that a basal kinase activity acts as a negative modulator of TRPM8 channel function, suggestingthat the phosphorylation level ofthis channeltunes its responses to cold and menthol.



89) Inhibitory and Excitatory Synaptic Contact Number and Distribution of in vivo Recorded Dopaminergic Neurons in the Mouse Ventral Tegmental Area.

Montero T[1], Gonzalez-Cabrera C[1], Henny P[1], [1]Anatomía Normal, Medicina, Pontificia Universidad Católica De Chile.

Midbrain dopaminergic neurons (DANs) exhibit two firing patterns, tonic and bursting. The former pattern is determined by intrinsic membrane properties that endow neurons with pacemaking firing, while the latter is greatly affected by incoming synaptic afferents. It is known that the distribution of synaptic inputs on the somatodendritic domain affects the activity and responses of neural cells. For instance, a recent report in rat substantia nigra pars compacta dopaminergic neurons, showed a correlation between the number of GABAergic synapses on distal dendrites and the strength of the response to a noxious stimulation. In this study, our aim was to understand how the number and distribution of synaptic contacts correlates with spontaneous and driven (aversive) activity of ventral tegmental area (VTA) DANs, a population of neurons involved in motivated behavior and preference formation. In urethane anesthetized mice, extracellular recordings and subsequent neurobiotin labelling of VTA single neurons were performed. Dopaminergic phenotype was confirmed by tyrosine hydroxylase (TH) immunopositivity. Afterwards, the entire somatodendritic domain was acquired using confocal microscopy, and a 3D reconstruction of each recorded neuron was generated with Neurolucida software (MBF Bioscience). The presence of glutamatergic or GABAergic synaptic inputs onto the recorded neurons was determined by double immunolabelling for neurobiotin and specific postsynaptic density markers. The number of contacts was estimated with the optical fractionator method and the distribution analyzed on the 3D reconstructions. Up to date we have recorded, labelled and identified 12 individual VTA dopaminergic neurons. Of these, 8 were inhibited by the aversive stimulus, 3 were activated and only 1 unresponsive (8,3%). We found no differences in spontaneous frequency, coefficient of variation or bursting activity between aversive-stimulus inhibited and activated neurons (students t-test, $P < 0.05$). Two neurons have been fully analyzed, which varied in surface area (20292 μm^2 and 4051 μm^2) and number of putative synaptic puncta, or PSP (1166 and 398). Finally, synaptic density did not seem to differ importantly between the two (0.0574 PSP/μm^2 and 0.0982 PSP/μm^2).

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91) Adolescent exposure of WIN55212-2 increases population activity of mesolimbic and nigrostriatal dopaminergic pathways.

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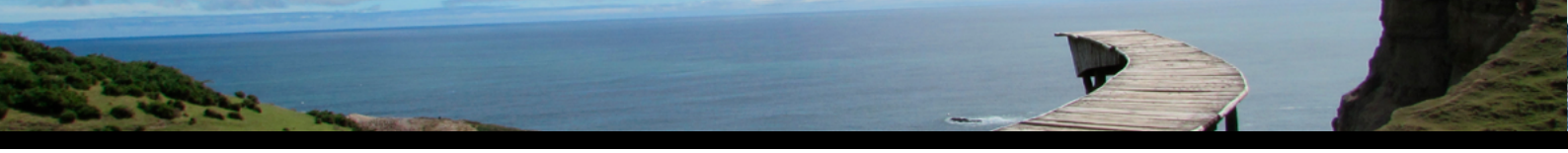
During adolescence, critical neuronal circuits changes to respond to physiological changes and to adapt to environmental stimuli (Sturman & Moghaddam, 2011). In particular, mesolimbic and nigrostriatal dopaminergic (DA) pathways are in constant change during the development of animals (McCutcheon & Marinelli, 2009). In early adolescence, the DA activity is lower compared to adulthood, but during the middle and late adolescence, the DA activity is higher than in adults (McCutcheon & Marinelli, 2009; Naneix, Marchand, Di Scala, Pape, & Coutureau, 2012). The dynamic changes observed in DA circuits suggest that adolescence is a period of high vulnerability to the long-term effects associated to drugs of abuse (Schneider, 2008). The most common illegal drug of abuse used in Chile by adolescents is cannabis (Servicio Nacional para la Prevención y Rehabilitación del Consumo de Drogas y Alcohol, http://www.senda.gov.cl/observatorio/estadisticas). Evidence indicates a relationship between an early use of cannabinoids and psychiatric disorders with abnormal DA system, such as schizophrenia, depression and addiction (Renard, Rushlow, & Laviolette, 2016). However, it remains unclear the impact of adolescent exposure to cannabinoids on mesolimbic and nigrostriatal DA pathways in adulthood. We hypothesize that repeated treatment with the CB1/2 agonist, WIN55212-2, during adolescence produces a long-lasting change in the DA activity of mesolimbic and nigrostriatal pathways. Male rats were treated with 1.2 mg/kg WIN 55212-2 daily during the adolescence period (postnatal day 40 – 65, 25 injections) and DA electrophysiological activity were assessed during adulthood (Postnatal day 72 – 78). The results show an increase of population activity of DA neurons in the Substantia Nigra (SN) and Ventral Tegmental Area (VTA) without changes in the firing rate and burst in both areas. These results suggest that adolescent treatment with WIN55212-2 produce a long-lasting increase of DA transmission in both pathways by changes on GABAergic input, that modulate the population activity, without modify glutamatergic input, that modulate burst pattern (Floresco, West, Ash, Moore, & Grace, 2003; Gomes, Rincón-Cortés, & Grace, 2016; Steiner & Tseng, 2017).

This work was supported by FONDECYT Project #1141088 and CONICYT Fellowship #21150450.



93) Endocannabinoid-mediated depolarization-induced suppression of a glycinergic synapse in the mammalian retina.

Quiroz C[1], Chavez A[1], [1]Centro Interdisciplinario de Neurociencias, Instituto de Neurociencias, Ciencias, Universidad de Valparaiso. (Sponsored by Supported By FONDECYT (1151091), Núcleo Milenio Nu-MIND (NC 130011) And The Millennium Institute CINV (P09-022F))

The neuronal endocannabinoid (eCB) system is known to depress synaptic inputs retrogradely in an activity-dependent manner by activating presynaptic type 1 cannabinoid receptors (CB1Rs). In addition, growing evidence indicate that some eCBs, such as anandamide (AEA), can also activate the transient vanilloid channel (TRPV1) to depress synaptic inputs in a non-retrogradely or autocrine manner. While these mechanisms have been described for excitatory glutamatergic and inhibitory GABAergic synapses, little is known about the role of eCB system in the modulation of inhibitory glycinergic synapses. Glycinergic inhibitory transmission plays an important role in regulating the processing of sensory information in the mammalian retina and there, anatomical studies have shown a high expression of the eCB system in almost all retinal layers and neurons. However, the functional consequences of eCB signaling in regulating synaptic function and retinal visual processing remains unclear. Here, we show that exogenous and endogenous cannabinoids alter spontaneous glycinergic synaptic transmission onto retinal ganglion cells (RGCs). Using whole-cell voltage-clamp recordings, we measured isolated glycinergic spontaneous postsynaptic currents ($_{gly}$SPSCs) in mouse RGCs. We found that the addition of an exogenous cannabinoid agonist, WIN55212-2 (5 µM), caused a significant reduction in the frequency, but not the amplitude of $_{gly}$SPSCs in a CB1R-dependent manner. In contrast, activation of TRPV1 channels with capsaicin (1 µM) did not cause any significant effect on $_{gly}$SPSCs, suggesting that eCB signaling solely attenuates glycinergic inputs in a retrograde manner by activating CB1Rs. Accordingly, brief depolarization of RGCs (50 mV, 5s), a well-known protocol to induce eCB release, also reduced the frequency but not the amplitude of $_{gly}$SPSCs. This effect on $_{gly}$SPSCs was CB1R-dependent and was also blocked by intracellular loading of inhibitors of eCB production. Together, these results indicate that glycinergic inhibition onto RGCs is subject to eCB-mediated regulation via CB1R but not TRPV1, and suggest that the eCB system might play an important role in the modulation of signal transmission and visual processing in the mammalian retina.

95) P2X7 receptor signaling in the retrotrapezoid nucleus contribute to breathing pattern irregularities in heart failure.

Toledo C[1], Andrade D[2], Diaz H[1], Alexis A[2], Lucero C[1], Rodrigo D R[2], [1]Biomedical Research Center Universidad Autónoma de Chile.[2]Departament of Physiology , Laboratory of Cardiorespiratory Control, Pontificia Universidad Católica de Chile.

Major hallmarks in heart failure with preserved ejection fraction (HFpEF) include enhanced central chemoreflex drive and resting breathing pattern irregularities. In HFpEF rats we found that both process rely on functional chemoreceptor neurons within the retrotrapezoid nucleus (RTN), a major region that controls the central respiratory drive, since selective ablation of chemoreceptor neurons results in reductions in central chemoreflex drive and restoration of normal breathing pattern in HFpEF. The precise mechanism underpinning the contribution of RTN chemoreceptor neurons to oscillatory breathing patterns in HFpEF remains to be determined. However, recent evidence suggests that purinergic signaling within the RTN may contribute to regulate breathing. Therefore, we aimed to determine if purinergic signaling in the RTN from HFpEF rats is associated to the development of heightened chemoreflex drive and altered breathing patterns. Adult male Sprague-Dawley rats underwent volume overload to induce HFpEF. Repetitive photoexcitation of pLenti-PRSX8-ChR2-YFP-expressing RTN chemoreceptor neurons was performed in conscious control rats to assess the contribution of RTN to resting breathing oscillations. Micropunches containing the RTN were obtained to determine $P2X_7$ receptor ($P2X_7R$) expression and ATP bioavailability levels. $P2X_7R$ knockout mice were used to study the contribution of the $P2X_7R$ on breathing stability. Activation of ChR2-expressing RTN neurons (light OFF vs. light ON, $p<.05$) leads to increases in minute ventilation (V_E 20±2 vs. 31±3 ml/min/100g). During the post-stimulation period (pre light vs post light, $p<.05$) there was a significant increase in breathing variability (SD1: 30±2 vs. 45±3 and SD2: 30±2 vs. 60±7, respectively) and in V_T amplitude (7±1% vs. 16±1%). HFpEF rats (Sham vs. HFpEF, $p<.05$) display decreased ATP bioavailability (78±2 vs. 21±10 pmoles/100µg of protein) and reduced $P2X_7R$expression (45±8% vs. 100±15%) in the RTN. Interestingly, injections of BzATP into the RTN, a $P2X_7R$ agonist, reduces breathing variability. Accordingly, $P2X_7R$deletion in mice recapitulates the altered breathing patterns observed in HFpEF (SD1: 25±4 vs. 38±2 and SD2: 29±2 vs. 45±3, WT vs $P2X_7R^{-/-}$) and increased V_T oscillations. No change in chemoreflex function was found in $P2X_7^{-/-}$ mice compared to wild type mice. In summary, our results show that repetitive RTN chemoreceptor neurons activation is capable of driving ventilatory disordersin normal rats. Also, our results suggest that $P2X_7R$is required for breathing regularity and a decreased purinergic signalling may be related to breathing irregularities in HFpEF.

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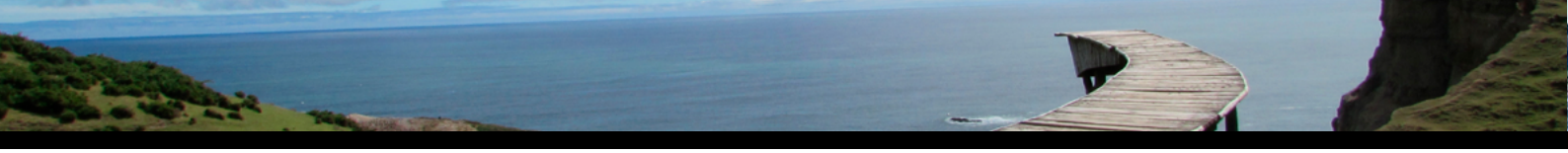


97) ATP sources for chemotransduction in rat olfactory cilia.

Acevedo C[1], Bacigalupo J[1], Vergara C[1], [1]Biologia, Ciencias, Universidad de Chile.

Odor transduction, which takes place in the sensory cilia of olfactory sensory neurons, is a metabotropic mechanism with high energy demands. We previously showed (Villar et al, J Neurosci 2017) that the cilia obtain ATP from oxidative phosphorylation in the dendrite and local glycolytic processing of glucose incorporated from the mucus. Electrophysiological experiments showed a prominent but not absolute reduction in the odor response when suppressing both processes, suggesting an additional supply of ATP for chemotransduction. We explored other possible ATP and glucose sources. Using immunohistochemistry, immunocytochemistry and Western blotting of ciliary membranes we detected the ATP shuttles adenylate kinase and creatine kinase in the cilia of the olfactory epithelium, suggesting that both pathways transfer ATP along the cilia, supplementing glycolysis and oxidative phosphorylation. We also found apical expression of glucose-6-phosphatase 3 in the olfactory epithelium sustentacular (SCs) cells and Bowman's glands (BGs), an enzyme that hydrolyzes glucose-6-phosphate to glucose that could be released to the mucus by glucose transporters. This suggests glucose from the SCs and the BGs glands would supply the glucose metabolized in the cilia. These results support that glucose from the olfactory mucosa blood vessels moves through the SCs and BGs that release it to the mucus, from where the cilia incorporate it to generate ATP. Also, ATP from the dendrite is transported by shuttles along the cilia.

FONDECYT 1140520.

99) Mechanisms of action of Loxosceles laeta venom on cultured human fibroblasts.

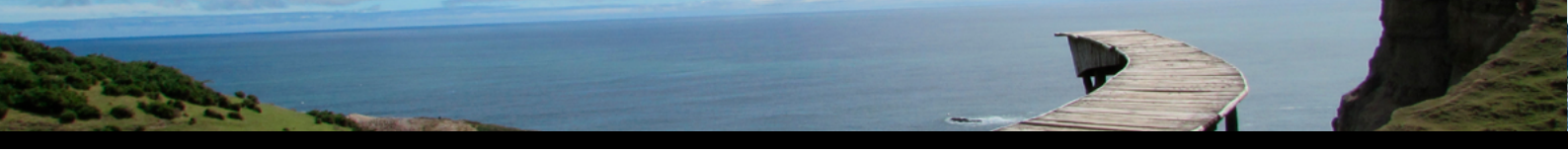
Bertea C[1], Flores C[1], Maripillán J[1], Martínez A[1], Schmachtenberg O[1], [1]Instituto de Neurociencias, Facultad de Ciencias, Universidad de Valparaíso. (Sponsored by Supported By The Millennium Institute CINV.)

The bites inflicted by *Loxosceles laeta* produce a dangerous and complicated clinical condition called Loxoscelism, which can trigger an inflammatory reaction and tissue necrosis, or produce renal and hepatic damage with potentially fatal complications.

Although many toxins contained in *L. laeta* venom are known, the mechanisms of pathogenesis remain poorly understood. Current research is mainly focused on phospholipase D, because this enzyme alone produces a large part of the clinical symptoms. This toxin is a phosphodiesterase that can react with many lipid substrates. In mammals, it acts mainly on sphingomyelin and lisophosphatidylcholine (LPC), whose cleavage generates choline and ceramide-1-phosphate (C1P) or lisophosphatidic acid (LPA), respectively. These metabolites have biological actions in the affected tissue, which contribute to the inflammatory condition.

In this study we seek to understand the mechanisms that trigger oxidative stress, cellular inflammation and cell death on primary cultures of human fibroblasts treated with *L. laeta* venom.

A venom extraction protocol based on electroestimulation was adapted to *L. laeta* using CO2 as anaesthetic. The protein contents of venom were determined by fluorometry the relationship between the protein concentration and programmed cell death rate in cell culture, assayed with TUNEL, was determined. Sub-lethal venom concentrations (<50% of death rate at 24 h), caused prominent changes in the expression patterns and total quantity of iNOS, Cx43, MTCO2, falloidine, ZO1, caspase-3 and YO-PRO-1 uptake after 4, 8 and 24 hours of exposure to the venom. Among others, iNOS expression is increased and redistributed from a perinuclear localization to the cytoplasm, whereas MTCO2 showed mitochondria network and shape changes after prolonged venom incubation, supporting a compromised cellular energy production. These results shed light on the cellular inflammatory pathways and mechanisms of cell death triggered by *L. laeta* venom in human fibroblasts, and may help develop effective treatment strategies for spider bites.



101) Enhancement of MOC activity prevents the onset of hidden hearing loss after acoustic trauma.

Boero L[2], Castagna V[2], Goutman J[1], Elgoyhen A[2], Gomez-Casati M[2], [1]INGEBI-CONICET Universidad de Buenos Aires.[2]Instituto de Farmacología, Facultad de Medicina, Universidad de Buenos Aires.

Noise induced hearing loss (NIHL) is growing as one of the most prevalent types of non-congenital hearing loss. It has been proposed that activity of the medial olivocochlear system (MOC) can ameliorate acoustic trauma effects. To address the role of the MOC in NIHL, we used two different mouse models: an alpha9 knock-in (KI), in which the alpha9 nicotinic cholinergic receptor (nAChR) subunit bears a mutation and leads to enhanced MOC activity; and also, one lacking the alpha9 subunit (KO).

We exposed WT, KI and KO mice at 3 weeks of age to loud sounds and tested their cochlear function 1 and 7 days after exposure. Large auditory threshold shifts were found one day after exposure in WT and KO mice, whereas KI mice were resistant to the same protocol. One week later, thresholds returned to normal in WT but KO ears did not recover. Permanent reduction in auditory brainstem responses (ABR) peak I amplitudes were found in WT and KO mice after exposure reflecting an ongoing process of hidden hearing loss. Notably, KI mice did not suffered any changes after acoustic overexposure.

Synaptophysin immunostaining evidenced a reduction of efferent terminals contacting outer hair cells (OHCs) at 7 days after trauma in WT mice. KO mice showed a distribution of efferent innervation shifted to minor contacts per OHC, whereas KI mice presented a wider innervation pattern. Finally, immunostaining for pre-synaptic ribbons and post-synaptic AMPA-receptors were performed to assess the degree of de-afferentation in inner hair cells (IHCs) followed by acoustic overexposure. Traumatized WT mice showed a reduction in the number of ribbons and afferent terminals at the apical turn. KO mice showed a decrease in the number of synaptic puncta mostly at middle and high frequencies after acoustic trauma. Interestingly, KI mice developed an increase in the number of synapses after exposure. Results obtained show that enhancement of MOC reflex can prevents hidden hearing loss as a consequence of noise exposure. Additionally, immunohistochemical data suggests that the MOC system is a key player on the balance between synapse formation and degeneration after exposure to loud noise in the inner ear.

103) Effects of opioid-induced analgesia on electroencephalographic markers of pain perception.

Egaña J I[2], Montefusco-Siegmund R[1], Blanch A[2], Rojas-Libano D[3], Rivera G[4], [1]Laboratorio de Neurosistemas, Facultad de Medicina, Biomedical Neuroscience Institute.[2]Departamento de Anestesiología y Reanimación, Facultad de Medicina, Universidad de Chile.[3]Departamento de Educación, Facultad de Educación, Univesidad Alberto Hurtado.[4]Departamento de Kinesiología, Facultad de Medicina, Universidad de Chile.

Chronic pain is a highly prevalent condition in modern medicine. Is the main cause of consultation, the principal cause of disability worldwide and represent enormous costs for all health systems. In most cases, chronic pain is a consequence of long exposures to untreated or subtreated acute pain. Efforts should be done in situation where acute pain is expected in order to prevent its transformation into chronic pain. Surgery is one of those situations. Nevertheless, chronic post-surgical pain (CPSP) is highly prevalent indicating that surgery-derived acute pain is not being correctly detected and/or treated. Mechanisms that account for acute to chronic pain transformation start acting rapidly after intense painful/nociceptive stimulation. That makes necessary to maintain adequate levels of analgesia during the surgery itself. Currently, there are no reliable intraoperative pain/nociception monitors.
EEG is a powerful tool that has proved its utility for monitoring the brain under general anesthesia. Unfortunately most of the achievements have been developed in the study of unconsciousness and amnesia with little progress in the pain/nociception field. Before the EEG can guide medical interventions, the electrical activity associated with pain and analgesia should properly be characterized.
Eight subjects were submitted to a 2 stages experiment while a 16+8 electrodes EEG was recorded. In the first stage they underwent a protocol of painful transcutaneous electrical stimulation of variable intensity. 3 consecutive stimuli of 4 different intensities, ranging from mild to moderate pain, were applied. Subject were instructed to report the amount on pain elicited by each of the stimuli in a 0-10 scale. During the second stage subjects repeated the previous protocol while they were exposed to increasing levels of analgesia. Analgesia was obtained by intravenous computer-controlled injection of remifentanil. Remifentanil is an ultrashort-acting synthetic opioid that allow quick effect and rapid recovery allowing rapid changes in analgesic effect.

We report the effects of opioid-induced analgesia on pain-associated Event Related Potentials (pERP) and on induced oscillatory activity.

Biomedical Neuroscience Institute (BNI).
Hospital Clínico Universidad de Chile.
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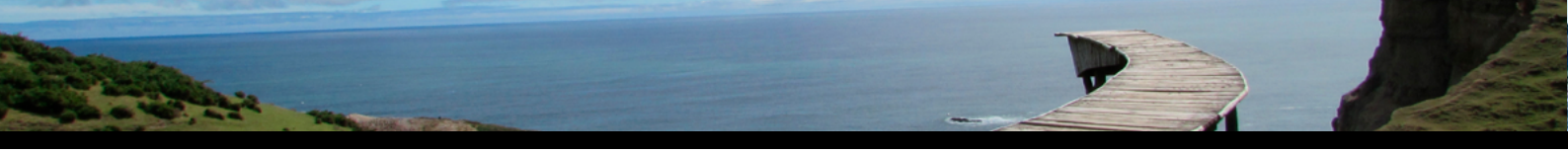

105) Frequency-dependent modulation of motor adaptation by cerebellar transcranial alternated current stimulation.

Mariman J J[1,2], Rojas-Libano D[3,1], Valero-Cabré A[4], Maldonado P E[1], [1]Department of Neuroscience, BNI & Faculty of Medicine Universidad de Chile.[2]Laboratorio de cognición y control sensoriomotor, Department of Kinesiology Universidad Metropolitana de Ciencias de la Educación.[3]Laboratorio de neurociencia cognitiva y social, Faculty of Psychology Universidad Diego Portales.[4]Cerebral networks, plasticity and rehabilitation team, Frontlab Institut du cerveau et la moelle, & CNRS umr 7225.

Human motor adaptation involves contributions from multiple cortical and subcortical regions organized in networks, in which the cerebellum plays a coordinating role, synchronizing interregional systems. We report a study where 18 participants carried out a visuo-motor task under the impact of cerebellar transcranial alternating current stimulation (tacs) using 20 hz, 50 hz or sham tacs delivered at 2ma for ~12 minutes. Participants must perform a reaching task with their right arm to bring a central dot towards a target distributed across eight eccentric locations. The participant's motor responses had to compensate a 45° counter-clockwise distortion of the screen's visual feedback on the online target location, while being under the effects of one of the tacs conditions. Kinematic analysis of individual trials allowed the identification of two sub-groups of ballistic arm responses: *accurate responses* (i.e., movements that reached the target in time) and *erratic responses* (i.e., responses in which the target was undershot or overshot at the end of response window). Analysis of *erratic responses* across tacs conditions revealed for the 50 hz tacs a significant decrease of the kinematic error, and a faster adaptation process to visual distortions across trials. Such effect proved specific for reaching movements towards targets displayed in the upper left and upper right side of the screen (but not for those displayed in the lower left and right-sided locations). No significant effect of tacs condition was found for any of the tested metrics indexing motor adaptation for *accurate responses*. Our results provide support to the notion of a direct modulatory enhance of error processing conducted by the cerebellum, likely induced by a local entrainment of frequency specific rhythmic activity at 50 hz. Moreover, our data support future promise for cerebellar tacs for the modulation of motor adaptation in healthy participants and also neurological patients with impaired motor learning abilities. CONICYT-Beca Doctorado Nacional

107) Perceptual Stability and Discrimination of Olfactory Representations.

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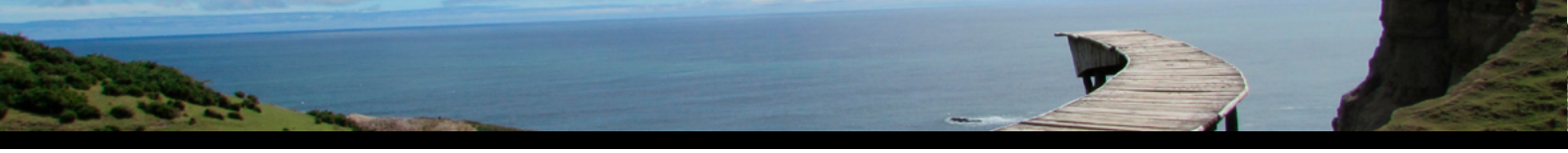
Olfaction is one of the most ancestral senses and a sophisticated neural circuit evolved to extract accurate relevant information from the environment to elicit behaviors critical for survival and reproduction. In vision, hearing and touch the physical properties of the stimuli are topographically represented in the sensory organ, representation that is maintained in the processing cortices. Odors, however, do not elicit meaningful representations through a continuous physical space and the olfactory system does not exhibit the typical topographical arrangement found in the other sensory systems posing the question of how the olfactory cortex (OC) process the information to generate an efficient neuronal code and adequate odor objects representations.

Olfactory sensory neurons project to the olfactory bulb (OB) where they make their first synapse with mitral and tufted cells (herein, MCs), which in turn directly and diffusely project to the OC. A particular MC project to multiple pyramidal cells (Pyr) in the OC and one Pyr neuron receives inputs from several MCs. Olfactory information is therefore coded in the OB by changes in MC's activity, information that is later integrated and ultimately decoded by a unique ensemble of Pyr in the OC representing a particular odor object. Interestingly, the OC identifies an odor mixture as one odor object without recognizing the different odorants that build them as independent units, even though the Pyr activation pattern will partially overlap to the ones of the single odorants. Therefore, the brain has to exhibit the ability to decorrelate partially overlapping patterns of Pyr activation and treat them as different, a process called pattern separation. Under certain scenario, however, it has to also recall a representation even though there are some features of the sensory stimulus missing (pattern completion). How is the subtle equilibrium to balance stimulus discrimination with perceptual stability regulated to generate adequate context-dependent sensory representations is not known.

The OC receives abundant cholinergic innervation and acetylcholine has been shown to play an important role in olfactory learning and discrimination. It has been suggested that it regulates intracortical fibers synaptic plasticity which diminishes the interference to generate new odor representations. Thus, we aim to study how cholinergic release in the OC could regulate the perceptual threshold of pattern completion and separation. Here, we show how animals in a go-no go task learn to discriminate between a rewarded and a not rewarded odorant and morphed the stimuli mixtures to promote either pattern separation or completion.

FONDECYT Iniciación 11150897.



109) Voluntary versus spontaneous control of biestable stimuli perception.

Osorio M[1], Rodríguez E[1], [1]Escuela de Psicología, Facultad de Ciencias Sociales, Pontificia Universidad Católica De Chile. (Sponsored by MO To Vicerrectoría De Investigación Pontificia Universidad Católica, Concurso De Investigación Pregrado Invierno 2014. ER To FONDECYT Regular 1120752.)

In bistable perception the brain transforms ambiguous stimulation into two mutually exclusive percepts, one of which is consciously perceived while the other is suppressed. This selection can occur either spontaneously or by the conscious decision of the viewer. Here we use this fact to find the perceptual stabilization periods of both, conscious and spontaneous control of perception. We presented 30 adult subjects with a version of the Stroboscopic Apparent Motion stimulus for 3 minutes. When rapidly shinned, this stimulus elicits vertical or horizontal motion perception. During continuous viewing, the perceived movement changes every few seconds. The task involved two conditions: In 'Spontaneous Condition' subjects were asked to report whenever perception spontaneously changed from vertical to horizontal or viceversa. In 'Voluntary Condition' subjects had to voluntarily hold a perception for as long as possible, reporting when perception changed. Analyzing the perceptual stabilization period allowed us to determine whether the Spontaneous control differs from Voluntary control. We found significant differences between conditions, as shown by the Kolmogorov Smirnov Test ($h=1$, $p = 0.0328$). Additionally, we determined the frequency distributions, evaluating whether they could be represented by Gamma distributions. We found that spontaneous and voluntary conditions were adequately described by Gamma distributions. Gamfit function showed gamma parameters for spontaneous condition of alpha = 1, and Beta= 27320. Gamma parameters for voluntary condition showed alpha= 1, and beta= 23889. Also, we found that the differences between the perceptual stabilization period of both Spontaneous and Voluntary control occurs only in a specific time range. Meaning that willful control of perceptual states succeeds only up to a particular time range, so conscious control of perceptual states is operational only to a certain extent. After some time, voluntary control of perceptions is lost and spontaneous reversions occur despite the intended voluntary control.

111) Role of Pannexin-1 in the post-natal maturation of the Organ of Corti.

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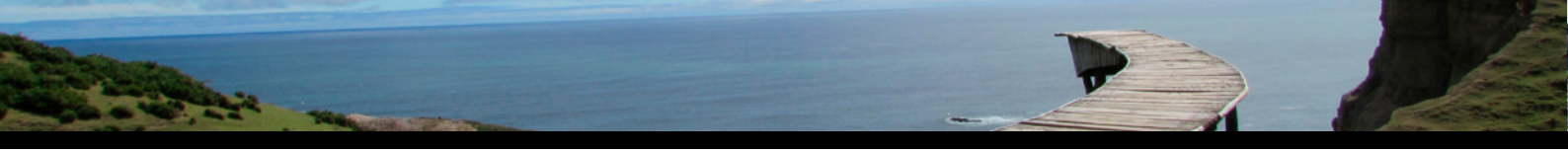
Pannexin 1 (Panx1) is a trans-membrane protein that forms non-selective plasma membrane channels permeable to ATP. In the cochlea, this molecule is expressed in different cellular groups, including the supporting cells of the organ of Corti (OC). Lack of Panx1 in the cochlea results in sensorineural hearing loss (SNHL). We hypothesized that this type of deafness might arise from the disruption of the cochlear purinergic signaling pathway, which finally results in the abnormal maturation of the OC. To get insight about the role of Panx1 in hearing, cochleae of wild-type mice with different postnatal ages were collected, and physiological properties of supporting cells were characterized as a function of the age and the effect of pharmacological agents that specifically block Panx1 channels. It was found that whole cell voltage-dependent ionic currents of isolated supporting cells increase with the maturational stage of the animal. The magnitude of the ionic currents was importantly reduced by acute treatment with Panx1 blockers (probenecid and the mimetic peptide ^{10}Panx1), suggesting a critical role of Panx1 channels in the excitatory properties of cochlear supporting cell. Furthermore, the basal release of the ATP by the cochlear supporting cells was also reduced when organotypic cultures of the OC were incubated with Panx1 blockers. Although still preliminary, difference in the single channel activity were observed among animals of different age brackets These results support the idea of an age-dependent expression of Panx1 channels in the murine cochlea, which might be important for the correct functioning of the Organ of Corti and the developing of hearing.

Work supported by FONDECYT 3150442 to PP



113) The endocannabinoid system shapes amacrine cell light-evoked responses in the retina

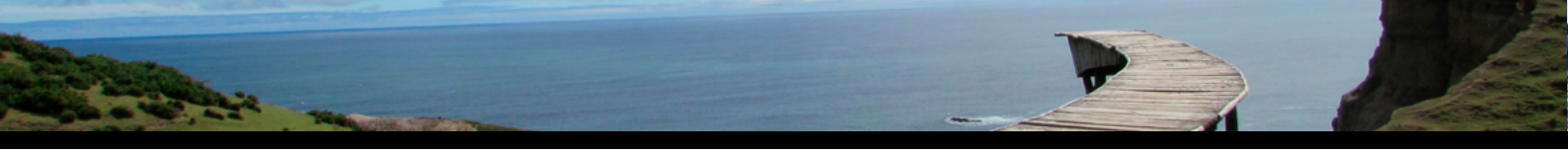
Tapia F[1], Chavez A[1,2], Vielma A[1], Schmachtenberg O[1], [1]CINV, Ciencias, Universidad de Valparaíso.[2]Núcleo Milenio NU-MIND, Ciencias, Universidad de Valparaíso. (Sponsored by FONDECYT 1151091, 1171228. Millennium Institute CINV, Millennium Nucleus NU-MIND NC-130011. CONICYT-PFCHA/Doctorado Nacional/2017.)

The endocannabinoid (eCB) system is widely distributed in the mammalian retina, suggesting that it may play an important role in retinal information processing. However, little is known about the physiological role of eCB signaling in retinal amacrine cells, the most diverse group of retinal neurons and a key cell in retinal information processing. Using whole-cell voltage-clamp recordings of amacrine cells in dark-adapted rat retinal slices, we investigated the effect of type-1 cannabinoid receptor (CB1) blockage on responses evoked by light stimulation. AM251 (5 µM), a CB1 inverse agonist, was applied to the inner plexiform layer using a puffer pipette, while the retinal slice was stimulated with green light flashes. Of 42 amacrine cells recorded, 22 were classified as ON, 11 as OFF and 9 as ON-OFF based on the pattern of their light-evoked responses. The recorded cells were morphologically highly heterogeneous, with horizontal dendritic tree extensions ranging from 34 to 176 µm, excluding cells extending their processes outside of the microscope field of view. Changes evoked by the application of AM251 also showed heterogeneous characteristics. Using the amplitude of the light-evoked response as the classification parameter, 5 functionally and morphologically heterogeneous cells (2 OFF, 2 ON and 1 ON-OFF), exhibited a change above 50% in the presence of AM251. Our results show that CB1 blockage produces changes in the amplitude of amacrine cell light responses, and that these effects are limited to certain amacrine cell sub-groups. The most prominent effect was an increase in response amplitude, which points to a regulatory role of eCB release on these cells light-evoked responses. Further studies are required to identify and classify the amacrine cells modulated by the endocannabinoid system, and the functional implications of this modulation on retinal information processing.

115) Cannabinoid receptors participate in the control of inhibitory activity in bipolar cells of rat retina

Vielma A[1], Tapia F[1], Chavez A[1], Fuenzalida M[2], Schmachtenberg O[1], [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.[2]Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso. (Sponsored by Regular FONDECYT #1171228 (OS, AHV), #1171006 (MF), And #1151091 (AEC). Millennium Institute CINV (OS, AEC) And Millennium Nucleus NU-MIND NC-130011 (AEC, MF).)

The cannabinoid receptor type 1 (CB1R), one of the most abundant G protein-coupled receptors in the brain, has been shown to mediate a number of physiological actions such as regulation of excitatory and/or inhibitory synaptic transmission. In the mammalian retina, CB1R is widely distributed in the synaptic plexiform layers, which suggests that this receptor may play an important neuromodulatory role in retinal synaptic function and information processing. However, the physiological significance of CB1R activation in the mammalian retina remains unclear. Here, using whole-cell voltage-clamp recording in light-adapted rat retinal slices we investigated whether activation of CB1R can regulate inhibitory synaptic input onto both ON and OFF bipolar cells (BCs). While BCs receive both GABAergic and glycinergic inhibitory synaptic inputs, we found two patterns of OFF BCs responses: some types receive spontaneous inhibitory inputs with a low frequency (LFC), whereas another types receive inhibitory inputs with high frequency (HFC), that are mainly mediated by glycine. Interestingly, perfusion of WIN 55212-2 (WIN; 1 µM), a specific CB1R agonist, increases the frequency of spontaneous activity in LFC but not in HFC. Moreover, this effect was eliminated when $GABA_A$ and $GABA_A$-ρ receptors were blocked with SR-95531 (SR, 10 µM) and TPMPA (50 µM), respectively, suggesting that activation of CB1Rs likely regulates GABAergic inhibitory inputs rather than glycinergic inputs onto OFF BCs. In contrast, inhibition of CB1Rs with AM251 (5 µM) increases the amplitude of glutamate-evoked GABA/glycine responses in OFF bipolar cells, opening the possibility that glycinergic inputs onto OFF bipolar cells may be regulated by CB1R. These results suggest that GABAergic, and perhaps glycinergic, inhibitory activity onto ON and OFF bipolar cells in the mammalian retina is regulated by the endocannabinoid system, which participates in the fine-tuning of the visual processing.



POSTER SESSION II

1) Prominence in sentence comprehension in schizophrenic subjets: An ERP study.

Alonso-Sánchez M F[1], Zepeda-Rivera L[2], [1]Escuela de Fonoaudiolgía, Salud, Universidad Santo Tomás.[2]AC3E Universidad Técnica Federico Santa María.

Schizophrenia is a chronic neurobiological disorder with recurrent tendency and wide heterogeneity of positive, negative and mood symptoms, In the communicaction with the use of ERP some authors have observed that subjects with schizophrenia are insensitive to syntactic and semantic violations, other authors have observed normal triggering of N400 of the semantic component and in the ELAN component, whereas the P600 wave has not been triggered against elicitation with syntactic incongruities. Likewise, it has been observed that subjects with schizophrenia have lower P600 wave amplitude in response to syntactic and semantic violations. Although there are several studies that present evidence of syntactic alteration, there are still discrepancies about the syntactic alteration in subjects with schizophrenia and their interrelation with the semantic level. In this line, the mayor concern of sentence interpretation is the semantic and syntactic interface. Particulary, in spanish the information that determine the prominence of a sentence element is the hierarchy stablished by the thematic role. The dative object-experiencer verbs makes the reanalysis of initial target object structure more easily, modulated by the tematic hierarchy and is associated with a N400 ERP. Furthemore, the prominence reversal of SVO senteces with a psych verb cued morphosyntactically elicits a P600 due to thematic mismatch. According to this, the aim of this study was to assess the prominence information span in schizophrenia subjects. An ERP study was made with sentences constructed with variation in the thematic structure of the verb (activity or psych verbs) and with manipulation of the word order (SVO or OVS). The schizophrenic subject were matched in age and education with healthy controls. The ERP were recorded with an 64 channel Biosemi EEG. The signal processing was made with Analizer Brain Vision. The analysis of the response time and the accuracy of response shown the performance deficit of the schizophrenic subjects. Additionally it was observed the differences in the SVO with psych verbs associated with de P600 component and the OVS activity verb associated with the N400 component among the schizophrenic and healthy subjects.

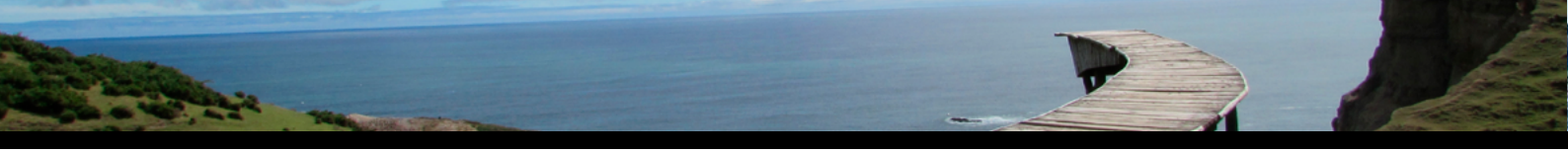
FONDECYT 11160212.

4) Autonomic nervous system impairment in children with pyramidal syndrome.

Arce-Alvarez A[1,3], Melipillan C[2], Andrade D[1], Toledo C[3], Díaz H[3], Lucero C[3], Del Río R[4], [1]Laboratory of Cardiorespiratory Control, Faculty of biological sciences, Pontificia Universidad Católica De Chile.[2]Research Unit Corporación de Rehabilitación Club de Leones Cruz del Sur.[3]Center of Biomedical Research Universidad Autónoma De Chile.[4]Department of Physiology, Faculty of biological sciences, Pontificia Universidad Católica De Chile. (Sponsored by Rodrigo Del Rio).

Pyramidal syndrome (PS) is a complex pathological condition characterized by increased muscle tone and hyperreflexia. However, brain imaging studies suggest that patients with PS may also display neuronal alterations in several brain regions. Interestingly, case reports studies suggest that PS patients are at higher risk of cardiovascular disease but no mechanistic explanation to these phenomena has been explored. We hypothesized that PS patients display autonomic nervous system (ANS) impairment, a condition closely related with cardiovascular diseases. Twenty-three infants (10.3 ± 4.8 months of age) were recruited and allocated into two groups: healthy (n=10; 40% females and 60% males) and PS (n=13; 46% females and 54% males) according to their neurological examination. RR intervals derived from heart rate recordings (10 min) acquire at rest with a heart rate monitor were used for ANS function estimation by means of heart rate variability (HRV) analysis. Time domain measures of HRV includes the root mean square (RMSSD), standard deviation of NN intervals (SDNN) and ratio of adjacent NN intervals differing by >50 ms to all NN intervals (pNN_{50}). Frequency domain measures were obtained using the following cut-off frequencies: low frequency bands (LF:0.04–0.3 Hz), high frequency bands (HF:0.3–1.2 Hz). For nonlinear analysis, Poincare plots from the RR interval were constructed. Compared to healthy subjects, we found that PS group showed (Healthy vs. PS, respectively):increased heart rate (133.2±11.8 vs. 143.9±10.4 bpm;$p<0.05$), decreased RMSSD (12.3±4.6 vs. 8.4±3.9 ms;$p<0.05$), increased LF component (80.3±4.8 vs. 86.7±5.7 ms^2;$p<0.05$), decreased HF component (19.7±4.8 vs. 13.3±5.7ms^2;$p<0.05$), increased LF/HF ratio (4.5±1.9 vs. 7.9±4.0;$p<0.05$) and reduced Poincare variability (SD1: 8.7±3.3 vs. 5.9±2.7 ms;$p<0.05$). No differences were found in SDNN, pNN_{50} and total spectral power between groups. Our results show for the first time that: i)childrens with PS display autonomic imbalance, ii)ANS impairment in PS may precede the onset of cardiovascular diseases, and iii)HRV analysis is a suitable tool to characterize ANS function in infants with PS. Future long-term follow-up studies are needed to establish the cardiovascular outcome in infants with PS.

FONDECYT # 1140275.



6) Alterations of reinforced and supervised motor learning in subjects with parkinson´s disease.

Burgos P[1], Gonzalez D[2], Verdugo C[2], Wimmer J[3], [1]Neurociencia,Kinesiologia, Medicina, Universidad De Chile.[2]Kinesiologia, Medicina, Universidad De Chile.[3]Applied neuroscience lab El Carmen Hospital Maipu. (Sponsored by Ramiro Zepeda, Paola Vargas, El Carmen Hospital Of Maipú)

Objectives: Sensorimotor learning presents several kindsof learning, two of these are Reinforced and Supervised learning. For the first one, basal ganglia is responsible and cerebellum for the second one. Parkinsons disease(PD) affects the function of basal ganglia thus altering reinforced learning. As there are connections between basal ganglia and cerebellum it may also be affecting Supervised learning. Therefore, the purpose of the study is to compare the level of impairment between Supervised learning and Reinforced learning in patients with Parkinsons disease in a visuomotor task.

Methods: A sample of 6 subjects with Parkinsons disease and 6 healthy subjects were recruited. All the subjects performed an adaptation visuomotor task (60 °) in a tablet pen with and without feedback during the trajectory and always with a final position feedback. Angular error (AE) and reaction time (RT) were used as adaptation metrics.

Results: Differences in performance between exposure, pre and post-exposure(after-effects) in healthy subjects and Parkinsons disease patients were found. Parkinsons disease group had a similar after-effect(measured by AE average) in comparison to the healthy group in the Supervised learning(with trajectory feedback) but significant differences in the Reinforced learning($p<0.05$) (without trajectory feedback). RT was significant slower in PD in all conditions($p<0.05$).

Conclusions: The altered results in the Parkinson's disease group in the Reinforced but not in the Supervised learning confirm previous evidence regarding the alterations of reinforced learning in this neurological disorder.

8) Outcomes of a novel visuospatial planning task coupled to eye-tracker and electroencephalogram systems.

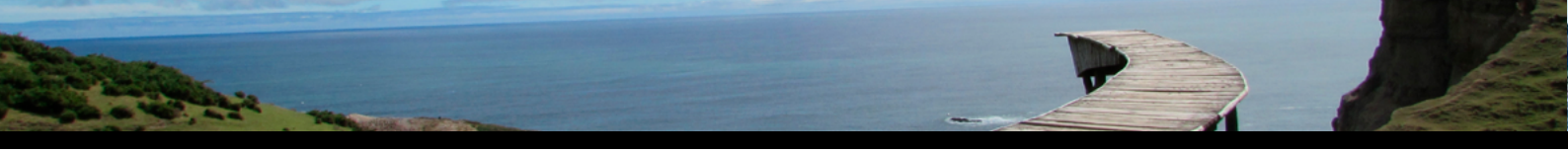
Domic M[1], Follet B[1], Wainstein G[1], Sánchez A[1], Valdés J[1], Medel V[1], Santander D[1], Perrone-Bertolotti M[2], Ossandón T[1], [1]Departamento de Psiquiatría, Facultad de Medicina, Pontificia Universidad Católica De Chile.[2]Laboratoire de Psychologie et NeuroCognition UMR5105 Université Grenoble Alpes. (Sponsored by Comisión Nacional De Investigación Científica Y Tecnológica - CONICYT).

Planning is the ability of developing a sequenced plan to achieve a goal in an organized, strategic and efficient manner. It requires several cognitive components, making the experimental manipulation difficult. The design of behavioral paradigms (with proper controls) that demand the start-up of planning and allow the acquisition of electrophysiological and ocular dynamics data combined in healthy, psychiatric and cognitive diseases population is an unsolved question. Here, we proposed to evaluate a novel experimental paradigm design in 10 healthy adult subjects. This experimental paradigm was based on Porteus Maze and Zoo Map Task using a control condition able to control confounding variables and is coupled to an electroencephalogram (EEG) and an Eye-Tracker (ET) systems.

The task consists on the presentation of mazes which represents a zoo map including several paths with animals inside. Participants were instructed to planning a path following a set of rules (planning period). Then, they have to trace the path planned before using their eyes movements through an online feedback given by the ET (execution period). The control condition is identical to the experimental condition, but with an already visually marked path and participants have to verify if these paths have been made following the rules (control period). This control condition allows the control of several other components confounds (such as working memory, visuoperceptual analyses).

Results show that participants require more time to solve the mazes when they have to plan a path relative to other condition (RT planning mean: 8.96, STD: 1.16; RT control mean: 6.27, STD: 1.31; Wilcoxon: P: 0.0039), suggesting that solve the planning period is more time consuming and reflect more cognitive demand. Moreover, lower accuracy rate was observed during experimental than control condition suggesting that experimental condition is, as predicted, more complex than control condition (Planning accuracy mean: 0.79, STD: 0.03; control accuracy mean: 0.94, STD: 0.04; Wilcoxon: P: 0.0020). Our preliminary results suggest that our experimental paradigm is optimal to evaluation of planning in combination with neuroimaging methods in several pathological population.

Research supported by Becas de Doctorado Nacional CONICYT: 21150295 and FONDECYT regular: 1140996.



10) Association between peripheral vestibular function and cognitive performance in elderly population from Santiago de Chile.

Faúndez J P[2,1], Martínez M[3,1], Soto Á[3,1], Delgado C[3,1], Délano P[1,5,4], [1]Auditory and Cognition Center, Medicine, University of Chile.[2]Hearing, Speech and Language Sciences, Medicine, University of Chile.[3]Neurology and Neurosurgery Clinic Hospital of University of Chile.[4]Otorhinolaryngology, Clinic Hospital , University of Chile.[5]Neuroscience, Medicine, University of Chile.

Introduction: Peripheral vestibular activity seems to be fundamental to integrate information in place cells and head-direction cells. Vestibular activity influences spatial memory and navigation processes. Subjects with bilateral vestibular loss, perilymphatic fistula, and vertigo haveneuropsychological deficits as attention disorders, visuospatial andexecutive function impairments and short-term memory problems.
Harun et al. reported in 2016 that in Alzheimer dementia (AD) patients exist a relation between peripheral vestibular impairment and disease onset.
The purpose of this study is to find associations between peripheral vestibular function and cognitive performance in elderly population.

Material and Method: The current study recruited forty-one participants (mean age 74,2 years; s.d. +/- 4,77). The exclusion criteria were conductive or mixed hearing loss diagnosis, non-typical tympanic membrane image or presence of occluding ear wax, history of vertigo or related symptoms and at least 6 years of formal education.
All participants went under neuropsychological testing and air-conducted cVEMP recordings.

Results: Non-parametric analysis show a significant correlation between cVEMP amplitude in the right ear and working memory performance (rho = 0.268, p = 0.045). Also, a significant correlation between cVEMP amplitude in the right ear and executive function performance (rho= 0.277, p=0.04) it was found. Analysis also shows a negative correlation between cVEMP amplitude in the left ear and long-term memory performance (rho= 0.277, p=0.04).
Other significant correlations were not found.

Conclusions: Data analysis shows a mild positive significant association between cVEMP amplitude and working memory and executive function performance. It has been shown that peripheral vestibular inputs has cortical connections with parietal cortex, which is involved in working memory function. About cVEMP and executive function, results suggest that vestibular inputs could have neural connectivity with prefrontal cortex. Results suggest that it is very necessary in this research to increase the sample size and that other neural pathways related to vestibular inputs and cognitive areas should be investigated in the future.

Supported by Proyecto Anillo ACT1403 from PIA CONICYT, FONDECYT 1161155 and Fundación Guillermo Puelma.

12) Influence of vocabulary skills on visual context and linguistic processing interaction in 2 year-old children.

Helo A[1], Azaiez N[2], Ommen S[3], Pannasch S[4], Rämä P[5,3], [1]Departamento de Fonoaudiología, Facultad de Medicina, Univeridad de Chile.[2]Department of Psychology University of Jyväskylä, Finland.[3]Laboratoire Psychologie de la Perception Paris Descartes.[4]Department of Psychology, Engineering Psychology and Applied Cognitive Research University of Dresden.[5]CNRS (UMR 8242) Paris, France.

Linguistic inputs typically occur within a visual context (i.e. natural scenes). Information from linguistic and visual modalities is integrated very quickly. In adults, perceptual features, semantic consistency and task demands are the principal factors guiding visual attention. Also, linguistic processing can guide visual attention. Interestingly, scene context can influence word processing in adults. In contrast, much less it is known about the interaction of these processes during development. During the second year of life, there is an important increasing in vocabulary size, with significant individual differences. By the same age toddlers are prone to spontaneous naming. We investigated the interaction of language and visual context processing in 2 year-old children; specifically, the effect of linguistic skills on: (1) visual attention guidance and (2) the influence of visual context on word processing. We examined how semantic violations, perceptual features and linguistic properties affected gaze distribution of toddlers with high and low vocabulary skills. We compared eye movements of toddlers and adults while exploring consistent (C-O; e.g., sock in a closet) or inconsistent (I-O; e.g., sock in a kitchen) scenes. Results showed that low producers looked longer to I-O while high producers looked equally long to both C-O and I-O. Toddlers looked longer to I-O only when they were highly salient while saliency did not affect semantic effect in adults. Our results indicate that perceptual features have a stronger influence in toddlers than adults and that language skills influence cognitive but not perceptual guidance of visual attention. In another experiment, toddlers with high and low vocabulary skills were presented with visual scenes (e.g., kitchen) followed by semantically consistent (e.g., spoon) or inconsistent (e.g., bed) spoken words while EEG was recorded. Inconsistent scene-word pairs evoked a larger N400 component over the right frontal areas (FA) of low-producers, while high-producers presented it over the left FA. Results suggest that contextual information facilitates word processing in toddlers and different linguistic skills present differential rehearsal strategies when linguistic and visual context interact (reflected by the FA differential activation). Altogether, our findings suggest that language and vision modalities closely interact in young children.

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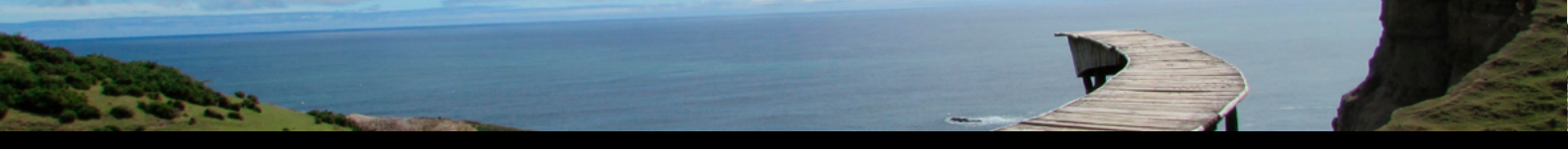


14) Temporal changes in the neural correlates during different stages of propofol-induced anesthesia using EEG.

Irani M[1,2], Sánchez A[3,2], Rana M[2,3], Fuentes C[4], Pedemonte J[4], Cortinez L[4], Ruiz S[3,2], Sitaram R[5,3,2], [1]Facultad de Ciencias Químicas y Farmacéuticas Universidad de Chile.[2]Laboratory of Brain-Machine Interfaces and Neuromodulation Pontificia Universidad Católica De Chile.[3]Department of Psychiatry, Interdisciplinary Center for Neuroscience, School of Medicine, Pontificia Universidad Católica De Chile.[4]Department of Anaesthesiology, School of Medicine, Pontificia Universidad Católica De Chile.[5]Institute for Biological and Medical Engineering, Medicine, Biology and Engineering, Pontificia Universidad Católica De Chile.

Electroencephalogram (EEG) is an important clinical tool for monitoring brain activity during anesthesia-induced unconsciousness. In clinical settings, anesthesiologists use different indices derived from EEG data to estimate anesthetic depth. However, these indices do not always represent the actual anesthetic depth, leading to a failure in preventing incidence of awareness during surgery (1-2 cases in 1000 general anesthesia cases). Recent studies have characterized the EEG spectral signatures for different stages of anesthesia. However, most of the studies have focused on the young adult. Pharmacodynamic studies have demonstrated that older patients (>65 years) require a significantly less amount of Propofol anesthesia to reach a specific anesthetic depth as compared to the younger adult, thus, concentrations which are suitable for young adult patients could lead to postoperative side-effects in elderly patients. Recent studies have characterized the effect of aging in Propofol EEG spectral signatures in loss of consciousness and recovery of consciousness by the occurrence of slow-delta and alpha waves along with a decreasing in gamma band power. Although EEG spectral signatures provide a better approximation in assessing anesthetic depth as compared to the existing clinical methods like BIS index, it has been reported that using EEG-parameters separately to define anesthesia depth is not as accurate as using them in combination. In this study, we explore the temporal changes in several frequency- (e.g. band powers, spectral entropy and spectral edge frequency) and time-domain (e.g. approximate entropy, Lempel-Ziv complexity) EEG parameters during different stages of anesthesia i.e. awake, induction, maintenance and recovery. In this study, we included EEG data from 5 elderly patients (>65 years) undergoing surgery who were administered continuous intravenous infusion of Propofol. The data was recorded at a sampling frequency of 89 Hz, using a SEDLine® monitor, which consists of four EEG electrode array over the prefrontal cortex, with the reference electrode and the ground electrode 1 cm above Fpz and at Fpz, respectively. Our preliminary results demonstrate the reproducibility of EEG spectral patterns as it has been previously reported in the literature. We observed a sustained activity of alpha and slow waves after the induction and an extinction of alpha activity when the patients recover from anesthesia. Taken together, these results would allow us to further characterize and classify different stages of anesthetic depth in terms of the parameters mentioned above.

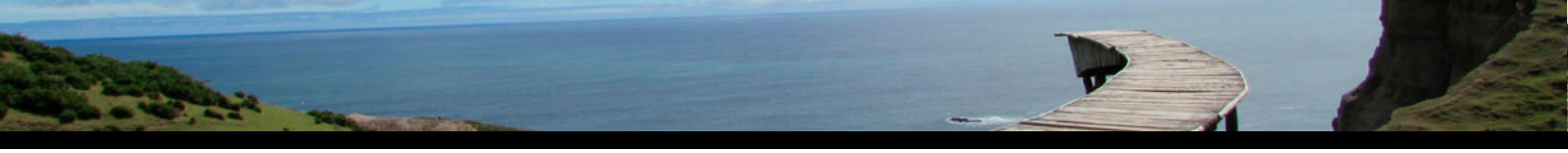
Supported by the Department of Anaesthesiology and Department of Psychiatry at Pontificia Universidad Católica de Chile School of Medicine and by the UT Austin-UC SEED Grant.

16) Difference in perseverative errors during a visual attention task with auditory distractors in alpha-9 nicotinic receptor subunit wild type and knock-out mice.

Jorratt P[1], Delano P[1,2], Delgado C[1,3], Dagnino-Subiabre A[4], Terreros G[5], [1]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.[2]Departamento de Otorrinolaringología Hospital Clínico de la Universidad de Chile.[3]Departamento Neurología y Neurocirugía Hospital Clínico de la Universidad de Chile.[4]Laboratorio de Neurobiología del Stress, Centro de Neurobiología y Plasticidad Cerebral, Facultad de Ciencias, Universidad de Valparaíso.[5]Instituto de Ciencias de la Salud Universidad de O'Higgins.

The auditory efferent system is a neural network that originates in the auditory cortex and projects to the cochlear receptor through olivocochlear neurons. Medial olivocochlear neurons make cholinergic synapses with outer hair cells through nicotinic receptors constituted by α9 and α10 subunits. One of the physiological function of the α9 receptor is the suppression of auditory distractors during selective attention to visual stimuli. In a recent study we demonstrated that the behavioral performance of alpha-9 nicotinic receptors knock-out (KO) mice is altered during selective attention to visual stimuli with auditory distractors since they made less correct responses and more omissions than wild type (WT) mice. As the inhibition of the behavioral responses to irrelevant stimuli is an important mechanism of the selective attention processes, behavioral errors are a relevant measure. These errors produced during a cued attention task can be classified as premature, target and perseverative errors. Perseverative responses can be considered an inability to inhibit the repetition of an action already planned, while premature responses can be considered as an index of the ability to wait or retain an action. Premature and perseverative errors reflect impulsive behaviors which are an important components to be inhibited during attention. Here, we studied premature, target and perseverative errors during visual selective attention (twelve-day behavioral protocol of a two-visual discrimination task) in presence of auditory distractor (clicks and 15 kHz tones, and broad-band noise) in WT and KO mice. We found that KO mice make fewer perseverative errors with longer latencies than WT mice during the auditory distractors. Also, although we found no significant difference in the number of target error between genotypes, KO mice increased the amplitude of the first peak of early of target error latency during the presentation of the click and tone distractors. These results suggest a reduced motivation for reward and an increased impulsivity during decision making with auditory distraction in KO mice.

Funded by Proyecto Anillo ACT1403, Fundación Puelma.



18) Aerial binocular strip visual stimulation triggers defensive responses in the Octodon degus.

Lopez-Jury L[1], Deichler A[1], Mpodozis J[1], Marín G[2,1], [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile.[2]-, Facultad de Medicina , Universidad Finis Terrae.

The degree of binocularity has been widely linked to nocturnality and active visual behaviors such as hunting and eye-hand coordination. However, prey mammalian species, such as rodents, possess a dorsal band of binocular superposition in their visual field, which we call aerial binocular strip (ABS), that has been associated to reactive visual responses such as freeze and escape. Previous studies in our lab have demonstrated that the ABS is conserved among rodents with independence of their visual habits (diurnal, nocturnal or subterranean). Behavioral studies in mice show that escape behavior can be triggered by an overhead looming stimulus. Furthermore, a small moving disk, simulating the course of a predator gliding overhead, induces freezing. We reproduce these experiments in the diurnal Chilean rodent Octodon degus with the aim of providing comparative evidence for the association between the ABS and reactive visual responses in rodents. To that end, we used a small arena featured with screen monitors and a video camera to track the animals reactions in response to controlled visual stimulation presented to either the dorsal or the ventral parts of the visual field.

Our results show a bias in the execution of reactive behaviors toward the stimulation of the ABS. Contrary to the results reported in mice, we were able to trigger escape responses in the degus with a sweeping stimuli presented in their ABS in addition to looming. However, the behavioral responses depended on the size and velocity of the moving disks, with larger and faster disks increase the probability of triggering escape responses.

The ABS therefore appears to be a visual field specialization devoted to aerial surveillance common to rodents and presumably other mammals with similar ecologies. Further experiments are required to unveil the neuronal substrates associated to the ABS and the execution of behaviors to which we propose it is linked.

FONDECYT 1151432.

20) Cognitive effort modulates otoacoustic emissions in individuals with high working memory capacity.

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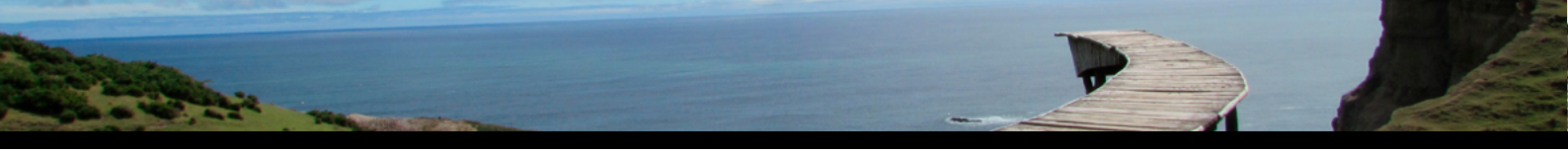
Otoacoustic emissions (OAEs) are sounds that are generated in the cochlea that are intimately related with outer hair cells (OHC). These cells are innervated by the medial olivocochlear efferent bundle, the final stage of the auditory efferent system that begins in the auditory cortex. Recent studies investigating cortical modulations of cochlear responses by using otoacoustic emissions shown differences in OAE depending in visual or auditory attention modality, but no studies have been made controlling visual working memory (VWM) load of the task and individual VWM capacity. Here we present a study using a visual task using the change detection paradigm, where the subject has to detect if a colored squared change its color among other colored squares. Two different VWM load were used, low (two squares) and high (four squares) load. At the same time, tones where elicited in different parts of the visual task to record distortion product otoacoustic emissions (DPOAE), a type of OAEs. These tones appeared in parts of the visual task with and without VWM load. Preliminary results show that OAEs are modulated by the mental effort of the task and not by VWM load, but only in participants with high visual working memory capacity. This study aim to clarify the role of auditory efferent pathway in the regulation of cochlear responses, and the role of VWM capacity in the modulation of auditory distractors.

Funded by FONDECYT 1161155 and Proyecto Anillo ACT1403.



22) Human intracranial EEG activity during a visuospatial working memory task.

Medel V[1], Valdés J[1], Follet B[1], Kahane P[2], Lachaux J[3], Ossandón T[1], [1]Psiquiatría, Medicina, Pontificia Universidad Católica De Chile.[2]Neurology Grenoble-Alpes University.[3]Brain Dynamics and Cognition, INSERM U1028 - CNRS UMR5292, Lyon University. (Sponsored by Funded By: Anillo ACT1414, FONDECYT 1140996.)

Visuospatial working memory (VWM) is the cognitive substrate that allow us to retain and use the visual information of our environment over brief time intervals and is important for complex human behavior. It has been shown that attention and WM recruit similar brain regions. Here we present a time-frequency analysis of intracranial EEG recordings during a visuospatial working memory task. The data was obtained from five neurosurgical patients with intractable epilepsy at the Epilepsy Department of the Grenoble Neurological Hospital (Grenoble, France). In the present analysis we determine the time-frequency components, their relation with the VWM task events, and the anatomical positions of the electrodes. Our preliminary results show that during the working memory encoding phase there is an increase in the power of the alpha(8-15 Hz), beta(16-31 Hz) and theta(4-7 Hz), while during the working memory recall we observe suppression in the alpha, beta and theta frequencies, and a strong activation of the broad gamma band (50-150 Hz). This findings support previous evidence relating the increase in the power of alpha, beta and theta band in a WM task, and suggest that the broadband gamma activity could correlate to working memory recall. We will present the complete time-frequency analysis of the five subjects, its correlation with the anatomical positions of the electrodes, the comparison with high and low working memory load conditions, and correlations with performance.

24) **Wave V latency of the Auditory Brainstem Response as a biomarker of working memory performance in healthy elders.**

Morales R[1], Leiva A[1], Espinoza M[1], Martínez M[1], Soto A[1], Eléspuru K[1], Délano P[1], Delgado C[1], [1]Neurociencias Universidad de Chile.

Background: Hearing loss (HL) has been recognized as a risk factor for dementia. Although the mechanisms underlying cognitive decline associated with HL are not yet clear, we propose that loss of auditory nerve neurons has a strong impact in complex cognitive performance such as working memory (WM). To study this we used supra-thresholds Auditory Brainstem Response (ABR), which provides information on the peripheral and subcortical hearing status through amplitude and time of responses from auditory nerve (wave I) to the inferior colliculus (wave V) and an auditory verbal working memory (AVWM) test.

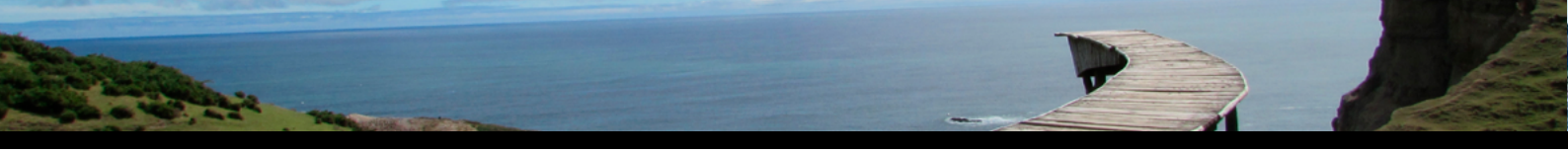
Objective: To determine if the electrophysiological function of the peripheral and subcortical auditory pathway is associated with the performance in an AVWM test in healthy elders.

Methods: 73 subjects >65 years old, without dementia from the ANDES study were screened with a Pure Tone Audiometry (PTA) resulting in normal hearing (PTA <20dB, n=21) or with mild (PTA 20-40dB, n=36) to moderate (PTA >40dB, n=16) presbycusis. They were evaluated with a comprehensive battery of neuropsychological test including visual and verbal WM domains and a supra-threshold ABR. We used the Speech Perception in Noise Test (SPIN) as a AVWM assessment with high cognitive load.

Results: The performance in AVWM test was significantly correlated with the measures of global cognition: Mini-Mental State Examination (MMSE)(r=0.33, p=0.005); visual WM: indirect span of the Corsi Test (r=0.31, p=0.012); and verbal episodic memory: free recall of the free and cued selective reminding test (r=0.41, p=0,001). AVWM did not correlate with the PTA. Using regression models, controlling for sex, age, education, MMSE and hearing status we found a significant correlation between the AVWM performance and the ABR wave V latency of the right ear (r=0.52, p=0,002).

Conclusions: The latency of wave V in the ABR may represent a reliably measure as a biomarker of the auditory working memory performance when high cognitive load is required, which could be related to the speed subcortical processing of auditory responses.

Funded by Proyecto Anillo ACT1403 and Fundación Guillermo Puelma.



26) Neural correlates of attentional networks in preschool children with and without attentional deficit hyperactivity disorder symptoms.

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Introduction: Attention deficit hyperactivity disorder (ADHD) is considered to be a neurological development disorder characterized by a lack of attention and/or hyperactivity-impulsiveness. Most ADHD diagnoses are made after 6 years of age. However, it is not clear what occurs to the executive functions during the formation of this disorder at the preschool stage. Our study aims to fill this gap by evaluating inattention symptoms (ADHD-S) in preschool children aged 5 years with Conners rating scale and attentional network task, the last one during a electroencephalographic recording.

Methods: Preschool children were recruited for research through their schools (n = 19; mean age = 65.6 ± 1.96 month; 51% female and 49% male). Parents and teachers completed the short version of the Conners test to identify the presence of symptoms of ADHD (ADHD-S). A pediatric version of attentional network task was evaluated in their schools during a electroencephalographic recording. This test measures different aspects of attention such as Alerting, orienting and executive attention.

Results: The percentage of TD children were greater than the percentage of ADHD-S children. The prevalence of symptoms of ADHD found for 5 years old children was 30%. The results of the main differences found in the ERP analysis shown that exist differences in the early ages in the modulation of different attentional networks. A lower amplitude of the contingent negative variation (CNV) in frontal regions of the head may be an indicator of lower modulation of alertness to external signals. Thus the smaller amplitude of occipital N1 component and frontoparietal P3 component may show that there is a decrease in the ability to redirect spatial attention. The lower amplitude of target P3 or also called P3b in parietal region of the head, may be an indicator of lower inhibitory control to incongruent stimuli in ADHD-S children.

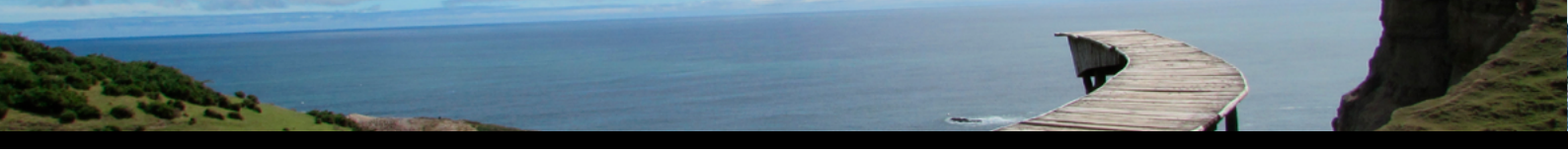
Conclusion: The results support the idea of ADHD as a neurodevelopmental problem because differences can be found in the modulation of different attentional networks before the age of clinical diagnosis. For this reason we suggest the preschool age as a therapeutic target oriented to the prevention of attentional deficit hyperactivity disorder.

FONDECYT regular Nº 1151262, Chile BecaCONICYTDoctoradoNacional, Chile.
Programa de Apoyoparatesis de Postgrado, Facultad de Medicina, Pontificia Universidad Católica de Chile.

28) Severity of some depressive symptoms can predict deep transcranial magnetic stimulation (dTMS) treatment efficacy.

Peña F[1], Linsambarth S[1], Cornejo F[1], Stehberg J[1], [1]Laboratorio de Neurobiología Universidad Andrés Bello. (Sponsored by FONDECYT 1160986).

Deep repetitive transcranial magnetic stimulation (dTMS) applied to the prefrontal cortex (PFC) has been proposed as an adjuvant for pharmacological treatment and has been shown to be effective in the treatment of several psychiatric pathologies, including depression, for which it is FDA approved. The main objective of this study is to determine to which extent initial patients´symptoms can be used to predict dTMS efficacy. Repetitive dTMS was administered to the PFC in a cohort of 213 patients with depression. The efficacy of dTMS was assessed using the HDRS scale (Hamilton Depression Scale) at the beginning, middle and end of the treatment, and their initial depressive symptoms were compared to the effectiveness of treatment. Although improvements over time were found in a large number of symptoms according to the HDRS scale, initial depersonalization, desrrealization and psychic Anxiety showed significant differences between the group that responded and the one that did not. Our data suggest that the beneficial effects of dTMS could be predicted before the treatment according to the HDRS scale, where severity of some symptoms could predict whether or not patients will respond to treatment.



30) Effect of Chronic Unpredictable Stress on 2-4 Hz Oscillations in the Basolateral Amygdala during Fear Memory Retrieval.

Pérez-Valenzuela C[1], Arriagada M[1], Dagnino-Subiabre A[1], [1]Laboratory of Stress Neurobiology, Center for Neurobiology of Brain Plasticity, Institute of Physiology., , Faculty of Sciences, Universidad de Valparaíso.

It has been shown that fear memory is associated to synchronous 4-Hz oscillations in the medial prefrontal cortex-basolateral amygdala (BLA) circuit. On the other hand, chronic unpredictable stress (CUS) induces both dendritic hypertrophy and decreases GABAergic neurotransmission in BLA. The aim of this study was to evaluate *in vivo* whether chronic stress affects the neuronal activity in BLA when rats recall a fear memory. Male *Sprague-Dawley* rats were trained in a classical Pavlovian fear conditioning paradigm. Afterward, animals were implanted in BLA with a microelectrode array (MEA) and following the post-surgery period, implanted rats were separated in control and stress group. Local field potentials (LFP) were recorded from BLA during fear memory retrieval with a wireless *in vivo* recording system (Multichannel System). We found that power of 2-4 Hz oscillations increased in BLA specifically during freezing behavior, a conditioned behavioral response to fear. Seven and fourteen days after retrieval, the 2-4 Hz oscillations in BLA were decreased in control animals, while it is remaining enhanced in the rats that were subjected to CUS protocol. Our results suggest that decreasing of 2-4 Hz oscillations power in BLA is related to extinction of fear memory, while enhancing of 2-4 Hz oscillations after CUS could be related to the persistence of fear memory in chronically stressed animals.

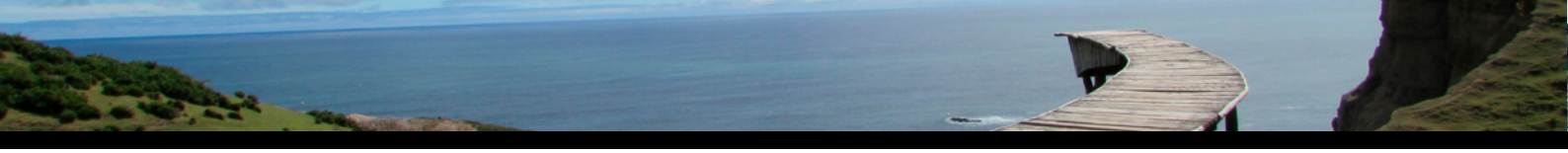
Support: This work was funded by FONDECYT Grant N° 1141276 and Anillo de Ciencia y Tecnología Grant Nº ACT1403 to Alexies Dagnino-Subiabre. Labsite www.stress.cl

32) In Vivo Recording in the Rat Dorsomedial Prefrontal Cortex During Fear Conditioning and Retrieval of Fear Memory.

Ramírez M[1], Dagnino-Subiabre A[1], [1]Laboratorio de Neurobiología del estrés, Facultad de Ciencias, Universidad de Valparaíso.

The dorsomedial prefrontal cortex (dmPFC) plays a key role in the expression of fear memories. Interestingly, a 2-6 Hz oscillations evoked from the dmPFC are associated to retrieval of fear memory in mice. Therefore, we aimed to analyze in this study the dmPFC neuronal activity during both acquisition and retrieval of fear memory in rats. Male *Sprague-Dawley* rats were implanted in the dmPFC with a microelectrode array (Microprobes) and following a post-surgery period, implanted rats were trained in a Pavlovian fear conditioning paradigm. Local field potentials (LFP) were recorded from dmPFC during habituation, fear conditioning and memory retrieval with a wireless recording system (Multichannel System). In addition, neuronal activity from dmPFC was also recorded in non-related fear behaviors in an open field test. We found that increased of power of 2-6 Hz oscillations from dmPFC was synchronized with fear behavior (freezing) in the conditioning and retrieval phases, independently of the context in which fear was evoked by tones exposure. On the other hand, the 2-6 Hz activity in dmPFC was decreased during exploratory and immobility behaviors in an open field test and habituation phase, respectively. These results suggest that the 2-6 Hz oscillations could be the fear memory oscillations in the rats. In addition, this finding opens a new avenue to explore the effect of chronic stress on neuronal activity in the dmPFC.

This work was funded by FONDECYT Grant N° 1141276 and Anillo de Ciencia y Tecnología Grant Nº ACT1403 to Alexies Dagnino-Subiabre. Labsite: www.stress.cl



34) Medial olivocochlear efferent feedback effects in Knockin alpha9-nicotinic cholinergic subunit in young and older mice.

Terreros G[1], Boero L[2], Silva S[3], Gomez-Casati M E[2,4], Delano P[5,3], [1]Instituto de Ciencias de la Salud Universidad de OHiggins.[2]Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, "Dr. Héctor N Torres" CONICET-UBA.[3]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.[4]Instituto de Farmacologia , Facultad de Medicina , Universidad de Buenos Aires.[5]Departamento de Otorrinolaringologia Hospital Clinico de la Universidad de Chile.

Medial olivocochlear (MOC) neurons comprise a negative-feedback gain-control system that can reduce noise-induced cochlear damage. Here, we explore the effect of MOC system in thelong-term maintenance of cochlear function in mice aged 6 months to 1 year. For this purpose, we used a mouse model in which the α9 nicotinic receptor subunit bears a point mutation that leads to enhanced MOC activity (Chrna9L9'T knock-in (KI)). Auditory brainstem responses (ABR) and distortion product otoacoustic emissions (DPOAEs) were used to verify the cochlear function. Afterward, we analyzed the effect of contralateral acoustic stimulation (CAS) on ABR wave 1 amplitudes as a measure of the individual strength of the MOC reflex.

As a sign of cochlear aging, we quantified the loss of synapses between hair cells and the terminals of auditory nerve fibers by whole mount immunostaining for pre-synaptic ribbons (CtBP2) and post-synaptic AMPA-receptor (GluA2). By 6 months, WT (WT_6) and KI mice (KI_6) showed no signs of cochlear synaptopathy and their auditory function was normal. Notably, the amplitude suppression of ABR wave 1 by CAS showed a significantly reduced effect in KI compared to WT mice (Suppression (µV): WT_6 = 0.42; KI_6 = 0.12; Mann Whitney test; $P< 0.05$). By 12 months (WT_{12} ; KI_{12}) we found a significant reduction in ABR wave I amplitudes compared to young mice, indicating some degree of cochlear neuropathy. Importantly, this reduction was smaller in the KI_{12} with an enhanced MOC activity (Amplitude (µV) : WT_6 = 2.074 ± 0.69; WT_{12} = 0.78 ± 0.46; KI_6 = 1.77 ± 0.64; KI_{12}= 1.13 ± 0.43; Mann Whitney test; WT: $P< 0.001$; KI: $P< 0.05$). Finally, we did not found a significant reduction in the strength of MOC effect in WT mice by 12 months (Suppression (µV) : WT_{12} = 0.21; KI_{12} = 0.12; Mann Whitney test; $P >0.05$).

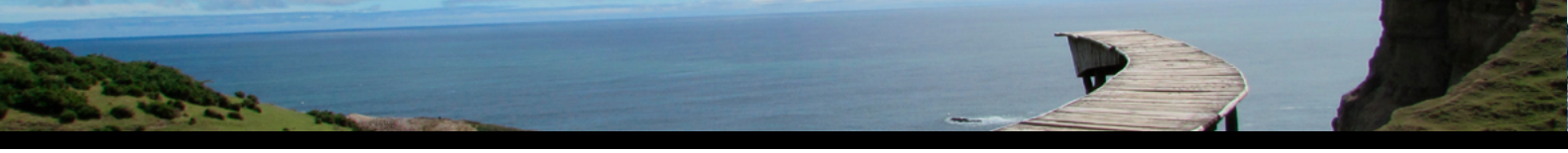
Our preliminary study might indicate that enhancement of the MOC system can slow the effects of aging.
Supporting by REDES 150134, FONDECYT 1161155 and FONCYT (Argentina).

36) Reduced power in alpha and theta bands in ADHD children during a visuo-spatial working memory task.

Valdés J[1], Ihnen J[1], Medel V[1], Ossandón T[1], [1]Neurodynamics of Cognition Lab, Department of Psychiatry - Medical School Pontificia Universidad Católica de Chile.

Deficits in visuo-spatial working memory (VSWM) are one the most common impairments in subjects with ADHD. VSWM is associated with amplitude modulations in theta, alpha, and gamma bands. Specifically, increases in the power of a theta fronto-central component and a posterior alpha component have been shown to occur in dependence of memory load. In this study, we sought to compare the modulations of alpha and theta power in control and ADHD children (9-13 yo). ADHD patients performed the task in two separate sessions, on- and off-medication, which in all cases was methylphenidate. We monitored the subjects during a visuo-spatial working memory task in a modified Sternberg VSWM task, using scalp EEG. In this task, the periods of encoding, retention and recognition are separated. In all groups, the time-frequency plots show clear increases in the encoding phase and retention phase in a frequency band from 4-12 Hz (theta and alpha) in more anterior electrodes (Fz and Cz) and from 4-30 Hz (theta, alpha, beta) in more posterior electrodes (Pz and Oz). In the recognition period, after the presentation of the probe, there is also an increase in power from 4-12 Hz (theta and alpha) in all electrodes, followed by a notorious suppression of power in the alpha and beta bands (12-25 Hz) in posterior electrodes (Pz and Oz). A between groups permutations test of the time-frequency plots shows that in the encoding and recognition phase unmedicated ADHD children present lower power in the theta band in Cz and lower alpha band in the encoding phase in posterior electrodes (Pz and Oz). These results suggest that impairments in VSWM in ADHD might be related to decreased local synchronization in the theta band and alpha bands in fronto-central and posterior electrodes, respectively which could explain their performance deficits in the task.

Supported by FONDECYT 1140996.



38) The role of visual cortex in self-generated thoughts: evidence from event-related potentials and fMRI functional connectivity.

Villena-Gonzalez M[1], Wang H[2], Sormaz M[2], Margulies D[3], Jefferies E[2], Smallwood J[2], Rodriguez E[2], [1]Laboratorio de Neurodinamica, Escuela de Psicología, Pontificia Universidad Católica De Chile.[2]Department of Psychology/York Neuroimaging Centre University of York.[3]Max Planck Research Group for Neuroanatomy & Connectivity Max Planck Institute for Human Cognitive and Brain Sciences. (Sponsored by We Acknowledge Support From CONICYT-PCHA/ Doctorado Nacional/2014-21140290 To MV, European Research Council (WANDERINGMINDS?646927) To JS And FONDEQUIP Grant EQM120027 And FONDECYT Grant 1120752 To ER).

When attention is oriented toward self-generated thought (SGT), the sensory processing of visual stimuli becomes attenuated. This reduction in processing has been understood as a decoupling or deactivation of sensory cortices during SGT. However, an alternative view is that visual cortex is actively involved in thought's construction, and therefore, visual cortex becomes less available to processing external information. In the present work we tested this latter hypothesis by carrying out two experiments. Experiment 1 was aimed to test if visual represented thoughts trigger a larger attenuation of visual response to external stimuli than an auditory represented thought. Experiment 2 aimed to test if functional connectivity from visual cortex into the default network (DMN) during resting state determines features of imaginative thought.

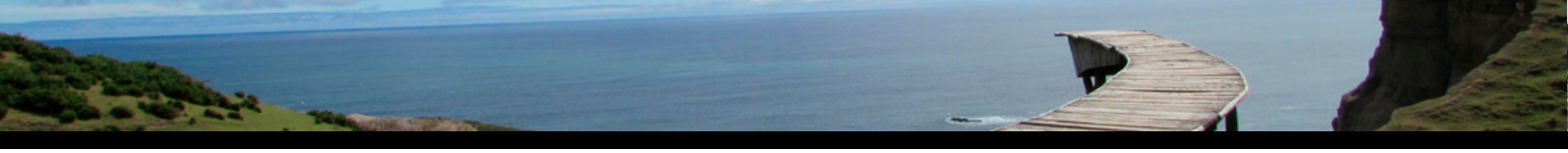
In the experiment 1, we found that visual processing of external stimuli is more attenuated when SGT is represented visually than auditory/verbally. In the experiment 2, we found that strong intrinsic communication between visual and retrosplenial cortex predicts the degree of social thoughts about the future. Using an independent dataset, we show that the same region of retrosplenial cortex is functionally coupled to regions of primary visual cortex as well as core regions that make up the DMN.

Together these findings suggest that information from visual cortex is integrated during SGT, modulating sensory processing depending on the modality of thoughts. Furthermore, this evidence showed that retrosplenial cortex may act as a possible "hub" of information by integrating sensory cortices with the DMN, which in turns determines some features of imaginative thoughts. We speculate that the role of the DMN in imagination may emerge from its capacity to bind together distributed representations from across the cortex in a coherent manner.

40) Therapeutic effect of stem cells in a sporadic Alzheimer´s disease rat model.

Zappa Villar M F[1], Morel G R[1], Trípodi L S[1], Lopez Hanotte J[1], García M G[2], Reggiani P C[1], [1]School of Medical Sciences - INIBIOLP National University of La Plata.[2]School of Biomedical Sciences - Gene Therapy Lab Austral University.

Alzheimer's disease (AD) is the most common form of dementia, representing a growing medical and socioeconomic challenge. AD is characterized by the degeneration of neurons and reduced brain glucose metabolism, as well as by the progressive decline of cognitive functions. Our objective is to develop therapeutic strategies that allow preventing and/or overcoming the degenerative changes in the brain with experimental AD. In this context, cell therapy emerges as a promising therapeutic approach. We set up a model of sporadic AD by the intracerebroventricular (icv) injection of streptozotocin (STZ) in rats. In a first study, we explored the therapeutic effect of mesenchymal stem cells (MSC) in our STZ-icv animal model. Intact, STZ and STZ+MSC groups were used. STZ and STZ+MSC groups received 3 mg/kg STZ-icv and, 24 hours later, the STZ+MSC group received 2x105 MSC-icv. STZ+MSC group showed a significant improvement in learning and spatial memory by the Barnes Maze (BM) and recognition memory by Novel Object Recognition test (NOR). We also assessed the effect of intravenous (iv) administration, as a non-invasive route, of hMSC on behavior and microgliosis in the dorsal hippocampus of AD rat model. Intact, STZ and STZ+MSC groups were used. After 24 days of STZ, when the damage was already established, animals received four times 1x106 MSC iv. We performed Open Field (OF), NOR, BM and Marble Burying (MB) tests to estimate memory, depression-like and anxiety-like behaviors. STZ group showed an increase in Iba1-immunoreactive microglial cells and a deficiency in all behavioral tests. STZ+MSC group improved its performance in OF, BM and MB. We concluded that MSC therapy is a suitable biological tool in neurodegenerative disorders, preventing the progression of cognitive impairment when injected in situ or restoring it when systemically administered for two months.



42) Comparison of Different Diffusion Approximation Implementations in a Conductance-Based Model of Slow Wave Parabolic Bursting.

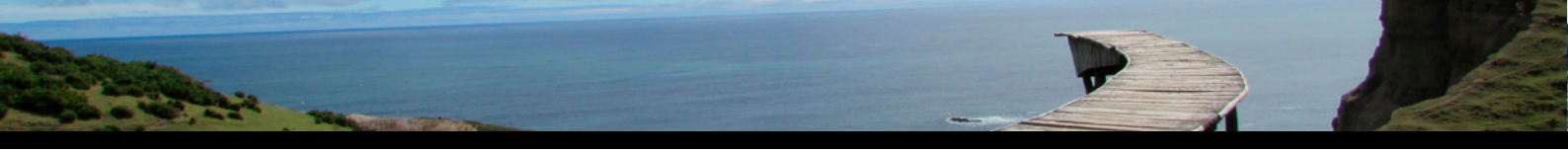
Maidana J[1,3], Gatica M[2], Nicolis O[1], Orio P[3,4], [1]Instituto de Estadística , Facultad de Ciencias, Universidad de Valparaíso.[2]Departamento de Matemática, Facultad de Ciencia, Universidad de Santiago De Chile.[3]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.[4]Instituto de Neurociencia, Facultad de Ciencias, Universidad de Valparaíso. (Sponsored by JPM Is Recipient Of A PhD Grant FIB-UV From UV, PO Is Partially Founded By Grants FONDECYT 1130862 (ACT-1113), AC3E (FB0008 CONICYT, Chile). The CINV) is A Millennium Institute Supported By The Millennium Scientific Initiative Of The Ministerio De Economía).

Noise can shape the dynamics of neural systems in unique ways. Stochastic opening and closing of ion channels is an important source of neural noise, and conductance-based models arise as a plausible and biologically relevant way to study it. This requires an appropiate numerical simulation of stochastic channel gating. An alternative to the time-consuming simulation of a large number of Markov Chains, the Diffusion Apporiximation (DA) converts the deterministic Ordinary Differential Equations (ODEs) into Stochastic DEs with a multiplicative noise term. However, several subtle errors can be made when implementing the DA, such as considering a fixed number of channels when varying membrane area or treating calcium dynamics equations in the same way as ion channels. To study the effects of these mistakes, we used a parameter-swipping approach in a simple model of burst generation, where we study how noise interacts with the slow subthreshold dynamics. We simulated the model with different noise implementations and quantified the different firing modes observed in a region of the parameter space. Firing patterns were compared using a non-parametric test for the similarity of the Inter-Spike Intervals distribution and Wavelet Cross Spectrum of the Voltage traces. Qualitatively, firing modes obtained with different noise implementations are similar with only a few differences in some critical regions of the parameter space. However the distributional test of similarity and time-frequency representation capture more differences. We conclude that in certain regions of the parameter space, an incorrect implementation of the DA algorithm can produce results with firing staitstics different to what is expected.

44) Is chaos making a difference? Synchronization transitions in chaotic and nonchaotic neuronal networks.

Xu K[1], Orio P[2], [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, University of Valparaíso,Chile.[2]Instituto de Neurociencia, Facultad de Ciencias, Universidad de Valparaíso. (Sponsored by KX Is Funded By Proyecto FONDECYT 3170342. PO Is Partially Funded By The Advanced Center For Electrical And Electronic Engineering (FB0008 CONICYT, Chile). The Centro Interdisciplinario De Neurociencia De Valparaíso (CINV) Is A Millennium Institute Suppor).

Chaotic dynamics of neural oscillations has been shown at the single neuron and network levels. Theoretical works suggest that chaotic dynamics enrich the behavior of neural systems. However, the contribution of chaotic neural oscillators to relevant network behavior has not been systematically studied yet. We investigated the synchronization of neural networks composed of conductance-based neural models that display subthreshold oscillations with regular and burst firing. By small changes in conductance densities, the model can be turned into either chaotic or non-chaotic modes . We study synchronization of heterogeneous networks where conductance densities are drawn from either chaotic or non-chaotic regions of the parameter space. Measuring mean phase synchronization in a small-world network with electrical synapses, we characterize the transition from unsynchronized to synchronized state as the connectivity strength is increased. First, we draw densities from fixed-size regions of the parameter space and find the transition to synchronized oscillations is always smooth for chaotic oscillators but not always smooth for the nonchaotic ones. However, non-smooth transitions were found to be associated to a change in firing pattern from tonic to bursting. Nevertheless, we noticed that chaotic oscillators display a wider distribution of firing frequencies than non-chaotic oscillators, thus making more heterogeneous networks. Next, we draw the conductance densities from the parameter space in a way that maintained the same distribution of firing frequencies (hence the heterogeneity of the network) for both chaotic and non-chaotic. In this case, synchronization curves are very similar, being second order phase transition for both cases. However, we cannot discard that non-chaotic oscillators become chaotic (or vice versa) when in a network, because of the extra parameter associated to the electrical synapse. Finally, when the chaos-inducing Ih current is removed, the transition to synchrony occurs at a lower value of connectivity strength but with a similar slope. Our results suggest that the chaotic nature of the individual oscillators may be of minor importance to the synchronization behavior of the network.



46) Long term effects of LL exposure during lactation on metabolic and circadian system.

Palma M[1], Osnaya Ramirez R I[2], Escobar C[2], [1]Anatomy, Facultad de Medicina, UNAM.[2]Anatomia, Medicina, UNAM.

Epidemiological and experimental evidence supports an association between constant light (LL) exposure and an increased incidence of overweight and metabolic disease in rats. The present study aimed to describe the effects constant light (LL) during lactation on the development of the suprachiasmatic nucleus (SCN), on body weight and metabolism in rat pups. New born rats were randomly assigned to one of three groups: Control lightdark cycle 12:12 (LD), Constant darkness (DD) or Constant light (LL). Lighting conditions were maintained along lactation from P0 to P21. In order to specifically evidence the effects of light conditions in the pups, the nursing mothers had a normal LD cycle. At P21 after weaning we determined daily rhythms of glucose, general activity, Vasoactive Intestinal Peptide (VIP), Arginine Vasopressin Peptide (AVP) and the clock protein PER1 in the SCN. General activity was assessed from P14 to P21 and we found that in LD conditions 100% of litters were rhythmic, 33.33% of litters in DD and 16.67% of litters in LL were rhythmic, In pups exposed to DD and LL the peptides AVP and VIP and the clock protein PER1 in the SCN showed arrhythmic patterns, additionally the number of positive immunoreactive cells of VIP and AVP was decreased as compared with the control group. In LLexposed animals body weight gain was significantly increased as well as fat mass, the glucose rhythm was lost in both DD and LL conditions. The body weight remained higher until day P90 in spite of exposing them after weaning to a normal 12:12 LD cycle. Our results show that LL, as well as DD, affect the development of the SCN leading to a decreased VIP and AVP cell number and for LL a loss of rhythmicity. These animals also had metabolic disturbance and increased weight gain. Present results point out a programming process early in development and indicate the relevance of a normal LD cycle for the development of the SCN.

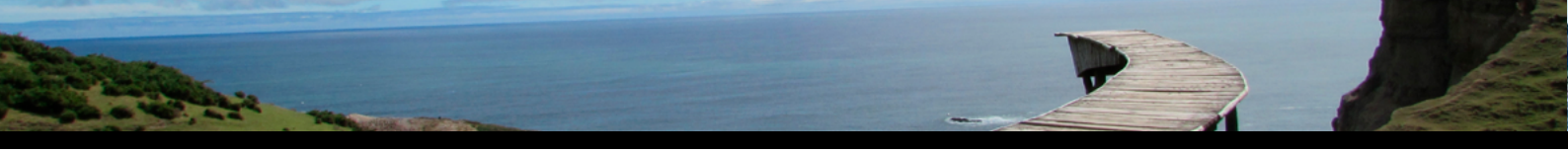
48)Searching for a Reelin-like protein in Drosophila melanogaster and its associated signaling pathway.

Rojo F[1], Marzolo M P[1], Campusano J[1], [1]Biología Celular y Molecular, Ciencias Biológicas, Pontificia Universidad Católica De Chile.

Reelin is an extracellular glycoprotein that plays a role in neuronal migration and plasticity. Deficient Reelin expression has been associated to neuropsychiatric disorders. Although Reelin has been historically considered a vertebrate signaling molecule, a recent report suggests that Reelin is also present in the filum Arthropoda, to which the D. melanogaster belongs. Drosophila also presents orthologous for the proteins involved in the Reelin canonical signaling pathway in vertebrates. Taking in consideration this information, we postulated the occurrence of a Reelin-like protein and signaling cascade in D. melanogaster.

Many reports show that Reelin treatment increases the number and length of neurites in primary cultures of hippocampal neurons, an effect that depend on Reelin receptors (ApoER2 and VLDL) and the Dab1 protein. We decided to assess whether mammalian Reelin was able to induce similar effects in cultured Drosophila neurons. We also studied the dependence for these effects on LpR1 and LpR2, orthologous for Reelin vertebrate receptors, and Dab protein.

Drosophila brain primary cultures were prepared from wildtype and mutant animals for these genes. These cultures were treated with Reelin and Sholl analyses were carried out in GFP-expressing Drosophila neurons. In addition, a BLAST homology study identified a putative Reelin-like protein in Drosophila which has not been previously characterized: CG17739. We studied the effect induced by mammalian Reelin on cultures prepared from mutant animals for this gene. Additionally, fly brain general anatomy was evaluated in these mutants. Results obtained show that mammalian Reelin stimulates the complexity of the neuritic tree in fly neurons in culture. This effect is not observed in cultured neurons from mutant animals. On the other hand, cultured neurons mutants for the putative Reelin-like protein exhibit poor neurite development which can be at least partially recovered by mammalian Reelin treatment. These results support the idea that there is a Reelin functional homolog in Drosophila, whose actions depend on LpR1, LpR2 and Dab. Preliminary experiments suggest that CG17739 could behave as the Reelin homolog in Drosophila, but further experiments are needed to support this idea.



50) RETIRADO

52) Characterization of mitochondria in response to spinal cord injury in Xenopus laevis.

Cavieres J[1], Lee-Liu D[2], Eisner V[3], Larrain J[1], [1]Laboratory of Developmental Biology and Regeneration, Facultad de Ciencias Biológicas, Center for Aging and Regeneration- CARE Chile UC, P. Universidad Católica de Chile..[2]Laboratory of Neuronal and Cellular Dynamics, Facultad de Ciencias, Geroscience Center for Brain Health and Metabolism (GERO), Universidad de Chile.[3]Mitochondrial Communication and Function Laboratory, Facultad de Ciencias Biológicas, P. Universidad Católica de Chile.

In mammals, spinal cord injury (SCI) is practically irreversible given the Central Nervous System (CNS) has a limited regenerative capacity. Unlike mammals, anuran larvae (for example, African clawed frog *Xenopus*) are capable of functional recovery after spinal cord injury in regenerative stages which correspond to the tadpoles stages. In contrast, *Xenopus* froglets are unable to regenerate following metamorphosis (non-regenerative stages). The presence of regenerative and non-regenerative stages makes *Xenopus laevis* a unique model organism to study regenerative biology. In this context, transcriptomic and proteomic analyses from our laboratory have shown differential expression of a gene set in regenerative stages when compared to non-regenerative stages in response to SCI. A large percentage of these genes are related with energy metabolism, and among them, we identified a cluster of mitochondrial proteins whose expression is significantly decreased in response to SCI in regenerative stages, while in non-regenerative stages we observed no significant changes. In this context, our primary goal is to compare mitochondrial architecture and abundance in cells of the spinal cord central canal zone. By evaluating the expression of mitochondrial protein COX IV, we observed that mitochondria of cells in the central canal zone show apical distribution patterns. Electron microscopy analyses suggest that the number of mitochondria decrease in response to SCI. Furthermore, we noted ultrastructural changes in response to SCI in regenerative and non-regenerative stages. In this regard, we observed mitochondria forming nanotunnels, and that these, in regenerative stages, apparently decrease in response to SCI. We also observed morphology similar to that of mitochondrial donuts, previously reported in cells after hypoxic conditions. As part of the work in progress of this study, we showed that only in regenerative stages, mitochondrial donuts increase in response to SCI. Considering our previous proteomic analysis and differences in abundance and architecture of mitochondria between the regenerative and non-regenerative stages, we propose that mitochondria could play a key role in the regeneration of the spinal cord.

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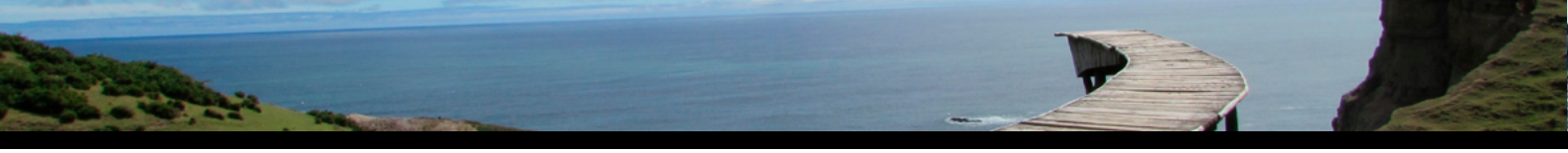

54) Motor effects of non-invasive spinal cord stimulation in a parkinsonian animal model.

Gallegos, S[1], Alamos, F[2], Martinez, A[3], Fuentes, R[4], [1]Neuromodulation and Control Motor Lab, Medicina, Universidad de chile.[2]BNI, Pontificia Universidad Católica de Chile.[3]Facultad Ciencias Fisicas y Matematicas Universidad de Chile.[4]Departamento de Neurociencias, Medicina, Universidad de Chile.

Parkinson's disease is one of the most common neurodegenerative disorders. Pathophysiological findings are related to the degeneration of dopaminergic cells in the substantia nigra pars compacta, which results in low striatal dopamine levels and abnormal synchronous oscillatory activity in the basal ganglia and cortex.

Among treatments, levodopa is usually effective in the early stages of the disease by improving the motor symptoms, but as time passes, these positive effects decrease. Other therapeutic strategy, the Deep Brain Stimulation (DBS), has become a recognized treatment modality with positive effects.

Recent evidence suggests that another neuromodulation procedure, spinal cord stimulation (SCS), is effective in the acute management of Parkinson Disease motor symptoms. Yet, both DBS and SCS requires surgical implants of stimulation devices, and are not used as treatment first options. Thus, having neuromodulation options that do not require surgery, would make this option available earlier and may be to a bigger number of patients.

In the present study we explored the motor effects of noninvasive spinal cord stimulation (NISCS), which uses electrodes on the surface of the skin, in a model of Parkinsons Performed in six rats divided into two groups (sham and intervention), the last group being noninvasively stimulated at medullar level (T12-L4). The parameters were defined through a previous electrophysiological study at 2500 uA, 300 Hz for 30 minutes during 12 days. The open field recording is carried out simultaneously during stimulation, the cylinder test, one minute post-stimulation and rotameter 45 minutes post-stimulation, to distinguish the acute and chronic effect of the NISCS.
The analysis of the motor effects resulted in a gain of the wight of the NISCS group over the sham group, in addition to an improvement in the rotameter test. However, the cylinder and open field results do not show a significant change.

Since this approach will be relatively inexpensive, safe, and easy to administer compared to other neuromodulation techniques, positive findings could be promptly translated into clinical practice and being available in the short term for a significant number of patients.

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56) Increased eaat3 expression in forebrain elicits ocd relevant behaviors.

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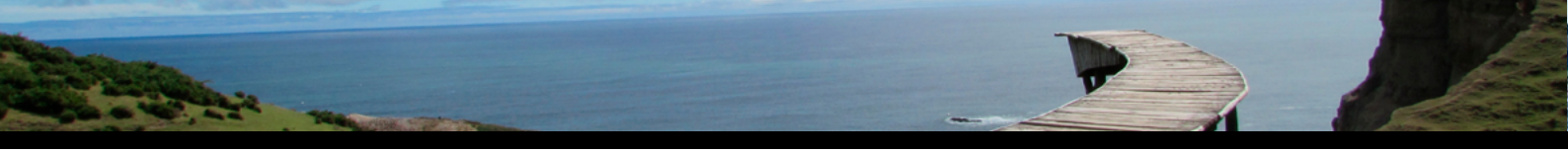
Obsessive-Compulsive Disorder (OCD) is a neuropsychiatric disorder characterized by obsessions and compulsions. Extensive evidence suggests altered glutamatergic transmission in cortico-striato-thalamo-cortical (CSTC) circuitry in OCD. As such, glutamatergic genes emerge as good candidates for association studies in OCD, particularly the *SLC1A1* gene encoding the neuronal glutamate transporter EAAT3. EAAT3 is expressed prominently in the CSTC circuitry, and plays multiple roles in regulating neuronal function. Consequently, it is of great interest to find out whether altered EAAT3 expression triggers OCD-like behaviors.

We generated conditional EAAT3 overexpressing (EAAT3glo) mice, and evaluated CamKIIa-driven expression at behavioral and molecular levels. EAAT3glo/CMKII mice were found to have increased EAAT3 mRNA levels in several brain regions, and increased protein levels were found by Immunohistochemistry. Also, the levels of GSH were analiyzed. EAAT3glo/CMKII mice were tested in a battery of behavioral paradigms relevant to OCD. We found increased anxiety-like and compulsive-like behaviors in EAAT3glo/CMKII mice, which were restored by chronic administration of fluoxetine and clomipramine. Thus, our novel mouse model has construct, face and predictive validity aspects that are relevant to this disorder.

Supported by Nucleo Milenio NuMIND (NC130011) and FONDECYT (1141272).



58) Behavioral characterization of a schizophrenia-related dysbindin mutant: possible contribution of the serotoninergic system.

Hidalgo S[1], Castro C[1], Campusano J[1], [1]Biología celular y molecular, Neurogenética de la Conducta, Ciencias biológicas , Pontificia Universidad Católica De Chile.

Dystrobrevin binding protein 1 (dysbindin) is a protein encoded by the dtnbp1 gene, associated with susceptibility to schizophrenia in humans. This protein is part of the biogenesis of lysosome-related organelles complex 1 (BLOC-1), an octameric complex involved in the endosomal trafficking of different cargoes. In the fruitfly, the dysbindin orthologue was found to be expressed in neural terminals and glial cells at the brain where it has the ability to modulate glutamatergic and dopaminergic function. It is also known that the serotoninergic neural system is affected in schizophrenia, but whether dysbindin mutants are affected in the serotonergic system is still unexplored. We conducted a behavioral screening using pharmacological approaches previously linked to the serotoninergic circuitry and different tests, to dissect out the contribution of this aminergic system to behaviors observed in dysbindin Drosophila mutants.

To assess olfactory acuity and locomotor activity, a single male fly is placed in a 3 mm-diameter arena where its behavior is recorded. After 3 minutes, the fly is exposed to the odorant benzaldehyde (1%) only in one side of the arena for 3 more minutes. A performance index is calculated comparing the time spent in the water side vs the odorant side. To assess the startle response, a group of 20 male flies is placed in a 20-cm test tube and allowed to settle for 30 minutes. Afterwards, flies are tapped down by gently hitting the test tube. Seven seconds later, the number of flies that climb up at least two thirds of the tube are counted and a performance index is calculated. The same process is repeated 15 times with 30 second breaks in between the trials to assess habituation. To assess serotoninergic contribution to those behaviors, flies are feed prior the experiments with 100 µM 4-MTA, a highly selective SERT ligand.

Our data show that dysbindin mutant flies present altered olfactory function as olfactory acuity is significantly diminished. Also, a decrement in the total distance traveled and in speed movement was found in dysbindin mutants, suggesting locomotor problems. Moreover, dysbindin mutants show defects in the startle response over time. Interestingly, 4-MTA induces an increased response to startle which is abolished in dysbindin mutants. This supports the idea of a change in SERT function in these mutants. Overall, our results suggest a possible dysregulation of the serotoninergic system, consistent with the abnormalities displayed on schizophrenia patients.

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60) Electrophysiological effects of non-invasive spinal cord stimulation in parkinsonian animal model.

Alamos F[1], **Martinez A[2]**, Gallegos S[3], Fuentes R[4], [1]Biomedical Neuroscience Institute, Facultad de Medicina, Pontificia Universidad Católica De Chile.[2]Biomedical Neuroscience Institute, Ciencias Fisicas y Matematicas, Universidad de Chile.[3]Biomedical Neuroscience Institute, Facultad de Medicina, Universidad de Chile.[4]Depto. de Neurociencia, Facultad de Medicina, Universidad de Chile.

Motor impairments are the most characteristic symptoms of Parkinson´s disease (PD), which affects one in every hundred people over 60 in the world. These motor impairments are commonly controlled with medications such as levodopa and therapies such as deep brain stimulation (DBS), but these treatments usually do not completely cover motor problems, such as the axial symptoms, related to posture and gait.

That is why new therapies such as spinal cord stimulation (SCS) have begun to take on great importance, as it largely alleviates axial motor problems, making people suffering from Parkinson´s disease walking more fluidly, improving posture and reducing tremors. Due to the SCS good results, we propose an improvement for this treatment, the non-invasive spinal electrostimulation (NI-SCS), which will avoid complications typical of surgery.

For this we placed superficial pads on the skin above the spinal cord of rats with parkinsonism condition (PC) to generate a stimulation current that will be propagated through the spinal circuits. Its effectiveness was estimated by analyzing the electrophysiological activity in supraspinal structures: primary motor cortex (M1), supplementary motor area (SMA), primary somatosensory cortex (S1), dorsolateral striatum (DLS), ventral posterolateral nucleus (VPL).

In these areas, we measured the change of Power Spectral Density (PSD) in the beta band [8-20] Hz, which is normally increased in PC, and how this change is maintained after receiving NI-SCS, as well as assessing the effects in higher frequency bands.Another important feature which has been detected in PD, is the rise of synchronization among cortical-basal ganglia circuit parts, so we established how strong is the synchronization under PC and how the synchronization changes when exposed to NI-SCS.

In general, SCS has shown to decrease both beta band potential and synchronization and in the same way, our results show that NI-SCS has strong modulatory effects over PC beta oscillations and changes in the synchronization of the areas previously mentioned.

This determined how effective NI-SCS is compared to other treatments, both pharmaceutical and with stimulation, and propose a non-invasive therapy, easy to implement, at a lower cost and that allows to treat one of the biggest problems that people with PD suffer, probably allowing them to resume the activities they performed before contracting this disease.

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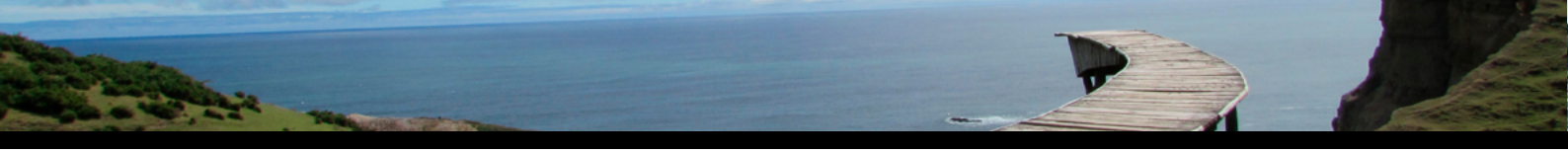
BNI Millennium Institute No. P09-015-F.



62) Interactions between epinephrine and corticosterone on the availability of insular β-adrenergic receptors and the modulation of anxiety.

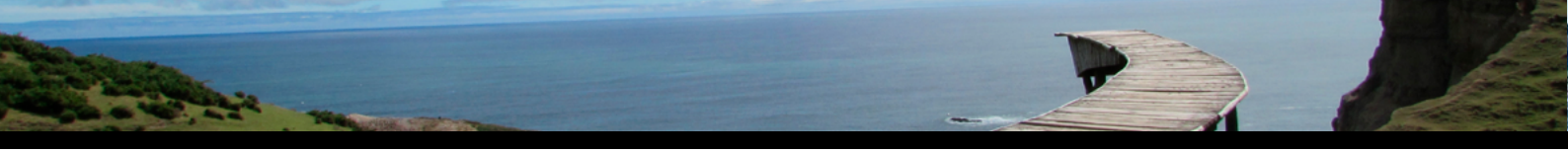
Palma F[1], Rojas S[1], Cornejo F[1], Tamburini G[1], Bahamonde T[1], Stehberg J[1], [1]Laboratorio de Neurobiología Universidad Andrés Bello. (Sponsored by FONDECYT 1160986).

Stress hormones, such as epinephrine and glucocorticoids are released in response to stress and mediate anxiety. However, their potential interactions in the modulation of anxiety have not been assessed to date. The present study aims at characterizing the mechanisms by which glucocorticoids acting at the insular cortex can affect anxiety induced by epinephrine treatment, and change the expression of insular β-adrenergic receptors. Here we show that corticosterone micro-injected into the insular cortex modifies the anxious behavior induced by subcutaneous administration of epinephrine, as measured using the elevated plus maze, which could be explained at least partially by changes in adrenoreceptor expression. Understanding the mechanisms that trigger anxiety in response to stressful stimuli is imperative for the development of novel therapies for the control of stress and anxiety.

64) Palmitic acid-mediated Free Fatty Acid Receptor 1 (FFAR1) activation stimulates ERKI/II and JNK and reduces insulin sensitivity in hypothalamic neurons.

Toledo-Valenzuela L[1], Hernández-Cáceres M P[1], Ávalos Y[1], Morselli E[1], [1]Physiology Department, Faculty of Biological Sciences, Pontificia Universidad Católica De Chile.

The saturated fatty acid palmitic acid (PA), abundant in high fat diet, crosses the blood-brain barrier and accumulates in the brain promoting hypothalamic inflammation, causing obesity and Type 2 Diabetes (DM2).The mechanism by which this occurs is the object of our investigation. We previously show that exposure to pro-obesigenic concentrations of PA (100µM) increases the levels of pro-inflammatory cytokines in the hypothalamic neuronal cell line N43/5, however how this occurs is still unclear. Our results indicate that the inhibition of the Free Fatty Acid Receptor 1 (FFAR1), expressed in hypothalamic neurons, reduces the level of pro-inflammatory cytokines in N43/5 cells exposed to PA, suggesting that this receptor might be involved in PA-induced inflammation. Previous studies show PA activates extracellular signal-regulated kinases (ERKI/II) and c-Jun N-terminal Protein Kinases (JNK) causing inflammation and reducing insulin sensitivity in several cell types. However, whether FFAR1 is implicated in the activation of these proteins causing inflammation and reducing insulin insensitivity in hypothalamic neurons is currently unknown.*We hypothesize that PA stimulates FFAR1 activating ERKI/II and JNK causing inflammation and reducing insulin sensitivity in N43/5 cells.* We treated the N43/5 cells with the FFAR1 antagonist GW1100 (1µM) followed by exposure to PA (100µM) and we measured pERKI/II and pJNK levels by Western Blot (WB). Additionally, cells were incubated with GW1100, followed by PA treatment and finally exposed to insulin (1nM) to tested insulin sensitivity as indicated by pAKT levels by WB. Our results show that FFAR1 activation by PA increases pERKI/II and pJNK in N43/5 cells, an effect prevented by GW1100. Additionally, treatment with PA reduced insulin-mediated pAKT increase in N43/5 cells. Interestingly, this effect was also prevented by GW1100. Altogether, these results suggest that PA-mediated activation of FFAR1 stimulates ERKI/II and JNK, which might lead to the increase in pro-inflammatory cytokines following PA exposure. Finally, our data indicate a role for FFAR1 in the regulation of insulin sensitivity in N43/5 cells. These results will help understanding the mechanisms by which PA leads to the onset of obesity and DM2.



66) Role and mechanisms of action of DYN-A2-17 in food intake in PVN.

Barrientos T[1], Alvarez B[1], Perez-Leighton C[2,1], [1]Center for Integrative Medicine and Innovative Science (CIMIS), Facultad de Medicina, Universidad Andrés Bello.[2]Department of Food Science Nutrition, Food Science Nutrition, University of Minnesota.

The dynorphin (DYN) peptides can be classified as opioid or non-opioid depending on whether they bind to opioid receptors. Opioid DYN peptides regulate food intake, but the physiological role of non-opioid DYN is not well understood. Recent evidence shows that administration of the non-opioid peptide DYN-A_{2-17} into the hypothalamic paraventricular nucleus (PVN) acutely increases chow intake and spontaneous physical activity, but there are still several questions about the behavioral effects and mechanisms of DYN-A_{2-17}. The present study aimed to understand the role and possible mechanisms of action of non-opioid peptide DYN-A_{2-17} in food intake in PVN. In male Balb/c mice cannulated aiming at PVN, we evaluated whether DYN-A_{2-17} increased food intake depending on PVN CRF signaling, whether it increased ACTH plasma concentration and activated PVN neurons measured by Fos immunohistochemistry. Pretreatment with the CRF receptor antagonist (αCRF9-41,1µg) into PVN blocked the effects of DYN-A_{2-17}(3nmol) on chow intake (n = 9). The injection of DYN-A_{2-17} (3nmol) into PVN increased plasma ACTH (aCSF=10; DYN-A_{2-17}= 8), while there are no significant effects on the activation of FOS in PVN (aCSF=8; DYN-A_{2-17}= 9). In summary, our data show that DYN-A_{2-17} is a neuropeptide that can promote food intake through its actions in PVN which seem to depend on local CRF signaling. This research was supported by grant FONDECYT Regular 1150274 (CONICYT, Gobierno de Chile).

68) How my hippocampus know where you are?.

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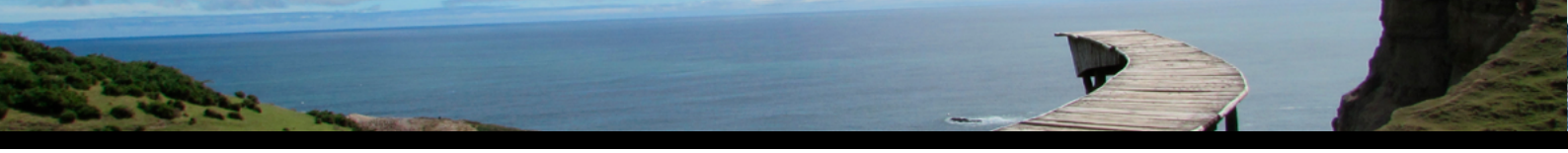
Observational or social learning is the ability to imitate a goal-directed behavior from the observation of a congener that acts as a demonstrator. The mirror neuron system is a proposed mechanism for social learning, but it has been described in humans and primates during motor paradigms. However, there is evidence about observational learning in other species and paradigms, suggesting that other neurophysiologic mechanisms could be responsible for this cognitive ability.

Rodents can learn from observation during spatial memory tasks. However, there is no evidence for the hippocampal role in this process, even though the well-documented involvement of this structure in spatial memory. Here, we assess the role of the hippocampus at the behavioral and hippocampal activity level, during an observational spatial learning task.

In brief, untrained rats could observe how an expert demonstrator rat, solves a spatial maze. After the observation, the untrained rat must solve the maze.

We found that the observer rat improves their performance after observation and this improvement was completely abolished after pharmacological inactivation of the hippocampus. In-vivo electrophysiological recordings in the observer animal brain, showed the existence of a population of CA1 pyramidal neurons capable of representing the position of the demonstrator during the observation (observational place cells, OPC). Half of those OPC was also regular place cells during navigation, and share several features between them. In summary, the hippocampus is critical for learning improvement induced by observation, and we proposed that the capacity of the hippocampus to represent the position of others could be a substrate for social or observational learning.

Biomedical Neuroscience Institute (BNI) - ICM #P-09-015-F.
Center for the memory neuroscience (CENEM) - ICM #P-10-001-F.
CONICYT Doctoral Fellowship .



70) ATP mediates the respiratory response to hypercapnia in the caudal medulla.

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ATP released by astrocytes in the retrotrapezoid nucleus (RTN) in response to hypercapnia increases the respiratory frequency in mice. However, in other caudal brainstem chemosensory nuclei, such as the raphe nucleus (NR) and the nucleus of the solitary tract (NTS), evidence supporting the role of ATP as a mediator of the respiratory response to hypercapnia has been elusive. We have shown that hypercapnia induces ATP release from caudal brainstem slices.

Since these slices do not contain the RTN, the source of ATP should be other chemosensitive nuclei. In this work, we evaluated whether ATP activates the respiratory rhythm in caudal brainstem slices and which purinergic receptors are involved. In addition we evaluated the effects of purinergic blockade in the respiratory response induced by hypercapnia using antagonists of P2X and P2Y1 receptors (PPADS and MRS2179.)

Fictive respiration was recorded in medullary slices (700 µm thick) of CF1 (P0-P8) mice with a suction electrode placed in the ventral respiratory column (VRC). In basal condition, superfused with artificial cerebrospinal fluid (aCSF) equilibrated with 5% CO2, 95% O2 and during hypercapnic acidosis equilibrated with 10% CO2, 90% O2 in the presence and absence of PPADS (200 µM) and MRS2179(75 µM) administered by superfusion.

Hypercapnia increased the respiratory frequency in 100% over basal (n = 8, P = 0.0079, Wilcoxon test). This increase in the respiratory frecuency was significantly reduced during hypercapnia when the slice was previously incubated with PPADS or with MRS2179, reaching to 5% (n = 8 P = 0.0079, Wilcoxon test) and -10% over basal (n = 8 P = 0.0079, Wilcoxon test). We conclude that ATP is a mediator of the respiratory response to hypercapnia in the caudal brainstem nuclei acting on P2 receptors, specifically on P2Y1 receptors.

72) Pro-inflammatory cytokines and reactive oxygen species in the nucleus of the solitary tract of hypertensive rats induced by chronic intermittent hypoxia.

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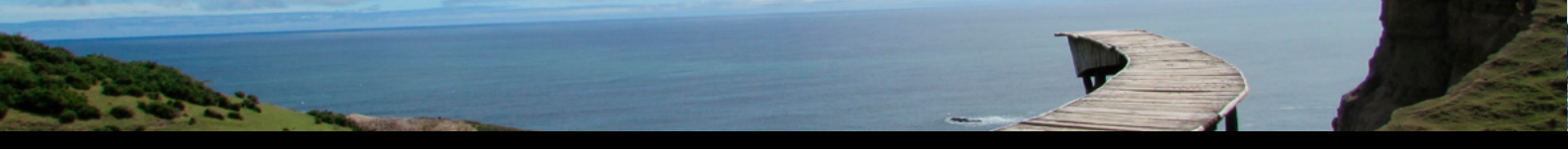
Chronic intermittent hypoxia (CIH) is the main risk factor for hypertension in obstructive sleep apnea (OSA). Oxidative stress, inflammation and sympathetic activation have been proposed as mechanisms underlying the hypertension in OSA. In rats exposed to CIH mimicking OSA, intermittent hypoxia enhances the carotid body (CB) chemosensory discharge, which in turn potentiates the sympathetic activity leading to an increase in arterial blood pressure of ~10 mmHg in 3-5 days. In addition, CIH increased CB levels of oxygen reactive species (ROS) and pro-inflammatory cytokines (PIC), which are potential mediators of the CB potentiation. We hypothesized if CIH may have similar effects on the central cardiorespiratory nuclei of the CB chemoreflex pathway. Accordingly, we studied if CIH increased ROS and PIC levels in rats in the caudal nucleus of the solitary tract (cNTS), which is the primary site for CB inputs. Male Sprague-Dawley rats (250g) were exposed to CIH (5% O_2, 12 times/h, 8 h/day) for 7, 14, 21 and 28 days. Rats were euthanized and brains were removed and processed to measure ROS by dihydroethidium (DHE) fluorescence and PIC levels (IL-1β, IL-6 and TNF-α) using qPCR and immunofluorescence in the cNTS. After 14 days of CIH exposure, we found a significant increase of DHE fluorescence in the cNTS compared to control rats. PIC mRNA levels increased at 21 day of CIH exposure compared with control ($p < 0.01$, one-way ANOVA followed by Dunnett's test). We found a significant increase of PIC immunoreactivity (PIC-ir) levels at day 28 of CIH exposure in the cNTS compared to the control group. The PIC-ir levels were (CIH vs. control, respectively): 1629.0 ± 160.1 vs. 879.3± 189.6 au, for IL-1β; 1342 .0 ± 75.9 vs. 863.3± 186.1 au for IL-6 and 723.2 ± 67.0 vs. 293.1± 48.3 au, for TNF-α; ($p<0,01$ one-way ANOVA followed by Dunnett's test). No significant changes were found in PIC levels at 7 or 14 day of CIH exposure related to control rats, measured with qPCR or immunofluorescence. Present results show that oxidative stress precedes the PIC increase in the cNTS. However, both events occurred when the rats developed hypertension. Thus, increased ROS and PIC levels in the cNTS may be involved in the maintenance of the hypertension of CIH-exposed rats.

FONDECYT 1150040.



74) Effect of exercise on hippocampal neural dynamics during acquisition and consolidation of memory in rats.

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It is documented that exercise promotes memory and cognitive improvement. It has been proposed that exercise facilitate structural changes in the hippocampus, increasing connectivity, synaptic plasticity, neurogenesis and the release of trophic factors like BDNF. Nevertheless, it still is unreported how the exercise could modify the neuronal hippocampal activity and dynamics, which could explain the cognitive improvement.

The Hippocampus is an essential structure in processes of learning and memory. Principal pyramidal neurons, known as place cells fire when subjects traverse discrete locations in space, which provides an internal representation of space required for spatial memory. During slow wave sleep, the hippocampus generates high-frequency oscillations (ripples), where pyramidal neurons replayed the patterns of activity observed during preceding wakefulness, this phenomenon is proposed as the neurophysiological substrate for memory consolidation. The aim of this study was to determine if voluntary exercise causes changes in memory acquisition and consolidation in rats at the behavioral and electrophysiological level. Thirty-one Sprague Dawley male adult rats were individually housed in its home cages, enabled either with (exercise group) or without (sedentary group), a running wheel during 21 days. After that sedentary and exercised rats were tested for acquisition and consolidation of memory, in the “Oasis Maze” task. Exercised rats showed a higher performance at the Oasis Maze task in all the parameters respects to the sedentary control group. To determine whether there are changes in the hippocampal neuronal dynamics we recorded the activity of hippocampal neurons in awake animals chronically implanted with tetrodes targeted to the CA1 region, during a spatial navigation task. Exercised rats showed a greater place fields stability, a higher level of neuronal reactivation during SWS and ripples oscillation with a higher frequency, compared with the control group. This data suggest that exercise may increase the acquisition and consolidation of memory, at the behavioral and neural dynamic level.

76) An endogenous inhibitor of calcium/calmodulin-dependent kinase II is up-regulated in the hippocampus after the induction of long-term potentiation .

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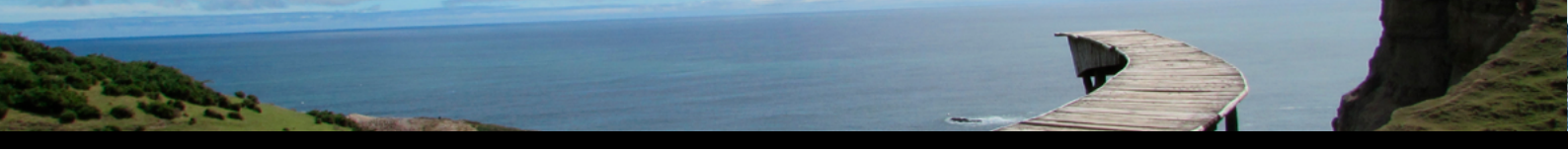
Ca^{2+}/calmodulin-dependent kinase II (CaMKII) is an abundant synaptic signaling molecule that plays a critical role in memory formation and induction of synaptic potentiation. CaMKII activation and autophosphorylation are required to induce long-term potentiation (LTP), a form of synaptic plasticity considered a cellular model underlying learning. CA1 hippocampal synapses expresses a type of LTP dependent on the N-methyl-D-aspartate receptor (NMDAR). After LTP induction, autophosphorylated CaMKII becomes enriched at postsynaptic densities, where it binds to the NMDAR GluN2B subunits. Mutations that prevent CaMKII autophosphorylation or disrupt the CaMKII-GluN2B complex cause a deficit in LTP induction and severe learning defects. Since CaMKII can be autonomously active by autophosphorylation or NMDAR binding, and considering its role in LTP induction and memory formation, it is expected that the kinase activity should be tightly regulated. This regulation may involve changes in the expression of two endogenous CaMKII-specific inhibitors: CaMKIINα and CaMKIINβ. Studies have revealed that CaMKIINα transiently increases its expression in the hippocampus and amygdala after fear conditioning, suggesting a role in controlling CaMKII activity in early stages of memory consolidation. Additionally, our previous studies showed that transient application of CaMKIIN-derived peptides to acute hippocampal slices disrupts the basal interaction between CaMKII-GluN2B and causes long-lasting synaptic depression in both naïve synapses and in previously potentiated synapses in which it reverses LTP saturation. However, it is not clear if CaMKIIN expression is regulated after induction of LTP. Here, we investigated whether CaMKIINα and CaMKIINβ gene expression is regulated after the induction of LTP in CA1 region of acute rat hippocampal slices. Quantitative PCR revealed that CaMKIINα mRNA expression was up-regulated 60 min after LTP induction. In contrast, CaMKIINβ mRNA expression did not change. These results and our previous findings, suggest that the up-regulation of CaMKIIN after LTP induction could be part of a negative feedback mechanism that facilitates the induction of subsequent synaptic plasticity events once basal expression levels are re-established.



78) Microtubule-associated protein 1B (MAP1B)-deficient neurons show structural presynaptic deficiencies in vitro and altered presynaptic physiology.

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Microtubule-associated protein 1B (MAP1B) is expressed predominantly during the early stages of development of the nervous system, where it regulates processes such as axonal guidance and elongation. Nevertheless, MAP1B expression in the brain persists in adult stages, where it participates in the regulation of the structure and physiology of dendritic spines in glutamatergic synapses. Moreover, MAP1B expression is also found in presynaptic synaptosomal preparations. In this work, we describe a presynaptic phenotype in mature neurons derived from MAP1B knockout (MAP1B KO) mice. Mature neurons express MAP1B, and its deficiency does not alter the expression levels of a subgroup of other synaptic proteins. MAP1B KO neurons display a decrease in the density of presynaptic and postsynaptic terminals, which involves a reduction in the density of synaptic contacts, and an increased proportion of orphan presynaptic terminals. Accordingly, MAP1B KO neurons present altered synaptic vesicle fusion events, as shown by FM4-64 release assay, and a decrease in the density of both synaptic vesicles and dense core vesicles at presynaptic terminals. Finally, an increased proportion of excitatory immature symmetrical synaptic contacts in MAP1B KO neurons was detected. Altogether these results suggest a novel role for MAP1B in presynaptic structure and physiology regulation in vitro.

FONDAP Geroscience Centre for Brain Health and Metabolism (15150012) and FONDECYT 1140325.

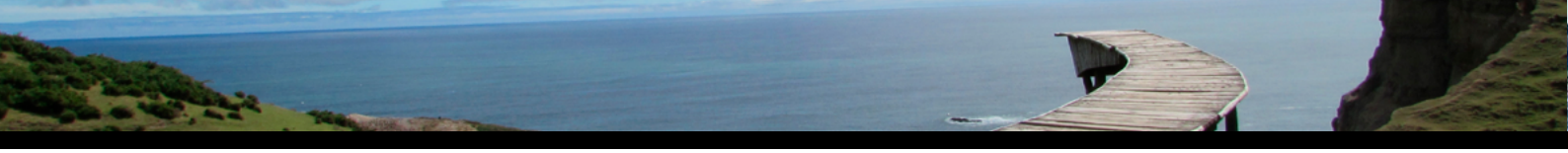
80) Cortical GABAergic system follows an abnormal trajectory of neurodevelopment in FXS.

Cea-Del Rio C[1], Nuñez-Parra A[2], Zuñiga N[1], Tobar H[1], [1]CIBAP, Facultad de Ciencias Medicas, Universidad de Santiago de Chile.[2]Laboratorio de Neurociencia de Sistemas, Instituto de Ciencias Biomedicas, Universidad Autónoma de Chile.
Fragile X syndrome (FXS) is the most common form of inherited mental retardation and the leading genetic cause of autism. FXS is caused by transcriptional silencing of the Fragile X Mental Retardation1 (Fmr1) gene. The Fmr1 gene is highly regulated early at postnatal ages during the critical periods of synaptic plasticity. Indeed, the disruption in the function of the (*Fmr1)* gene during the neurodevelopment, results in a variety of neurological consequences including abnormal network excitability across different brain regions. Although there is an incipient field studying the FXS development, most research has focused on understanding alterations in the excitatory components of the network, leaving the inhibitory counterpart largely unexplored.

In this study, we hypothesize that the GABAergic system of the somatosensory cortex in the FXS animal model undergoes an abnormal developmental progression, which would accounts in part for the hyperexcitability phenotype of the neuronal network. To address this hypothesis, we combined both *in vitro* and *in vivo* electrophysiological approaches in control and *Fmr1* KO mice.

First, analysis from sensory responsiveness to whisker stimulation and neuronal cell activation in L2/3 of somatosensory cortex *"in vivo"* revealed that the baseline rate of the recorded units is higher in *Fmr1* KO mice, consistent with the overall hyperexcitability phenotype found in this model. Second, whole cell recordings on layer 2/3 pyramidal cells showed that while control animals underwent a constant increase in sIPSC frequency through development, *Fmr1* KO sIPSCs exhibited high sIPSC frequencies throughout all ages, similar to those found in adult control animals. Third, the neuromodulation of the GABAergic function mediated by the metabotropic glutamate receptor (mGluR), a relevant molecular component in the FXS, is also abnormally developed. It fails to increase sIPSC frequency and amplitude in pyramidal cells of somatosensory cortex throughout the development in FXS animals. Lastly, inhibitory long term depression (I-LTD), which largely depends on mGluRs activity, was also developmentally unregulated in the FXS mouse model. Either chemically or electrically induced I-LTD failed to be detected in adult FXS mice, but was successfully evoked in the young (P14) FXS animals. Altogether, our data suggest that the correct maturation of the GABAergic system is principal to the proper synaptic function of the somatosensory cortex and further support the network hyperexcitability found in the FXS mice model.

FONDECYT Iniciación 11150816.
Return to Home Fellowship, International Brain Organization (IBRO).



82) Temperature-dependence of activation parameters in a potassium channel from an antarctic limpet.

Ferrada J[1], Barria J[2], Juanchuto N[1], Ugarte G[1], Madrid R[1], Pertusa M[1], Rojas P[1], [1]Departamento de Biología, Química y Biología, Universidad de Santiago de Chile.[2]Departamento de Biologia., Química y Biología, Universidad de Santiago de Chile.

The nervous system of antarctic organisms living in the intertidal ecosystem have developed different adaptations to survive the harsh environment of the antarctic peninsula, where water temperature reaches -4 °C during winter and ice cover all the intertidal zone. During summer the water temperature is 2 °C, and the intertidal is free from ice reaching air temperature in the range between -5 to 10 °C. In this work we clone an ortholog of the voltage-dependent potassium channel Kv1 from the antarctic limpet Nacella Concinna (NCKv1), in order to study the biophysical properties of activation and inactivation process at different temperatures. Whole-cell patch clamp recordings were performed in HEK cell lines expressing NCKv1 and mouse Kv1.1, at temperatures of 15, 23 and 30 °C.

NCKv1 channels present conductance levels three times higher than mKv1.1 suggesting higher expression level.The channel from Nacella also present a higher activation time constant and right-shift of $V_{0.5}$ at all temperatures. In addition, the time-dependent inactivation of NCKv1 channel is less sensitive to temperature compared to mKv1. Due to its role in repolarizing the membrane potential during the action potential, is possible that this channel can allow reliable firing rate in a broad range of temperatures, which can occur during antarctic summer.

Funded by INACH RT_15-12.

84) Axons provide the secretory machinery for trafficking of voltage-gated sodium channels in peripheral nerve.

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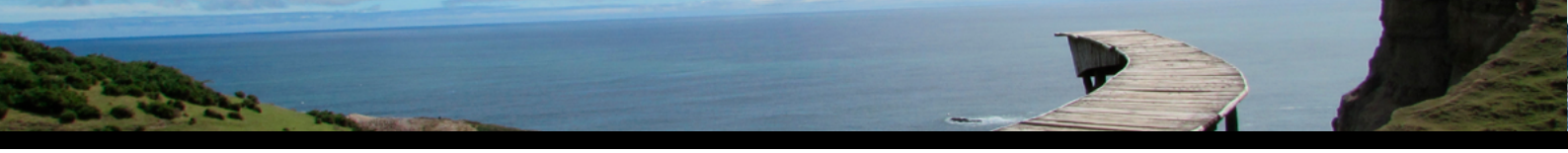
Neurons are responsible for the generation and propagation of electrical impulses, a mechanism that allows information transfer between the external and internal environment. Voltage-gated sodium channels (NaVs) are responsible for the generation and propagation of action potentials and are mostly concentrated in nodes of Ranvier. However little is known about the trafficking mechanisms governing their surface availability. We hypothesize that trafficking through the axonal secretory pathway is necessary for delivery of NaVs and is up-regulated in a model of unfolding protein response (UPR) mediated by the over-expression of XBP1 in peripheral axons.
WT and XBP1 transgenic mice were transected injured in the left sciatic nerve and sham in the right nerve. 14 days after injured, sciatic nerve and dorsal root ganglia (DRG) were extracted and analyzed by *ex-vivo* and *in-vitro* approaches. The effect of UPR on axonal secretory pathway was evaluated in wild type and XBP1 transgenic mice before and after transection.

Distribution of XBP1, NaVs, endoplasmic reticulum (ER), endoplasmic reticulum to Golgi intermediate compartment (ERGIC) and Golgi components were evaluated in DRG and sciatic nerve by immunofluorescence and real-time PCR. Axonal length and branching points were evaluated in 3 days *in-vitro* DRG culture.
Endoplasmic reticulum, ERGIC and Golgi components were detected in nodal and internodal regions. Sciatic nerve transection markedly increased axonal length, NaVs and axonal secretory pathway components, and this effect was more prominent in XBP1 mice.

Our data suggest that early secretory organelles in peripheral axons participate in the trafficking of NaVs to the plasma membrane. The increase in XBP1 transgenic mice exposed to damage suggests a potential impact in nerve regeneration.



86) Presynaptic Dlg regulates the calcium dynamics in synaptic boutons of Drosophila melanogaster, through the traffic and membrane localization of Cacophony and dPMCA.

Köhler A[1], Lopez E[2], Sierralta J[3], [1]Programa Doctorado Ciencias Biomédicas; Departamento Neurociencia, BNI, Facultad de Medicina, Universidad de Chile, Universidad de Chile.[2]Laboratorio de Neurobiología Celular y Molecular, Departamento Neurociencia, BNI, Facultad de Medicina , Universidad de Chile.[3]Neuroscience Deparment, Program of Physiology and Biophysics, ICBM and Biomedical Neuroscience Institute (BNI), Facultad de Medicina , Universidad de Chile.

Introduction: At the presynaptic level, the release of neurotransmitters critically depends on the location and arrangement of Ca_Vs and Ca^{+2} extrusion mechanisms. The existence of clearly defined pre-synaptic nano domains during cytosolic calcium dynamics allows for an emphasis on the precise localization of proteins involved in Ca^{+2} transport. Astorga et al. (2016), showed a role for presynaptic Dlg in synaptic boutons of the Drosophila neuromuscular junction (NMJ9. It was shown that *dlg* mutants have a lower probability of synaptic vesicles release and altered calcium dependence; both defects are rescued by the directed expression of Dlg in motoneurons and not in muscle, which indicates a presynaptic Dlg function on the Ca^{+2} dynamics in the NMJ. This work suggested that Dlg-MAGUK scaffold protein family play a role in the anchoring and traffic of CaVs and dPMCAs to presynaptic active sites. The main objective of this project is to determine the role of Dlg in traffic and membrane localization of Cacophony and dPMCA in motoneurons D. melanogaster NMJ.

Methods: Using third-stage Drosophila larvae with modifications on the expression of Dlg, and immunostaining techniques, we aim to determine the role of Dlg in motoneuron trafficking and localization in presynaptic nanodomains of Cacophony and dPMCA. Calcium dynamics experiments will be performed using the GCamp genetic tool, expressed in Drosophila larval motoneurons.

Results: We have observed that dlg mutants present membrane localization problems in active zones of Drosophila larvae when expressing constructs reporters for Cacophony. Preliminary experiments have evidenced alterations in the traffic of CaVs in motoneurons of third stage larvae. At present, work is underway to show alterations in the membrane localization of dPMCA and evidence alterations in the calcium dynamics with the genetic tool GCamp.

Funding: FONDECYT 1171800.

88)Study of the cholinergic and octopaminergic signals contributing to olfactory information processing in Drosophilamelanogaster Antennal Lobe.

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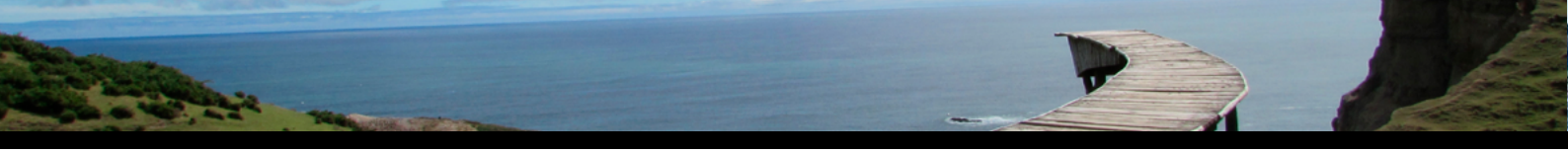
The ability to decipher odor signals is fundamental in animals, as it allows them to interact with each other or eventually generate memories of environments that are beneficial or dangerous for their survival. In this sense, it is essential to understand how these signals are received and processed in the brain. The organization and operation of the olfactory system is similar in a wide range of species, ranging from invertebrates to mammals. One of the most conserved regions in the olfactory system of different animals throughout evolution is the olfactory bulb (OB), the brain region that first receives and processes olfactory information. In flies the brain region that is homologous to the OB is the antennal lobe (AL). Projection neurons in this fly brain region receive and process olfactory information before it is sent to higher processes center. As in the vertebrate OB, AL receive information of modulatory systems, including aminergic neurons. This work focuses on the study of the signals activated in the AL by octopamine, the functional homologue of vertebrate noradrenaline in invertebrates, and acetylcholine muscarinic receptors, which could contribute to the processing of olfactory information in *Drosophila*.

Imaging experiments in cultured AL neurons show a muscarinic modulation of calcium levels in projection neurons, consistent with data in literature showing high expression of these receptors in AL. On the other hand, no changes in intracellular calcium levels is observed in AL neurons exposed to octopamine. Interestingly, calcium responses induced by cholinergic activation is modulated by octopamine. This data would suggest a cross-talk between aminergic and cholinergic components in *Drosophila* AL. Behavioral tests demonstrate the importance of the Octopamine beta 3 receptor in modulating olfactory discrimination in *Drosophila*.

FONDECYT 1141233.



90) Mechanism of hypercapnia-induced D-serine release from brainstem astrocytes.

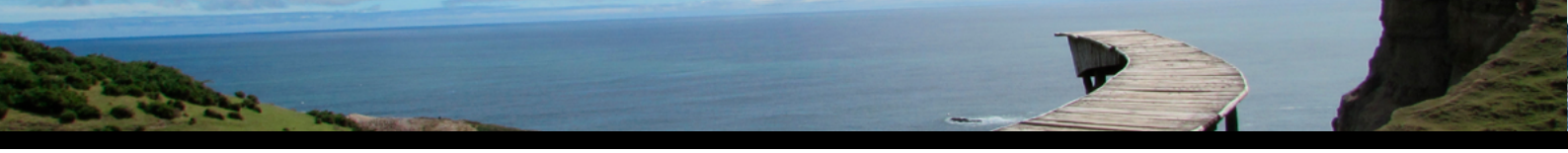
Olivares M J[1], Beltrán-Castillo S[1], Contreras R[1], Zuñiga G[1], Von Bernhardi R[2], Eugenín J[1], [1]Biología, Química y Biología, Universidad de Santiago de Chile.[2]Neurología Pontificia Universidad Católica de Chile. (Sponsored by FONDECYT Grant 1130874, FONDECYT Grant 1131025, FONDECYT Grant 1141132, CONICYT Grant 21140669.)

Central chemoreception is important for brain CO_2 and H^+ homeostasis. Astrocytes play a key role as chemosensory interoceptors in the brainstem, they can release ATP, D-serine (D-ser) and glutamate in response to hypercapnia (increased levels of CO_2). D-Ser is an endogenous agonist with high affinity for the glycine-binding site of the N-metil-D-aspartate glutamate receptor (NMDAR). Although activation of the NMDAR is not essential for the generation of the respiratory rhythm, it activation contributes to central chemoreception, but the mechanisms are poorly understood. Determining the mechanism of D-Ser release from brainstem astrocytes of the is very important to understand the modulation of respiratory response to hypercapnia. In the present work, we evaluated whether cultured astrocytes from the caudal brainstem are able of releasing D-Ser and mechanisms of released D-Ser. Two days old CF1 mouse neonates were anesthetized (3% isoflurane), decapitated, and their brains were extracted, disaggregated, and cultured in DMEM-F12 medium equilibrated with air containing 5% CO_2at 37°C for 2 weeks. During experiments, DMEM-F12 medium was replaced by artificial cerebrospinal fluid. Astrocytes cultures were exposed to 5% $CO_2$for 30 min (basal condition), followed by 10% $CO_2$for 30 min (hypercapnic acidosis), returned to 5% CO_2at 37°C, and finally the response to high K^+. Samples were collected at 5, 15 and 30 min at basal and hypercapnic conditions. The concentrations of D-Ser were measured using high-performance liquid chromatography technique. Posteriorly we evaluated the contribution of intra and extracellular Ca^{2+} (aCSF without Ca^{2+}, with Mg^{2+} and EGTA) or gap junctions hemichannels (probenecid and carbenoxolone) on the hypercapnia-induced D-Ser release. Our results reveal that medullary astrocytes release D-Ser in response to hypercapnia and suggests that gap junction hemichannels are involved in this mechanism. We found that carbenoxolone and probenecid also blocked the high K^+-induced release of D-Ser, which also supports the evolvement of pannexin-1.

92) Pannexin 1 channels blockade mitigates synaptic plasticity deficits in Alzheimer´s disease model.

Ponce D[1], Gajardo I[1], Silva G[1], Muñoz P[1], Ardiles A O[1], [1]Escuela de Medicina, Medicina, Universidad de Valparaíso.

The activity of N-methyl-D-asparte receptors (NMDARs) is essentials for brain functions including cell survival, synaptic plasticity and memory. However, the dysfunction of these receptors has been associated to synaptic disruptions as commonly observed in diverse synaptopathies such as Alzheimer's disease (AD). AD is a degenerative condition characterized by an early accumulation of soluble oligomeric forms of amyloid β peptide (sAβos) that induces synaptic loss and later cognitive deficits. Growing evidences suggest that the deleterious effects of soAβs may be mediated by activation of GuN2B-containing NMDARs and downstream signaling, including calcineurin activation, which are involved in the induction of long-term depression (LTD) and dendritic spines retraction. In this regard, transgenic mouse models of AD exhibit impaired excitatory synaptic plasticity, namely decreased LTP and increased LTD. Previously, we found that Pannexin 1 (Panx1), a protein forming non-selective channels, can modulates glutamatergic neurotransmission and NMDAR-dependent synaptic plasticity. Indeed, we observed that the blockade or the absence of Panx1 channels increase long-term potentiation (LTP) and reduce LTD. Interestingly, when we incubate hippocampal slices obtained from AD mice with probenecid (PBN), a Panx1 channel blocker, we found an increase in LTP and a decrease in LTD. Furthermore, we found that PBN incubation also reduced glutamatergic receptor-induced activation of CaN and the phosphorylation of S845 GluA1 according with a reduction of the sAβos signaling. plasticity. Our preliminary results show that the blockade of Panx1 channels in a transgenic mouse model of Alzheimer´s disease reverts the deleterious effects of soluble amyloid beta oligomers (sAβos) on excitatory synaptic plasticity.



94) Age-related changes in the activation of canonical and non-canonical TGFβ pathways contributing to the pathogenesis of Alzheimer's Disease.

Rojas-Vidal C[1], Cornejo F[1], Von Bernhardi R[1], [1]Department of Neurology, Faculty of Medicine, Pontificia Universidad Católica de Chile. (Sponsored by This Study Is Supported By FONDECYT Grant 1171645 (RvB)).

Aging is the major risk factor for most neurodegenerative diseases, including Alzheimer´s disease (AD). TGFβ1 is a potent regulator of cytotoxicity and neuroinflammation. Increased production of TGFβ1 in response to inflammatory conditions is one of the regulatory mechanisms in cellular activation. Binding of TGFβ1 induces TGFRI transphosphorylation by TGFRII, and results in the activation of SMAD and non-SMAD signaling pathways. The SMAD-independent (non-canonical) pathway includes signaling of mitogen-activated proteins (MAPKS p38, ERK and JNK), and PI3K/AKT. The modulation exerted by TGFβ1 via the canonical pathway is mediated by the activation of Smad3, which basal activity is increased but its activation in response to inflammatory activation is down-regulated in AD patients and aged individuals. The aim of this work is to evaluate at what levels of the activation of TGFβ1 pathways affects aging, and whether the modification of TGFβ1 signaling could be responsible for the neuroinflammatory profile observed in aged individuals and facilitate the development of AD. Young and aged wild type (WT) and APP/PS1 mice were used to assess the basal and inflammation-induced activity of TGFβ, as well as its effect on the regulation of glia activation, both in cell culture and *ex vivo* experiments. TGFβ1 was evaluated by ELISA and the expression of receptors and activation of signaling pathways by WB. The participation of the various signaling pathways was dissected by the use of specific inhibitors. We show that the modulation of the inflammatory activation by TGFβ was partially mediated by the activation of the TGFβ Smad3 pathway, with little participation of non-canonical pathways. We observed increased levels of TGFβ in the hippocampus during aging of WT mice, increase that was observed earlier in APP/PS1 mice. Similarly, aging-dependent increase in TGFRII was observed earlier in APP/PS1 than in WT mice. Furthermore, the age-dependent decrease in activation of Smad in response to inflammation was more robust in APP/PS1 than in WT mice. Our results show that age-dependent TGFβ increase appeared earlier and was more robust in an AD model than in WT mice. Down-regulation of the Smad3 pathway, which is responsible for important regulation by TGFβ1.

96) Characterization of intrinsic oscillatory behavior of CA1 pyramidal neurons in a rat model of blood-brain barrier dysfunction-induced epileptogenesis

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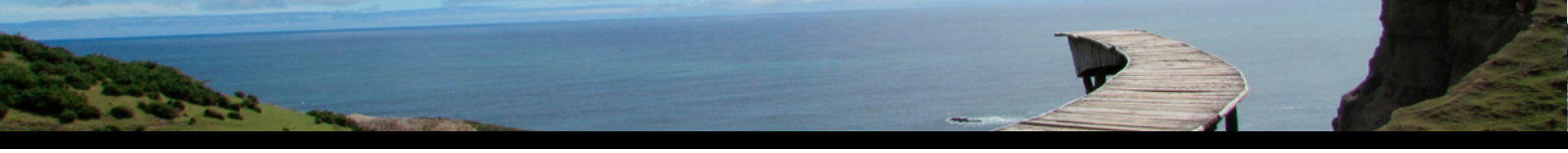
Insults like stroke, traumatic brain injury, brain tumors or infections are often leading to blood-brain barrier-dysfunction (BBBd), which may underlie post-insult seizures and epilepsy. Besides seizures, epilepsy patients suffer from neurological comorbidities, e.g., learning disabilities, memory impairment or anxiety associated to changes in brain physiology. The mechanisms causing post-insult epilepsy and cognitive comorbidities are still ill-defined. By using an adult rat model of cortical photothrombosis is possible to induce post-insult BBBd in the ipsilateral hippocampus leading to early seizures in two-thirds of animals. Manipulated animals show alterations in background hippocampal activity *in vivo*, displaying an increase in power at theta range (3-8 Hz) and a reduction in gamma range (30-45).

It is well known that CA1 pyramidal neurons from the hippocampus promote population theta activity through the intrinsic generation of subthreshold membrane potential oscillations and by displaying increased voltage response when stimulated in theta frequencies (i.e. they resonate). Here, we are characterizing the intrinsic neuronal properties of CA1 pyramidal neurons *in vitro* that might contribute to seizure generation and the associated increase in theta frequencies in the rat model of BBBd. One week after photothrombosis induced hippocampal BBBd, we are measuring resonant behavior, spike threshold, firing probability at theta frequencies, and subthreshold oscillations, among other intrinsic properties. Our preliminary data show that CA1 neurons from treated animals present a higher resonant frequency at hyperpolarized potential and a reduced phase-lag response under oscillatory stimulation, suggesting that intrinsic properties are modified. This detailed characterization will allow us to determine changes in intrinsic excitability of CA1 neurons that contribute to epileptogenesis and associated oscillatory alterations in the hippocampus.

Postdoctoral FONDECYT 3150668 (JV) and The Grass Foundation, Grass Fellowship 2017 (JV and KL).



98) Electrical epidural stimulation disentangles and rearranges oscillatory activity of supraspinal motor cortices in a model of parkinsonism.

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Parkinson's disease is a neurodegenerative disorder characterized by a progressive decline in motor and cognitive function. Despite the evidence points to the death of dopaminergic neurons located in the substancia nigra pars compacta (SNc) as the cause of the disease, the neurophysiological activity show changes in many areas. Recordings from animal models and patients show an increase in the oscillatory activity around 8-30 Hz, the so called ß band, in many areas of the cortical-thalamic-basal ganglia (Cx-Th-BG) circuit. Pharmacological and neuromodulatory therapeutic strategies, such as levodopa and deep brain stimulation (DBS) have a direct influence diminishing the spectral power of this ß oscillation although the mechanism is not understood. The epidural spinal cord stimulation (SCS), a neuromodulatory strategy originally used to treat chronic pain, is currently being explored in animal models and patients to treat PD. The SCS chronically delivers current pulses over the dorsal columns and it is able to modify the motor signs, but also the electrical activity of many areas of the Cx-Th-BG circuit.

To understand the characteristics of the SCS underpinning the effects in the cerebral electrical activity we investigated the effect of single current pulses in a bilateral neurotoxic model of parkinsonism. We induced parkinsonism by injecting the neurotoxin 6-OHDA in both striata of Sprague Dawley rats to destroy the dopaminergic terminals. Later we delivered electrical current pulses by epidural electrodes located at thoracic level. Electrical activity of different areas of the Cx-Th-BG circuit was recorded with tungsten electrodes. Our results indicate that pulses of SCS resets the phase of ß activity in premotor and motor cortices and striatum, as pulse-triggered field potential average shows clear oscillatory beta activity after the pulse. The evoked beta oscillations are not likely to be simply an increase in beta power, as the average beta power during pre and post-pulses periods presents no difference. We conclude that single SCS pulses cause a re-arrangement of the ß oscillations in the motor circuit. Whereas the pulses are applied in the spinal cord, it is remarkable that distant areas such as secondary motor cortex are being affected. We expect to keep exploring these effects in other areas of the Cx-Th-BG circuit and also to unravel the pathways that underpin its effect on the motor behavior to improve the SCS as a therapeutic alternative for patients suffering from Parkinson's disease

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100) Atlastin regulates the intracellular trafficking of synaptic vesicles, independent of BMP signaling, in Drosophila melanogaster motor neurons.

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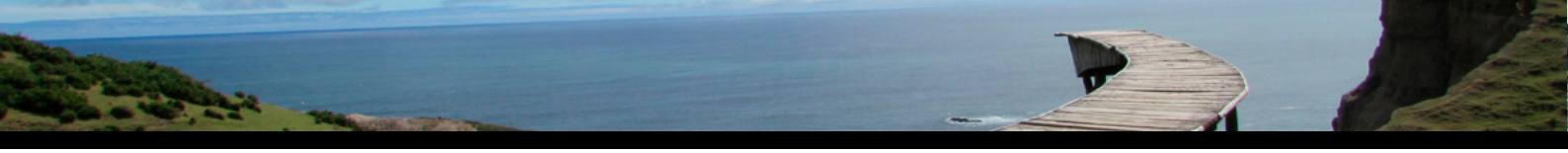
Motor neurons are polarized cells whose physiology requires membrane trafficking, process in which Rab proteins participate regulating the endosomal trafficking involved in various signaling pathways and synaptic vesicle (SV) cycle. The extensive presences of the endoplasmic reticulum(ER) in the neuron and the formation of ER-endosomes contact sites have conferred the ER the role of long-distance communicator. This requires a membrane flexibility of the ER, a process where the Atlastin (Atl) protein participates. Atl is a GTPase located on the ER membrane that regulates its structural dynamics. Atl also participates in the inhibition of the BMP pathway, involved in the development and maintenance of the neuromuscular junction (NMJ). As well, Atl colocalizes and interacts with several Rab proteins. However, a modulator function of Atl over endosomal traffic is unknown. Mutations in Atl are correlated with Hereditary Spastic Paraplegia (HSP), a group of genetic diseases characterized by spasticity of the lower extremities. In *Drosophila*, Atl knockdown (Atl-KO) in neurons associates to locomotion defects, increased BMP signaling and SV accumulation defects. The molecular basis of Atl-dependent defects and their implication on SV traffic remains unknown. We propose that Atl regulates SV trafficking, independent of BMP signaling, in *Drosophila* motor neurons. Using *Drosophila* third-instar larvae control and with modified Atl expression in the motor neurons we will characterize SV abundance and their colocalization with recycling and late endosomes. We also will determine whether these SV defects arise from deficiencies in the recycling of these vesicles and evaluate their dependence on an increased BMP signaling. We observed that Atl-KO causes a reduction in SV accumulation in the NMJ. As well, Atl-KO is related with alterations in the NMJ morphology and synaptic bouton size, suggesting endosomal traffic disturbances. Preliminary results reveal that Atl-KO could correlate with a decreased SV recycling in distal motor neurons, suggesting a length-dependent effect. Our study contributes to understand the pathogenic mechanisms underlying Atl-dependent HSP and suggests that an ER-organizing protein influences SV trafficking in motor neurons.



102) Schwann cells and Pericytes: Defense and repair at the dentin pulp interface.

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Dental pulp responses to caries comprise defense mechanisms against pathogens, triggered by nervous and vascular changes. Until now it is known that neurogenic inflammatory and angiogenic responses are dynamic processes mediated by reorganization of Schwann cells and pericytes, however, the characterization of their phenotype changes are not well described.The purpose of the present study was to define cellular changes during neurogenic and angiogenic responses in carious teeth. Human permanent healthy (n=10) and carious (n=10) teeth extracted under clinical indication and donated by informed consent, were fixed and demineralized. Cryosection were assayed through double immunohistochemical labeling, using specific markers for Schwann cells (S100, GFAP and p75NTR), and for pericytes (αSMA, NG2). Dental pulp sections from healthy and carious teeth were analyzed with confocal microscopy. Increased expression of S100, GFAP, p75NTR markers were observed for Schwann cells and αSMA in pericytes. Sprouting of nerve terminals in association with activated Schwann cells and enlarged blood vessels were evidenced; changes which are in correspondence to the infiltration of immune and inflammatory cells. Phenotype changes in Schwann cells evidence their ability to dedifferentiate to preserve innervation. On the other hand, pericytes are playing an important role in angiogenesis to insure oxygen and nutrient supply. This first approach helps to understand the cellular mechanisms of defense against pathogens in carious teeth, the maintenance of homeostasis and mechanisms of dental pulp repair.

104) Context modulates early visual cortex and motor performance during a visuomotor adaptation task.

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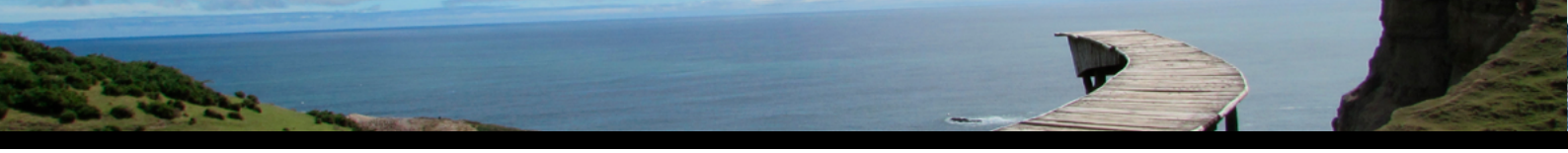
Acquisition of new internal models during motor learning has been widely studied. However, the mechanism involved in changes in the acquisition dynamics are not well understood. We conjectured that natural environment, usually with high content richness, modify the needs of the early sensory cortex, which can modify the changes in motor performance about the neutral contexts used in this type of tasks. We hypothesized that a natural context is capable of improving the dynamics of internal model acquisition, which would present a neurophysiological correlate related to modulations of early sensory cortex.

To verify our hypothesis, we used a visuomotor adaptation paradigm with a kinematic distortion of 135 ° counterclockwise with three different background screen of different content. 20 healthy subjects were recorded simultaneously during a kinematic adaptive behavior, along with eye movements (Eye Tracker) and EEG. We computed evoked potentials to the visual fixation (fERP) and motor performance to compare changes of early fERP components with motor learning dynamics.

About the kinematic behavior, we find improvements in motor performance modulated by more realistic background screen during initial stages of learning. This is related to variations in the electrical activity of early visual cortex, where early components of the fERP (P1 and N1) present greater amplitude while the higher natural content has the context of the task. However, for late learning stages performance improvement is matched by background screen at the expense of less variability of early visual cortical activity. These results suggest that a natural context in which the task of visuomotor adaptation is embedded could influence the processes of acquisition of new internal models.

Therefore, there is a differentiated visual cortical contribution generated by changes in the background screen of the task that modifies the motor performance. This reflects the importance of natural paradigms in the motor learning process.

Supported by Iniciativa Científica Milenio ICM P10-001-F, P09-015-F, Fundación Guillermo Puelma, FONDECYT postdoctorado 3160403 a R.V.



106) Glycine receptor β subunit: a critical target for pain sensitization.

Mariqueo T[1], Ferrada J[2], Argandoña Y[3], Solorza J[3], Arenas M[3], [1]Escuela de Medicina Universidad de Talca.[2]Química y Biología Universidad de Santiago de Chile.[3]Bioinformática Universidad de Talca.

Impairment in Glycine (GlyR) mediated inhibitory neurotransmission is thought to play a critical role in the disinhibition that account for the development and maintenance of central pain hypersensitivity. Our experimental results showed that modulator βGlyR subunit was increased in tissue lysates derived from animals subjected to neuropathic and inflammatory pain. We evaluated the expression of βGlyR subunit in neuropathic (Chronic Constriction Injury, CCI) and inflammatory (Zymosan injected) models of chronic pain. RT-qPCR analysis of spinal cord samples showed increased β gene expression after 3 days of CCI surgery, and similar results were obtained by Western blot analysis. Inflammatory pain model showed increased level of β gene expression after 4 hours of zymosan A injection. Thus, remarking the β subunit regulation as a common component in both pain models. These results were associated with increased expression of interleukin 6 (IL-6), which is reported to reduce glycine-induced currents, and therefore promoting spinal neural hyper-excitability, characteristic of chronic pain status. We are performing electrophysiological experiments to understand the molecular determinants of this modulation. Our results suggest that auxiliary βGlyR subunit may play a substantial role in establishing and maintaining GlyR-mediated pain sensitization during neuropathic and inflammatory injury. Taking together, these findings suggest an important, albeit underappreciated, role of auxiliary β subunit in the allosteric modulation of glycine receptors in chronic pain development.

108)Synchrony of neural oscillations in the olfactory system of rainbow trout (Oncorhynchus mykiss).

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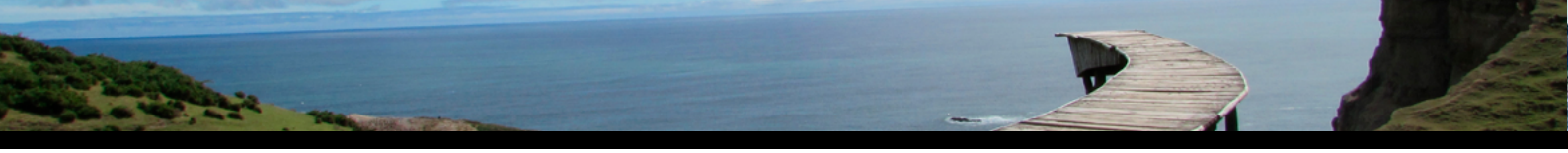
The olfactory system is highly conserved in evolution, presenting a similar general scheme of functioning in vertebrates and invertebrates. By recording electrophysiological activity in the olfactory system of rainbow trout and stimulating it through the application of odorants, chosen to represent natural odor stimuli for fish, local field potential (LFP) neural oscillations were observed. Raw recordings show an increase in the signal amplitude in frequencies restricted to specific bands. The dominant frequencies, corresponding to the frequencies in which the maximum power is observed using wavelet based spectral analysis, seem to be in the same frequency band for all the stimuli applied in this study. When oscillations recorded in the olfactory bulb (OB), ventral nucleus of the ventral telencephalon (Vv) and dorsal posterior area (Dp) of the telencephalon of *O. mykiss*, where olfactory information is analyzed, were compared, we observed a high degree of synchrony, given by the coherence calculation, suggesting a functional connectivity of the electrophysiological activity between these regions. The frequencies in which this high degree of coherence was observed in rainbow trout, belong to the bands denominated theta (θ), beta (β) and gamma (γ) in humans, and can also be found in many animal species, although their meaning, at the level of olfactory information processing, is still being investigated. Support: Beca de Estudio de Doctorado en Chile, CONICYT; CINV Millenium Institute; FONDECYT 1171228.



110) Characterization of melanopsin-driven pupillary responses in Octodon degus, a natural animal model for aging and neurodegeneration.

Palanca-Castan N[1], Neira D[1], Palacios A[1], [1]Centro Interdisciplinario de Neurociencia de Valparaíso Universidad de Valparaíso.

In vertebrates, photoreceptive "non-image forming responses"(NIFRs) include calibration of the circadian cycle, pupillary light reflex (PLR), melatonin suppression, and increase or decrease in alertness in response to changing light levels. Malfunctions of NIFRs are connected to widespread human health and quality of life issues. Although NIFRs have been described for long, the system that drives them remained unknown until recent years. The discovery of this system, based on intrinsically photosensitive retinal ganglion cells (ipRGCs) present in the vertebrate retina has created a revolution in visual science and opened new avenues of research. These ipRGCs, unlike the majority of retinal ganglion cells, contain a pigment named melanopsin more akin to invertebrate rhodopsins than to vertebrate visual pigments. Recent research has highlighted the role of iPRGCs in human health. Disruption of the circadian system is a risk factor for psychiatric and coginitive disorders, obesity, diabetes and breast cancer as well as an early symptom of Alzheimer's disease, which has been shown to selectively affect ipRGCs. The common degu (*Octodon degus*) is a rodent native to central Chile that lives up to 9 years in captivity and develops cognitive impairments, glaucoma and other aging-related diseases. Since dysfunction of the melanopsin system is one of the early symptoms of neurodegeneration, it could theoretically be used to detect individuals in the early stages of the disease before more obvious symptoms are present. We tested a protocol based on pupillometry to evaluate melanopsin function in degu. Monochromatic LED light (λ = 490 nm and λ = 505 nm) was used to evaluate ipRGC-driven components of the light-induced pupillary reflex. Our preliminary results show a drastic reduction of PLR in most animals over 3 years old when compared to younger animals. In an older animal that retained PLR, sensitivity to cone-stimulating light (λ = 505 nm) was comparable to younger animals, while sensitivity to melanopsin-stimulating light (λ = 490 nm) was dramatically reduced. This suggests that a deterioration of the melanopsin system is tied to aging in degus, and that our protocol could be used for repetitive, simple and non-invasive monitoring of said deterioration.

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112) Spatio-temporal characterization of the feedback signals mediating stimulus selection in the optic tectum of the pigeon.

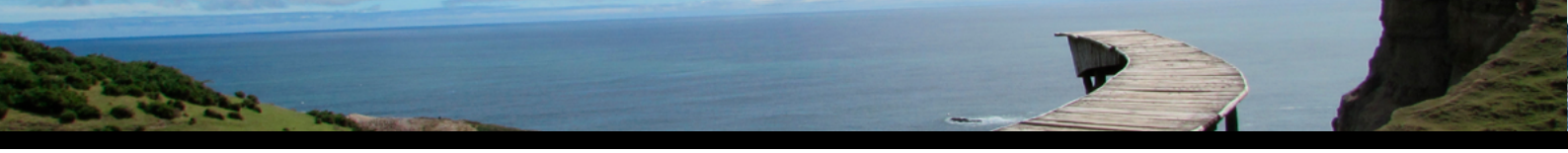
Reynaert B[1], Lopez-Jury L[1], Letelier J[1], Mpodozis J[1], Marín G[1,2], [1]Biología, Ciencias, Universidad de Chile.[2]Medicina, Medicina, Universidad Finis Terrae.

In all amniotes, a bilateral tectofugal pathway transmits visual inputs from the optic tectum (TeO), or superior colliculus, to the nucleus rotundus or caudal pulvinar. This pathway arises from wide-field tectal ganglion cells (TGCs), which in birds receive prominent feedback signals from axon terminals from the nuclei isthmi pars parvocellularis (Ipc). It has been shown that upon retinal stimulation, this feedback produces a gating effect on the ascending transmission of retinal inputs, while at the same time a diffuse GABAergic projection from the nucleus isthmi magnocellurais (Imc) exerts a suppressing effect over complementary locations in TeO and Ipc.Thus, under conditions of stimulus competition, this circuit implements a “winner-take-all” mechanism that promotes the selective transmission of visual activity representing the most salient stimuli.

However, given the complex topology of this network it is difficult to predict the spatio-temporal configuration of the Ipc feedback that is generated in a particular visual context, and consequently the activity pattern transmitted by the TGCs. In this study, using up to 12 microelectrodes regularly disposed on the superficial tectal layers of anesthetized pigeons, we recorded the bursting feedback signals from Ipc axons in response to static and moving visual stimuli. We found that the presentation of a point visual stimulus generates a wave of feedback activity that expands centrifugally from the tectal zone receiving the retinal input, encompassing a tectal area of about 1 mm. When the stimulus moves, the source-point follows the stimulus in a saltatory fashion and the speed and direction of the stimulus modify the response intensity. In the case of two competing stimuli, tectal activity is transferred from one region to the other instantly.

Ipc feedback might generate a priming effect, ahead of the tectal zone receiving the retinal input. To study the consequences of these feedback patterns upon the TGC responses, we modeled this network using leaky integrate-and-fire neurons that represent how the tectal, retinal and isthmotectal afferences interact to generate the tectofugal output. We explored the topological and physiological parameters that lead to the networks operation, as found in vivo. The model reproduces motion preference on the TGCs, with increasing firing rates for faster motion; and even stronger responses to looming stimuli. These findings and the continuing analysis of the model under different stimulus conditions help to elucidate the rules by which the operation of the isthmotectal network modulates the visual activity patterns that are relayed by the TGCs to the thalamus.

This work is supported by FONDECYT Grant 1151432.



114) Functional connectivity self-regulation of cerebellum and primary motor areas with real-time fMRI neurofeedback.

Vargas P[2,3,1], Sitaram R[2,3,5,4], Sepúlveda P[6], Montalba C[1], Rana M[2,3], Torres R[2], Tejos C[1,7], Ruiz S[2,3,5], [1]Biomedical Imaging Center Pontificia Universidad Católica de Chile.[2]Department of Psychiatry, Faculty of Medicine, Pontificia Universidad Católica de Chile.[3]Laboratory for Brain-Machine Interfaces and Neuromodulation Pontificia Universidad Católica de Chile.[4]Institute for Biological and Medical Engineering Pontificia Universidad Católica De Chile.[5]Institute of Medical Psychology and Behavioral Neurobiology University of Tübingen.[6]Institute of Cognitive Neuroscience (ICN) University College London.[7]Department of Electrical Engineering, Faculty of Engineering, Pontificia Universidad Católica de Chile. (Sponsored by CONICYT/FONDECYT Postdoctorado 3150391, CONICYT/FONDECYT Regular 1171313, CONICYT/FONDECYT Regular 1171320 And CONICYT-PIA-Anillo ACT1416)

Introduction: Real-Time fMRI neurofeedback (rtfMRI-NF) can be used to train voluntary regulation of neural activity, leading to behavioral changes depending on the functional role of the targeted brain regions.
Stroke is based in a lesion that also induce network dysfunctions. If stroke affects the primary motor cortex (M1), it is common to observe a subsequent "deactivation" of the contralateral cerebellum (Pantano et al., 1986). The restoration of this connectivity is essential for motor rehabilitation.

The aims of this study were to test the feasibility of achieving volitional control of M1-cerebellum functional connectivity with an rtfMRI-NF system and evaluate its influence on motor performance. The study included healthy subjects to set up the protocol before to use it in stroke patients.

Materials and methods: Nine healthy subjects (22.8±3.8 years, males, right-handed) were trained during 3 sessions and 6 runs of alternating baseline (Base) and up-regulation (Upreg) blocks. The feedback signal F was computed using BOLD signal and correlation (functional connectivity) between the regions of interest (ROIs): left M1 and right cerebellar hemisphere:

$$F = ((BOLD_{Upreg} - BOLD_{Base})_{Cerebellum} + (BOLD_{Upreg} - BOLD_{Base})_{M1}) * (1+Correlation)$$

We trained a first group of subjects (n=5) with feedback that weighted equally in terms of the contribution of each ROI (EFG: equal-feedback group; Cerebellum=M1=0.5) and a second group (n=4) with a differential weighted ROIs (WFG: weighed-feedback group; Cerebellum=0.3 and M1=0.7). Motor performance was evaluated using a button-pressing task.

Results: During overt movement, there was a significant higher percentage BOLD change (PBC: percentage between activation or up-regulation and baseline blocks) of cerebellum than M1 ($p<0.001$). During up-regulation, we found a similar pattern in the EFG ($p<0.001$), but not in the WFG. Moreover, compared to the WFG in up-regulation, overt movement had a significant higher PBC in cerebellum ($p=0.005$), but no differences in M1 were observed.

In the third session, the WFG had significant higher correlation coefficients compared to EFG ($p<0.001$) and to overt movement ($p=0.002$). Also, there was a significant correlation between the mean BOLD signal during up-regulation and the motor scores for the WFG in the third session.

Discussion and conclusion: The results indicate that even slight modification of the feedback can produce significant differences in the outcome measures. Voluntary self-regulation of cerebellum-M1 connectivity is feasible with an rtfMRI-NF. The effects in motor performance need to be further studied.

CONICYT/FONDECYT Postdoctorado 3150391, CONICYT/FONDECYT Regular 1171313, CONICYT/FONDECYT Regular 1171320 and CONICYT-PIA-Anillo ACT1416.

116) The avian visual DVR indeed contains hidden laminae.

Weiss-Garrido C[1], Fernández-Collemann S[1], Fernández M[1], Marín G[1], Mpodozis J[1], [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile.

In mammals, the sensory pallium is organized as a cortex formed by six layers densely interconnected by radially arranged processes, whose local circuitry gives rise to functional columns. In birds, the predominant structure of the pallium is a dorsal intraventricular protrusion known as the dorsal ventricular ridge (DVR). The DVR consists of two dorso-ventrally apposed cellular masses: the nidopallium (N) and the mesopallium (M). The internal most aspect of the N contains discrete areas receiving ascending afferents from different sensory modalities. Previous studies have shown that the auditory as well as the visual regions of the DVR follow a “laminar/columnar” arrangement, in such a way that cells of these areas are reciprocally linked by “columnarly” organized axonal processes. Moreover, recent gene expression studies have shown that these DVR areas differentially express mammalian layer-specific molecular markers. These findings prompt to study in more detail the laminar organization of the DVR.Of particular concern for this study is the entopallium (E), the thalamo-recipient area of the visual DVR. Previous studies have partitioned the E into a ventral portion (Ei) surrounded by a dorsal band of cells (Ex), based on cytoarchitecture, immunohistochemistry and differential density of thalamic terminals. Studies from our Laboratory have recently shown that most of the columnar intrapallial projections arise from the Ex, while the Ei mostly originates projections to the subpallium, specifically, to the lateral striatum (LSt). Here we performed tract tracing studies and *in situ* hybridization essays aiming to further characterize the differential projections of these entopallial regions, together with a presumptive differential expression of cortical layers markers. We found an expression pattern of RORß (in mammals a specific layer 4 marker) that is consistent with the parcellation of E: the internal E shows less RORß + cells than its external aspect. On the other hand, our tract tracing studies showed that the E-LSt projecting neurons were conspicuously restricted to the RORß- region. In addition, our results confirm that the “columnar” projections arise mainly from cells in the Ex region and, in a minor proportion, from cells in the RORß- region. Thus, our results indicate that the E contains two superposed sublayers: one external, “layer 4-like” and another internal, “layer 5-like”. The former exhibits a higher expression of RORß and exclusively originates intrapallial projections, while the latter lacks RORß expression and originates, mainly but not exclusively, projections to subpallial targets.

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