

C101. METHYLPHENIDATE IMPROVES CUE NAVIGATION IN RATS AT THERAPEUTIC DOSES IN THE MORRIS WATER MAZE Zeise ML, Espinoza S, Rozas C, González A, Miranda ML, Cerda FS, Nacarate J, Sanchez C, Yáñez CG and Morales B
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Methylphenidate (MPD) is amply used therapeutically to treat Attention Deficit/Hyperactivity Disorders, mainly in school children. Despite this, its mechanisms of action and collateral effects are not well known yet.

We tested whether therapeutic doses change goal-directed behavior in male Sprague Dawley rats and if there are changes in synaptic transmission *in vitro*.

In a Morris Water Maze, latencies were monitored of rats who had ingested pellets containing MPD (1 mg/Kg) an hour before the experiment (n=9) comparing with those of control rats (n=10), to reach a visible goal platform (All rats same age; experiments performed between 7 and 9 weeks after birth). Rats under the influence of MPD were much faster in getting to the platform than controls (10.7 ± 1.24 seconds vs. 24.9 ± 2.90 seconds S.E.M.; $p < 0.001$; ANOVA-2) beginning with the very first session.

In hippocampal brain slices from Sprague Dawley rats, MPD (5 μ M/L) failed to exert significant changes in synaptic field responses to Schaffer Collateral stimulation (CA1 pyramidal cell layer recording).

These data are compatible with the view that MPD, while improving goal-directed behavior, does not change normal synaptic transmission.

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C102. PHASE SYNCHRONIZATION IN THE VISUAL CORTEX OF THE RAT DURING A VISUAL DISCRIMINATION TASK Marcelo Aguilar, Bethany Snyder, and Pedro E. Maldonado. CENI y Programa de Fisiología y Biofísica. Facultad de Medicina, Universidad de Chile

In the visual system, physical attributes of object such as orientation and direction of movement activates different early anatomical pathways. Yet, perception of objects is a unitary and continuous experience. A neuronal mechanism, the Temporal Correlation Hypothesis has been proposed to account for the ability of the visual system to recognize multiple patterns and objects. This hypothesis proposes that relations among visual features are established when visual cortical neurons responding to those features transiently synchronize their discharges, thus constituting neuronal ensembles.

Here we investigate whether phase synchronization between local field potentials (LFP) signals on the visual cortex is apparent during a visual discrimination task. Using tetrodes, we recorded LFP signals in the primary and secondary visual areas of three rats while they performed a visual task requiring the discrimination of orthogonally oriented bars. We found that the animals performed the task quickly, with a mode response time of 900 ms from stimulus onset. We also found significant differences of phase synchronization in the Beta and Gamma frequency bands, approximately 200 ms after of the stimulus onset ($P < 0.05$) and differences between the correct and incorrect response condition ($P < 0.05$).

Our results demonstrate that phase synchronisation is strongest during the early part of the visual response and that the magnitude of this synchronisation is related to the performance of the animals. Supported by ICM P04-068-F and Fundación Guillermo Puelma

C103. THE EXPRESSION PATTERNS OF ALPHA-SNAP AND N-CADHERIN IN DIFFERENT EPENDYMAL DOMAINS CORRELATE WITH THE NEUROPATHOLOGICAL PHENOTYPE OF *HYH* MUTANT MICE. Luis Federico Bátiz, Cristian Oliver, Sara Rodríguez, Esteban M. Rodríguez. Instituto de Histología y Patología, Facultad de Medicina, Universidad Austral de Chile. federicobatiz@uach.cl

Background. The *hyh* mutant mouse develops fetal-onset neuroepithelial/ependymal denudation that precedes cerebral aqueduct obliteration and hydrocephalus. Recently, a point mutation in alpha-SNAP protein has been identified as responsible of the *hyh* phenotype. Alpha-SNAP is involved in the intercompartmental traffic of proteins; however, the expression of this protein during brain development and the molecular mechanisms leading to ependymal denudation, have not been studied. Considering that (i) the pattern of ependymal denudation matches that of ependymal differentiation, which involves changes in the intercellular junctions, and (ii) the ependyma of circumventricular organs, endowed with a special set of junctions, never detach; it is proposed that a failure in the traffic of some adhesion/junction proteins leads to ependymal denudation during early stages of development. The aim of the present investigation was (i) to study the temporal expression of alpha-SNAP, NSF, and proteins involved in intercellular junctions, (ii) to evaluate the expression of these proteins in different ependymal domains, and (iii) to correlate these patterns with the neuropathological process occurring in *hyh* mice.

Materials and Methods. Brains of non-hydrocephalic and hydrocephalic (mutant) mice were studied by immunocytochemistry and transmission electron microscopy at various developmental stages. Protein homogenates from telencephalum, brain stem and cerebellum were analyzed by immunoblotting. Expression of mRNA encoding for alpha-SNAP and NSF was analyzed by semi-quantitative and real-time PCR.

Results. (1) alpha-SNAP and NSF are preferentially expressed in the CNS and at early developmental stages; (2) ependymal cells express N-cadherin but not E-cadherin; (3), there is a differential expression of alpha-SNAP and N-cadherin between the dorsal and ventral ependyma of Sylvius ; (4) expression of alpha-SNAP and N-cadherin varied among the various ependymal subpopulations studied; (5) in hydrocephalic *hyh* mice, ependymal domains that express higher levels of N-cadherin were resistant to the denudation process.

Conclusions. The differential expression alpha-SNAP at distinct brain regions and cell types may contribute to the understanding of the molecular mechanisms underlying *hyh* phenotype. Differential expression of N-cadherin appears to be associated to both, ependymal denudation and resistance to ependymal detachment. It may be postulated that alpha-SNAP mutation occurring in *hyh* mice leads to abnormal traffic of N-cadherin to the plasma membrane of the detaching ependymal cells.

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C104. DESIPRAMINE BUT NOT HALOPERIDOL PREVENTS THE STRESS INDUCED DEPRESSION-LIKE BEHAVIOURS IN RATS, AND A REDUCTION IN HIPPOCAMPAL TGF- β 1 MRNA EXPRESSION. Javier A. Bravo¹, Gabriela Díaz-Veliz², Sergio Mora², Sandor Arancibia³, Hernán E. Lara¹, Jenny L. Fiedler¹. ¹Biochemistry and Molecular Biology, Fac. of Chemistry and Pharmaceutical Sciences, Universidad de Chile.

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In several psychopathologies there are changes in the expression of numerous growth factors. Depressed patients have lower levels of circulating TGF- β 1 than healthy subjects. TGF- β 1 has been related to neuroprotection in several animal models, but little is known of its modulation in the central nervous system by stress and antidepressants. We studied how TGF- β 1 expression changed in an animal model of depression, and under chronic antidepressant and antipsychotic treatment.

Male Sprague-Dawley rats were subjected to 2,5h/day of restraint for 14 days, and were chronically injected with either the antidepressant Desipramine (DMI 10mg/kg ip.) or the antipsychotic Haloperidol (HAL 50 μ g/kg sc.).

Stressed animals had higher corticosterone levels, anhedonia, avoidance conditioning impairments, and behaved helpless in forced swim test. These behaviours were prevented by chronic DMI but not by HAL treatment. In stressed animals, hippocampal TGF- β 1 mRNA was reduced, as shown by *in situ* hybridization. This reduction was prevented by DMI but not by HAL treatment.

This result suggests that DMI but not HAL modulates hippocampal TGF- β 1 expression, and probably promotes neuroprotection.

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C105. EFFECT OF CHRONIC ADMINISTRATION OF BRAIN INHIBITORY DRUGS ON VISUO-SPATIAL LEARNING IN THE RAT. Burgos H¹, Castillo A², Gaete P¹, Dominichetti E¹, Flores M², Covarrubias ME², Olivares X², Iturrieta A², Balbontín L², Muñoz P², Fernández V³, Hernández A⁴. ¹Escuela de Psicología Universidad de las Américas, ²Escuela de Psicología, Universidad Santo Tomás; ³Facultad de Odontología, Universidad Diego Portales; ⁴Facultad de Química y Biología, Universidad de Santiago de Chile.

Brain inhibitory drugs such as anxiolytic and anticonvulsants are effective for the treatment of anxious disturbances, panic crisis, bipolar disease and even for epileptic syndromes. There exist scanty evidence of effect of anxiolytics on learning, despite the fact central inhibitory effects of drugs might influence the cognitive performance. We studied the effects of chronic administration of diazepam, clonazepam and valproic acid (drugs largely prescribed in medical practice) on rat visuo-spatial memory using the Olton's eight-arm radial maze. The results showed that diazepam (10 mg/kg daily during 16 days), clonazepam (2 mg/kg daily during 16 days) and valproate (30 mg/kg daily during 16 days) produced significant dose-dependent decrement on maze performance (number of errors and time spent). These results indicate that activation of central inhibitory systems by drugs acting mainly on gabaergic transmission exerts a negative influence on visuo-spatial learning.

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C106. TUBERALINS: NEW ADENOHYPOPHYSEAL HORMONES? Carvajal AM, Aguilar A, Vasquez P, Guerra M and Rodriguez EM. Instituto de Histología y Patología, Área de Neurociencias, Facultad de Medicina, Universidad Austral de Chile.

The pars tuberalis (PT) is the only region of the adenohypophysis which displays a very high number of melatonin receptors. Although PT function has not yet been clarified there is evidence that it plays a role on the release of *pars distalis* (PD) hormones through the secretion of specific compounds called “tuberalins”. Previous studies from our laboratory have (i) identified two compound of 72 (tuberalin I) and 21 (tuberalin II) kDa secreted by PT-cells of the bovine and rat, (ii) detected the presence of these compounds in the blood of the hypothalamo-hypophyseal portal system and (iii) found that secretion of both tuberalins is regulated by melatonin. All these properties support the hormonal nature of tuberalins I and II. Our current aims are to purify both tuberalins, and to investigate their function(s). Bidimensional electrophoresis followed by immunoblotting using antiserum raised against tuberalin II revealed eight immunoreactive spots with a mass of 20-25 kDa and electrofocussing pHs ranging between 5 and 9. Immunochemical evidence indicates that one of these spots corresponds to luteinizing hormone (LH), suggesting a molecular relationship between tuberalin II and PD-glycoprotein hormones. Studies on the effect of PT-conditioned medium upon prolactin (PRL) and luteinizing hormone (LH) release by bovine PD cell culture, are in progress. The molecular characterization of tuberalins I and II and the clarification of their function(s), would further support the existence of a pineal-pars tuberalis-pars distalis neuroendocrine axis.

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C107. A Ca^{2+} -ATPASE IS PRESENT IN THE OLFACTORY CILIA. Castillo K., González C., Cabello S. and Bacigalupo J. Department of Biology, Faculty of Sciences, University of Chile, Santiago, Chile

Ca^{2+} concentration increases in the chemosensory cilia of olfactory receptor neurons (ORNs) during the odorant response. Calcium influx occurs through cyclic nucleotide-gated channels confined to the cilia and activates Cl^- or K^+ channels. In order to end the olfactory response, the Ca^{2+} ions must be removed from ciliary lumen. Ca^{2+} removal from the cilia is thought to rely on a $\text{Na}^+/\text{Ca}^{2+}$ exchanger (NCX). Immunoblots of purified rat olfactory cilia membranes confirmed the presence of a NCX, but also revealed that they are enriched in plasma membrane Ca^{2+} -ATPase (PMCA). Immunocytochemistry confirmed the ciliary presence of PMCA in toad ORNs, where it co-localizes with NCX. Immunohistochemistry shows enrichment of PMCA in the ciliary layer. We obtained inside-out ciliary membrane vesicles that were preloaded with Fluo 5N. We measured an ATP-dependent Ca^{2+} transport in such vesicles. The activity of the pump as a function of $[\text{Ca}^{2+}]$ exhibits a bell shape, with a peak at $\sim 5 \mu\text{M}$. Carboxieosin ($50 \mu\text{M}$), a specific PMCA blocker, reduced Ca^{2+} transport. Calmidazolium ($10 \mu\text{M}$), a calmodulin (CaM) blocker, also decreased PMCA activity. In contrast, the addition of CaM increased the pump activity ($K_{0.5} = 31 \text{ nM}$). These results demonstrate a Ca^{2+} /CaM-dependent PMCA is found in olfactory cilia. We propose that the PMCA plays a key role and that work in coordinated way with NCX on removing Ca^{2+} ions from the olfactory cilia, the that entered during the odorant response.

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C108. PERINATAL NICOTINE EXPOSURE AFFECTS THE RAPHE NEURONS IN NEONATAL MICE. V. Cerpa¹, I. Llona², F. Torrealba¹ and J. Eugén^{2, 1} P. Universidad Católica de Chile, ² Universidad de Santiago de Chile.

Nicotine would be responsible of the tight epidemiological association between maternal cigarette smoking during pregnancy and Sudden Infant Death Syndrome (SIDS). Infants who died from SIDS, showed several respiratory dysfunctions and reduced arousal responses induced by hypoxia and hypercarbia. We found that P0-P3 perinatal nicotine exposed neonates hypoventilate, had reduced responses to both hypercarbia and central chemoreceptor stimulation. Since raphe nuclei are involved in arousal responses and chemosensory control of respiration, we were interested in studying whether perinatal nicotine exposure affects raphe nuclei neurons.

Osmotic minipumps were implanted subcutaneously into 5-7 days CF1 pregnant mice to deliver saline (controls) or nicotine ditartrate 60 mg Kg⁻¹ day⁻¹. P1-P5 neonates were placed in a temperature-controlled plethysmographic chamber and were allowed to breath air spontaneously during 10 minutes, followed by 10 minutes inhaling air enriched with 10% CO₂ (21% O₂, N₂-balanced). After 1 ½ hr the neonates were anesthetised with ether, perfused transcardially with 4% p-formaldehyde and 0.01% picric acid, their brains removed and fixed for 42 hr. Cryostat made sections were processed for immunohistochemistry anti- Tryptophan Hydroxylase (serotonergic marker) and anti-c-Fos (neural activity marker).

In both, control and nicotine exposed, the number of c-Fos positive neurons in the raphe obscurus did not vary after CO₂ inhalation. However, the number of serotonergic (TpH-positive) or not serotonergic c-Fos positive neurons in P1-P3 nicotine exposed neonates was lower than that found in controls ($p < 0.01$ and $p < 0.05$, respectively, Newman-Keuls Multiple Comparisons). Even more, in P5 nicotine exposed neonates, somata of serotonergic neurons within the raphe obscurus showed smaller areas than those found in controls ($p < 0.01$ Kolmogorov Smirnov Two-Sample Test).

Our results show that perinatal nicotine exposure reduced the population of activated neurons of the raphe obscurus in neonatal mice affecting the somata size of serotonergic neurons. These findings have relevant implications for understanding the mechanisms underlying nicotine-induced deficit in respiratory central chemoreception

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C109. PHOTOBIMODULATION BY NEAR INFRARED LIGHT ATTENUATES RETINAL DETERIORATION INDUCED BY KCN Tatiana Cevo, Adrian G Palacios Centro de Neurociencia de Valparaiso, Fac de Ciencias, Universidad de Valparaiso.

The use of near the infrared light as neuroprotector has been considered from evidence that shows its antiapoptotic effect. An in vivo retinal model of chemical hypoxia was induced by intravitreal injection of 300 μ M of KCN. Retinal dysfunction was studied with electroretinogram (ERG) 30 minutes and 24 hrs post treatment, with or without pre-treatment with NIR (670 nm) light (n=6). Rats treated only with KCN showed a noticeable diminution, 50 to 100% (n=2) of the control ERG *b*-wave amplitude, 24 hrs after the injection, in all measured intensities. The pre-treatment for ten minutes with NIR light previous to the KCN injection showed to be effective in the prevention, showing a diminution of only a 23 to 36% in *b*-wave amplitude 24 hours later (n=2).

This is the first study to observe the effect of NIR light in an in vivo retinal model of chemical hypoxia by intravitreal KCN. Our results suggest that light of frequency NIR has a neuroprotective effect in retina from chemical hypoxia induced by KCN.

PBCT ACT45, Conicyt Doctoral Fellowship

C110. INCREASE OF LAYER IV-IPSCs DURING DEVELOPMENT AND INDUCED BY EXPERIENCE REGULATE THE CRITICAL PERIOD IN VISUAL CORTEX. Juan Fco. Codocedo and Bernardo Morales. Laboratorio de Neurociencias, Facultad de Química y Biología, Universidad de Santiago de Chile.

The experience-dependent synaptic plasticity in visual cortex have a critical period of around 5 weeks in rats. Recently, we demonstrated that the maturation of IPSCs of the layer II/III it is correlated with the timing of critical period. However, the “gates” hypothesis for synaptic plasticity in visual cortex has been proposed in the layer IV. In this work using the whole cell recording we directly test the changes of IPSCs in star piramidal cells of layer IV during development and induced by experience. Acute visual cortex slices (300 um) were obtained from 2-5 week-old Long Evans rats normal rearing and dark rearing and maintained in a storage chamber containing artificial cerebrospinal fluid for 1 hour before recording. GABAergic whole cell currents were evoked by electrical stimulation with electrodes localized on the white matter and recorded from layer 4. We found for the first time an increase of the IPSCs during development in a similar way to that observed in layers II/III. This effect was experience-dependent since in dark reared animal, the raise in the IPSCs was postponed. In contrast, the EPSC in the layer IV showed no changes, which confirms that the excitatory currents reach their maturation before the third week.

These results confirm our evidence previous and shows for first time of direct manner the gate hypothesis.

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C111. REVERSIBLE INACTIVATION OF THE INSULAR CORTEX SUPPRESSES PLACE PREFERENCE IN ADDICTED RATS AND MALAISE INDUCED BY LITHIUM. Contreras M., Ceric F., Torrealba F. Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

The Insular Cortex (IC) processes interoceptive information. Recent studies showed an increase in neuronal activity of the IC in addicted individuals that was positively correlated with self reports of drug craving. We evaluated the effect of the reversible inactivation of the IC with lidocaine on the conditioned place preference (assesses craving) induced by chronic amphetamine. The rats were under a protocol of addiction and conditioned place preference, where one of two chambers was repeatedly paired with amphetamine and the other was paired with saline. Amphetamine progressively increased locomotor activity and produced a significant preference for the amphetamine-paired chamber in all conditioned rats. Conditioned rats showed a significant increase in the number of Fos-ir neurons in the IC. The transient inactivation of the IC but not the saline injection, totally and reversibly suppressed the place preference in addicted rats. To test common interoceptive mechanisms in craving and malaise, we inactivated IC in rats injected with LiCl i.p. and assessed malaise by video recording lying on belly, pica and grooming. The transient inactivation of IC suppressed these behaviors. Our findings suggest that the IC is essential in sensing the internal physiological conditions, and we propose a key role of the Insular Cortex in the generation of craving for amphetamine in addicted rats, and in sensing malaise induced by lithium.

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C112. NON-AUDITORY RESPONSES IN THE AUDITORY CORTEX OF BEHAVING CHINCHILLAS. Paul H. Delano ^{1,2}, Fernando Ramírez^{1,2}, Luis Robles ¹ and Pedro E. Maldonado^{1,2}. 1. Programa de Fisiología y Biofísica. ICBM. Facultad de Medicina. Universidad de Chile. Santiago, Chile. 2. Centro de Neurociencias Integradas, Iniciativa Científica Milenio. Santiago, Chile.

There is evidence that neurons from the auditory cortex can be activated by visual or tactile stimuli in deaf subjects. However, in normal people, sensory cortices are generally considered to be modality-specific. To challenge this presumption, we recorded 181 units from the left auditory cortex in awake chinchillas performing a frequency discrimination task. Simultaneously cochlear potentials were recorded from the right cochlea. Auditory target discrimination was cued by a light that turned on for a period of two seconds before target presentation. The presence of the visual cue reduced reaction times to the auditory targets. We demonstrate that the visual cue influences the activity of units recorded from the auditory cortex of chinchillas during the auditory frequency discrimination task. The discharge rates of 9.4 % of the units recorded were modulated by the visual cue. In addition, the first-spike latencies of 18.2 % of these units were also modulated by this cue. By measuring the cochlear microphonic potential, we confirmed that an auditory artefact did not produce these visual-cue responses. In 103 units in which there were at least 10 correct responses we calculated peri-event time histograms (PETH) in relation to lever pressing. We found that 37 % of these 103 units changed their activity in relation to the execution of a lever response. We conclude that the activity of auditory cortex neurons could be modulated by heteromodal stimuli or by behavioural states during an auditory task that requires attention.

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C113. MORPHOLOGICAL AND VOLUMETRIC ANALYSIS OF THE HUMAN HABENULAE. Díaz E., Bravo D., Härtel S., Villalón A., Cifuentes D., Célis M., and Concha M.L. Programa de Anatomía y Biología del Desarrollo, ICBM, Facultad de Medicina, Universidad de Chile.

The habenulae is an evolutionary conserved dorsal diencephalic nucleus linking the limbic forebrain and the midbrain. Despite the large number of morphological studies of the habenulae in different vertebrates and the fact that it has been implicated in pathological conditions such as psychosis, schizophrenia and addictive behaviours, little is known of this nucleus in humans. We present a cytoarchitectonic and immunohistochemical approach of the human habenula focused on the organisation of functional sub-nuclei, the development of left-right asymmetries, and the co-evolution of habenular structures and limbic forebrain regions. Serial sections stained with Nissl and Kluver-Barrera techniques were used to analyse the spatial organisation of cell bodies and nerve fiber bundles. We revealed two main habenular subdivisions, which seem homologous to medial and lateral habenular sub-nuclei described in rodents. The medial subnucleus faces the wall of the third ventricle and is formed by densely packed neurons displaying small and rounded cell bodies. The lateral subnucleus is more heterogenous and comprises neurons of larger size, which are loosely distributed among the neuropile. Preliminary 3-dimensional reconstructions and volumetric analyses indicate that left and right habenular nuclei are symmetric, and that the volume ratio between lateral and medial habenular sub-nuclei is considerably larger than in rodents.

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C114. LONG-TERM TIME-FREQUENCY SPECTROGRAPHICAL DESCRIPTION OF 24-HOURS OF CONTINUOUS ELECTROCORTICOGRAPHIC RECORDING OF A RAT IN A RESTING STATE. Hernán Díaz M.^{1,3}, Javiera Castro F.^{2,3} and Ennio Vivaldi V.⁴. ¹

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Long-term description and analysis of brain electrocortical signals are scarce in the literature and barely used as research tool. Major part of temporal dynamics of nervous system processes are understood almost only exclusively at microtemporal scale (range of milliseconds) giving a very narrow temporal observation window for studying long-term brain electrical activity.

Using Sprague-Dawley rats tested for REM sleep experimental setup (12/12 Light/Dark cycle), we describe and FFT frequency decomposition analyze, 24-hours of continuous ECG signal (skull implanted electrodes, sample rate 300 Hz, cutoffs: 0,1-30Hz) to obtain time-frequency-amplitude representation (spectrograms) of the rat brain activity. Spectrograms were computed and analyzed using IgorPro/BSound FFT procedures.

We describe several brain activity patterns classified by their spectral characteristics, the criterion include three stages of background activity intensity: Low, Medium and High (-10dB→ -5dB / -5dB→ 0dB / 0→ ≥5dB) on four frequency bands: 0,1-7 Hz; 8-14 Hz; 15-21 Hz; 21-28 Hz. (graphical frequency resolution $1 \pm 0,5$ Hz / graphical time resolution: 3,2 s.).

Over the dynamic background activity, we found discrete events characterized by particular and multiple narrow frequency band arrangements, described here as harmonic resonance also finding some incidents showing frequency modulation. Time-freq long range background activity amplitude modulation is common but punctuated in their transitions. We also found tiny discrete low frequency activity burst (~ 2 s duration , ≤ 1 Hz). Frequent and long lasting uninterrupted activity (→7,5 min) is typical around 7 Hz, also occurring in simultaneous appearing with different background levels and in conjunction with discrete resonance patterns. Long intervals with very low activity are also observed.

C115. EFFECTS OF ELECTRICAL STIMULATION OF OLIVOCOCHLEAR FIBERS ON COCHLEAR RESPONSES IN THE CHINCHILLA. Diego Elgueda^{1,2}, Paul H. Delano² and Luis Robles². ¹ Facultad Ciencias Veterinarias y Pecuarias, ² Programa Fisiología y Biofísica, ICBM, Facultad Medicina. Universidad de Chile.

Two types of receptor cells exist in the mammalian cochlea, inner hair cells, innervated by VIII nerve afferent axons, and outer hair cells, which receive an important efferent innervation from the brainstem. In spite of this remarkable presence of efferent fibers in the cochlea, their function in the auditory system remains unknown. The effect of electrical stimulation of efferent fibers has been studied in cat and guinea pig. However, due to anatomical differences in the distribution of cochlear efferent fibers in the different species, it is important to evaluate this effect in the chinchilla. We stimulated olivocochlear fibers in 24 anesthetized chinchillas, applying current pulses through a bipolar electrode placed on the fourth-ventricle floor. Compound action potential (CAP) and cochlear microphonics (CM) were acquired in response to clicks and tones of different frequencies. Electrical efferent stimulation produced CAP-amplitude reductions, reaching up to 12 dB, which were higher for low to moderate sound levels and were also higher for larger current pulses. In addition, efferent stimulation produced concomitant CM amplitude increments, which were greater for tones of low frequencies and low levels. The CM increments (≤ 2.5 dB) were of smaller magnitude than the CAP reductions. We also found CAP-latency increments that were not equivalent to simple decreases in sound level, and CM-phase changes that were larger at low intensity tones. These results show the characteristics of the efferent control of sensitivity in the chinchilla cochlea.

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C116. EFFECTS OF HISTAMINE RECEPTOR ANTAGONISTS ON MOTIVATED BEHAVIOR. Farías, P., Valdés JL and Torrealba, F. Laboratorio Neurobiología, Facultad Ciencias Biológicas, P. Universidad Católica de Chile.

Food search is accompanied by an increase in arousal correlated with the activation of the histaminergic neurons of the tuberomammillary nucleus (TMN). Histamine probably plays a fundamental role in initiating and maintaining a motivated behavior. The postsynaptic H₁ histamine receptors facilitate excitatory function in the central nervous system. Histaminergic neurons express the H₃ autoreceptor which inhibits the synthesis and release of histamine. Since the motivation needs an increase in the arousal probably by the increase in the activity of the histaminergic neurons we evaluated if the changes in cerebral histamine receptor activity produce corresponding changes in motivation. Rats were maintained on a restricted feeding and trained to discriminate between one arm of a T-maze with high food reward from the other with low reward. ICV injection of thioperamide (H₃ antagonist; 100µg/µl) and pyrilamine (H₁ antagonist; 50µg/2µl) were administered. We measured the locomotor activity, time delay to eat, choosing of arm and c-Fos expression in the TMN.

Pyrilamine decreased the exploratory locomotor activity respect to control saline and inhibited the activation of the TMN approximately to a 5% of the TMN neurons compared to a 60% in the saline condition. Our results suggest that H₁ receptors located in the histaminergic neurons contribute to their activation, and that H₁ receptors in target neurons are necessary to express the arousal that characterizes a motivated behavior. FONDECYT 1060476

C117. REGULATION OF CONNEXIN43 DURING NEUROGENESIS OF P19 AND OLFACTORY EPITHELIAL CELL LINES. V. Figueroa¹, C. Pacheco¹, L. Sülz², C. Gatica³, J.C. Sáez³ and A.D. Martínez¹. ¹Departamento de Neurociencias, Universidad de Valparaíso. ²Facultad de Ciencias, Universidad de Chile. ³Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Connexin43 (Cx43) is a gap junction protein subunit highly regulated during brain development. Cx43 may influence neuronal differentiation by changing critical cellular features like gap junction channel permeability. To address this hypothesis we studied *in vitro* neurogenesis in P19 cells (mouse embryonic carcinoma pluripotent cell line) and OLF442 (olfactory epithelial cell line). Immunoblots and indirect immunofluorescence analysis showed that both cell lines express Cx43 and were coupled (diffusion of microinjected-Lucifer yellow to neighbouring cells) indicating the presence of functional gap junction channels. Retinoic acid (RA) plus cellular aggregation induced neurospheres formation and high levels of neuronal differentiation in P19 and OLF442 cultures (neuronal marker expression: β -III tubuline, GAP-43, neurofilament and NeuN). In addition, a progressive and concomitant reduction in both, total levels of Cx43 and dye coupling incidence were observed in the cultures during and after RA treatment. Free-serum culture condition induced differentiation of OLF442 cells and reduction of Cx43 levels. On the contrary, treatment of P19 cells with ciliary neurotrophic factor and cellular aggregation induced progressive increase of Cx43 and low levels of differentiation. Neurogenesis was reduced in P19 cells stably transfected with Cx43. These results suggest an inverse relationship between Cx43 expression and neurogenesis. (Supported by grant: FONDECYT 1050857, DIPUV-33, ANILLO ACT-46).

C118. FUNCTIONAL EXPRESSION OF *SHAKER* POTASSIUM CHANNEL MUTATIONS CARRYING AN ADDITIONAL CHARGED RESIDUE IN THE VOLTAGE SENSOR. Vivian M. González^{1,2} and David Naranjo¹ ¹Centro de Neurociencias de Valparaíso. Universidad de Valparaíso. ²Doctorado en Neurociencia, Fac de Ciencias, Universidad de Valparaíso.

The activity of voltage gated ion channels underlies the generation and propagation of electrical signals in excitable tissues. All these channels contain a voltage sensor domain in each of its four subunits that confers its exquisite sensibility to membrane potential. Under a depolarization, highly conserved basic amino acids, which are located at the fourth transmembrane segment (S4) of each subunit, move across the membrane electric field and promote a conformational change leading the opening of the conduction pathway. Recent structural model put some of the S4 basic residues in direct contact with lipid bilayer. We carried out punctual substitution for either arginine or aspartate, in 7 hydrophobic residues surrounding the S4 basic amino acids of *Shaker* potassium channel. The 14 mutations obtained were tested for expression in *Xenopus* oocyte. All mutations showed currents corresponding to functional voltage gated potassium channels and some of them shift the activation curve versus wild type. Negative mutations in each position showed better membrane expression level than its positive homologous. From our charge scanning we propose that most residues in S4 contact an aqueous environment.

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C119. THE SH-3 DOMAIN OF VOLTAGE GATED CALCIUM CHANNEL B-SUBUNIT PROMOTES ENDOCYTOSIS VIA DYNAMIN INTERACTION.

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High voltage-gated calcium channels (VGCC) enables calcium entry into cells in response to membrane depolarization. Association of the auxiliary β -subunit ($\text{Ca}_v\beta$) to the α -interaction-domain (AID) in the pore-forming subunit ($\text{Ca}_v\alpha 1$) is required to form functional channels. $\text{Ca}_v\beta$ belongs to the membrane associated guanylate kinase (MAGUK) class of scaffolding protein family containing a Src-homology 3 (SH3) and a guanylate kinase (GK) domain. While the latter is responsible for the high affinity binding to the AID site, the functional significance of $\text{Ca}_v\beta$ -SH3 remains elusive. Here, we show that injection of isolated $\text{Ca}_v\beta$ -SH3 into *Xenopus laevis* oocytes expressing $\text{Ca}_v\alpha 1$ reduces the number of channels in the plasma membrane. This effect is reverted by coexpressing $\text{Ca}_v\alpha 1$ with a dominant-negative mutant of dynamin, a GTPase involved in receptor-mediated endocytosis. Full length $\text{Ca}_v\beta$ also downregulates VGCCs but only when lacking the AID site. Moreover, isolated $\text{Ca}_v\beta$ -SH3 and full length $\text{Ca}_v\beta$ were found to interact *in vitro* with dynamin and to internalize the distantly related *Shaker* potassium channel. These results demonstrate that $\text{Ca}_v\beta$ regulates the turnover of VGCCs and other proteins in the cell membrane. This effect is mediated by dynamin and depends on the association state of $\text{Ca}_v\beta$ to the pore forming subunit. Our findings describe a novel function for $\text{Ca}_v\beta$ and establish a link between VGCCs activity and the cell endocytic machinery.

This work was supported by grants from the Deutsche Forschung Gemeinschaft (DFG) (FOR 450, TP1, to PH.) and Fondo para el Desarrollo de Ciencia y Tecnologia (FONDECYT - 1020899) and Anillo de Ciencia y Tecnologia (ACT-46) to AN. GG is financed by PhD CONICYT scholarship.

C120. AUDITORY CORTEX ACTIVITY MODULATES COCHLEAR RESPONSES.

Carlos M. Hamame, Paul H. Delano and Luis Robles. Programa de Fisiología y Biofísica, ICBM, Facultad de Medicina, Universidad de Chile.

The cochlea has two types of receptor cells, inner and outer hair cells. Inner hair cells are ordered in a single row and contact directly with the ganglionar neurons, whose fibers conform the auditory nerve and the beginning of the auditory afferent pathway. Outer hair cells are located more laterally in three rows and receive major efferent terminals, with scarce afferent synaptic contacts. The efferent auditory pathway has been classically described as the olivo-cochlear system. However, there is morphological evidence showing that the efferent pathway begins in the auditory cortex. Electrical potentials were recorded in 8 anesthetized (Ketamine/Xilazine) chinchillas using two electrodes. The auditory nerve compound action potential (CAP) and cochlear microphonics (CM) were acquired with an electrode placed on the round window of the cochlea. Lidocaine (intracortical injection) inactivation was assessed by measuring the auditory evoked potential with an electrode located at the primary auditory cortex. Cortical inactivation showed correlated changes in the magnitudes of CAP and CM. However, the direction of the effects varied in different animals: CAP decrease and CM increase (2), CAP and CM decrease (3), CAP increase and CM decrease (2), CAP and CM increase (2). These results show the existence of a tonic modulation of the cerebral cortex on the auditory periphery. The diversity of the observed effects may be due to inactivation of different regions of the primary auditory cortex, which could be the source of different corticofugal pathways.

Supported by Fundación Puelma.

C121. CALCITONIN GENE RELATED PEPTIDE MODULATES THE OVERFLOW OF ATP FROM SYMPATHETIC NERVE ENDINGS. Diego Hermosilla, M. Veronica Donoso, J. Pablo Huidobro-Toro. Centro Regulación Celular y Patología, Instituto MIFAB, Departamento Fisiología, Facultad Ciencias Biológicas, P. Universidad Católica de Chile, Casilla 114-D, Santiago, Chile.

To ascertain the role of calcitonin gene related peptide (CGRP) as a modulator of sympathetic transmission, we investigated whether this neuropeptide modulates the release of adenosine 5' triphosphate (ATP), the sympathetic co-transmitter. To further ascertain whether the ATP overflow is derived from sympathetic nerve endings, the release of NA and NPY, chemicals exclusive of sympathetic nerve endings was assayed in parallel. Methods: The prostatic portion of adult Sprague Dawley rat vas deferens was mounted in bath chambers and maintained with Tyrode buffer (37°C) supplemented with 1 μ M desipramine, gassed with 95% O₂/5% CO₂; the buffer was superfused at a flow of 2 ml/min. Neurotransmitter release was elicited by field electrical stimulation (16 Hz, 60 V, 1ms during 1 min), a stimuli that elicited indirect isometric contractions recorded through a force displacement transducer. ATP, NA and NPY were analytically quantified from a same aliquot sample of the superfusion buffer. Neurochemicals were separated by HPLC procedures. NA was quantified by electrochemical detection, while ATP was quantified by fluorescence; a RIA quantified NPY. Results: Following electrical nerve ending depolarization, the overflow of ATP, NA and NPY was 103 $\pm$ 17 pmol, 42 $\pm$ 8 pmol and 43 $\pm$ 6 fmol respectively (n=15); the NA overflow was delayed as compared to ATP. Application of 10 nM CGRP reduced the overflow of ATP, NA and ir-NPY to 21 $\pm$ 8 pmol, 12 $\pm$ 4 pmol and 18 $\pm$ 3.2 fmol (P<0.05) respectively, and halved the electrically evoked twitching. Moreover, 10 nM CGRP reduced the muscular contractions evoked by exogenous ATP and NA applications, revealing an additional inhibitory post junctional effect. To examine whether other neuropeptides evoked similar responses, 10 nM angiotensin II elicited a dramatic decrease on ATP and total purines (70%) overflow; however, it increased 2-fold the contraction evoked by exogenous ATP applications, indicating in addition facilitatory post-junctional modulator role. The peptide fragment CGRP₈₋₃₇ will be assessed to elucidate the nature of the CGRP receptor mediating pre and post junctional actions. Conclusions: CGRP modulates the release of ATP, which based on the parallel decrease in NA and NPY release supports the proposal that the ATP released might derive from sympathetic nerve endings. In addition this sensory neuropeptide exerts in addition a postjunctional modulator role. AII mimics the pre-synaptic inhibitory effect of CGRP on ATP overflow, but differs in its postjunctional role. Present results highlight the modulator role of neuropeptides in sympathetic co-transmission. Funded by FONDAPE 13980001 and MIFAB Institute.

C122. INTRAPERITONEAL ADMINISTRATION OF STI571 PREVENTS SPATIAL MEMORY IMPAIRMENT ASSOCIATED TO A β FIBRILS INJURY IN DORSAL HIPPOCAMPUS Hernández, D.E., Cancino, G.I. and Alvarez, A.R. Laboratorio de Señalización Celular, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile

Morris Water Maze (MWM) paradigm allows *in vivo* spatial memory evaluation in animal models of memory impairment pathologies such as Alzheimer's disease (AD). AD is a neurodegenerative pathology characterized by the presence of neurofibrillary tangles and senile plaques formed by amyloid β -peptide (A β) aggregates. A β fibrils induce neuronal dystrophy, neuronal dysfunction and apoptosis process that are underlaying to progressive dementia and memory impairments. Previous *in vitro* studies in our laboratory demonstrated that A β fibrils activate the c-Abl/p73 signaling transduction module inducing neuronal apoptosis. To analyze the role of c-Abl/p73 in neurodegeneration induction in animals models, we injected A β fibrils bilaterally into rat dorsal hippocampus, analyzing memory impairment response with MWM paradigm. A β injected animals showed higher escape latency and lower spatial acuity values than control animals, indicating cognitive performance loss and behavioral impairments. Then, we analyzed the effect of the co-treatment of the intraperitoneal (i.p.) administration of STI571, c-abl specific inhibitor, plus A β fibrils bilaterally injected. In this co-treatment we found that STI571 induces lower escape latency and higher spatial acuity values than A β alone animals, obtaining values similar to control animals. The results show that STI571 i.p. administration prevents A β injury effects and suggest that c-Abl/p73 signaling transduction module could be a possible therapeutic target for AD.

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C123. EFFECTS OF DOPAMINE MODULATING DRUGS ON NOCICEPTION INDUCED BY MECHANIC, THERMIC AND CHEMICAL TESTS: STUDY ON THE RAT Laurido, C.¹, Constandil, L.¹, Hernández, A.¹, Pelissier, T.² ¹Facultad de Química y Biología, Universidad de Santiago de Chile; ²Programa de Farmacología Molecular-Clínica, ICBM, Facultad de Medicina, Universidad de Chile.

Recent studies suggest that the D₂ receptor activation of dopaminergic mesolimbic neurons, arriving from cell bodies of the ventral segmental area and projecting to the nucleus accumbens, play an important role in the mediation and pain suppression. We used male Sprague-Dawley rats, to establish the role of endogenous dopamine on the antinociceptive mechanisms utilizing amineptine (selective dopamine reuptake inhibitor), deprenyl (selective monoamino oxidase B inhibitor) and sulpiride (dopaminergic D₂ receptor antagonist) subcutaneously administered on thermic, mechanic and chemical pain by using the tail immersion test, paw pressure test and the formaline test. The results show that amineptine, deprenyl and sulpiride induced a significant antinociceptive effect on the three tests studied. We can conclude the existence of a dopaminergic nociceptive modulation through D₂ dopaminergic receptors.

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C124. MORPHOLOGICAL ALTERATIONS OF CHOLINERGIC SEPTAL NEURONS IN NPC-/- MICE ; A MODEL OF NEURODEGENERATION OF NIEMANN-PICK DISEASE TYPE C. Lazo OM ^(1, 2), Figuerola A ^(1, 2), Mauna J ^(1, 2), Klein A ⁽³⁾, Alvarez AR ^(1, 4), Zanolungo S ⁽³⁾, Bronfman FC ^(1, 2)

Centro FONDAP de Regulación Celular y Patología Joaquín V. Luco. 1. Departamento de Fisiología. Facultad de Cs. Biológicas. P. Universidad Católica de Chile. 2. Departamento de Gastroenterología. Facultad de Medicina. P. Universidad Católica de Chile. 3. Departamento de Biología Celular y Molecular. Facultad de Cs. Biológicas. P. Universidad Católica de Chile

Niemann-Pick disease type-C (NPC) is an inherited disorder characterized by hepatosplenomegaly and progressive neurodegeneration leading to premature death during childhood. NPC common symptoms are ataxia and dysarthria, psychotic episodes and dementia due to neuronal degeneration in different areas of the brain. The NPC1 gene is mutated in most NPC patients. NPC1 protein is localized mainly in late endosomes and lysosomes and participates in cholesterol transport. Several evidences suggest that neuronal loss and dysfunction are related to a lipid traffic jam, due to a redistribution of proteins associated to vesicular compartments or membrane domains. In addition, neurons from NPC brains are positive for some hallmarks of neurodegeneration -shared by other neurodegenerative diseases exhibiting endosomal abnormalities- such as neuroaxonal swellings and neurofibrillary tangles. NPC1-/- mice are considered a good model of NPC, exhibiting several neurological symptoms of NPC patients. We have hypothesized that retrograde neurotrophic signaling, which depends on endosomal traffic, may be affected in NPC brain. To test our hypothesis, we are studying the morphology of cholinergic neurons, which relay heavily on neurotrophic support for survival and differentiation. We found no significant differences in the number of septal cholinergic neurons, but they appear atrophic (showing increased neuronal area) in NPC1-/- mice compared to wild type, consistent with cholesterol accumulation visualized by filipin staining. Additionally, the cholinergic dendrites appear altered and partially reduced. We are currently investigating the response of cholinergic septal neurons to NGF after axotomy of the septo-hippocampal pathway and intracerebroventricular infusion of NGF in the NPC mice. (Fondap 13980001, Fondecyt 1040999, F. Andes, ARA Parseghian Medical Research Foundation Grant)

C125. P2X RECEPTORS FACILITATE THE INDUCTION OF LTP IN CA1 OF HIPPOCAMPUS. Ramón Lorca^{*}, Héctor Duchens[#], Juan Pablo Huidobro-Toro^{*} and Bernardo Morales[#]. ^{*}Centro de Regulación Celular y Patología e Instituto MIFAB, Departamento de Fisiología, P. Universidad Católica de Chile. [#]Departamento de Biología, Universidad de Santiago de Chile.

Purinergic receptors may modulate long-term potentiation (LTP), a model widely accepted in learning and memory processes, since ATP and a non-hydrolyzable analog potentiate LTP in the CA1 area of rat hippocampal slices. Nevertheless, the cellular mechanisms and receptor subtypes involved in this modulation remain unclear. Our aim is to identify the subtypes of P2X or P2Y receptors involved in the LTP induction, expression or maintenance. Hippocampal slices (400 μm thick) were obtained from 3-5 week-old Sprague-Dawley rats and maintained in artificial cerebrospinal fluid for 1 hr before recording. LTP was recorded in CA1 by electrical stimulation of high frequency (HFS) applied from Schaeffer collaterals, using field excitatory postsynaptic potentials (fEPSP) technique. We found that 1 μM ATP, incubated 10 min before and 10 min after HFS, potentiates the induction and expression of LTP, while application of ATP 35 min post HFS reduces the potentiation, suggesting an inhibitory effect on the maintenance of LTP. Higher concentrations of ATP (5 and 10 μM) inhibit basal fEPSPs and LTP induction. Furthermore, the P2Y-selective agonist, 2MeSADP (100 nM) have no effect on LTP induction or maintenance. These results suggest that P2X purinergic receptors play an important role in the modulation of LTP in hippocampus. Funded by FONDAP 13980001 and MIFAB Institute.

C126. INHIBITORY EFFECTS OF TUTIN ON GLYCINE RECEPTORS IN SPINAL NEURONS. [§]Paula Manríquez-Navarro[§], Jorge Fuentealba, [§]Leonardo Guzmán, ^{*§}Claudia Pérez, ^{*§}Mario Silva, ^{*§}José Becerra, [§]Luis G. Aguayo [§]Department of Physiology, and ^{*§}Department of Botany. University of Concepcion, Chile.

Coriaria ruscifolia is a variety native to Chile and is known for its highly poisonous properties, especially in children that ingest its fruits. However, it was previously reported that tutin, in the micromolar range, inhibited GABA induced depolarizations in the frog spinal cord. It is presently unknown if tutin can interfere with GlyRs, which are expressed in several regions of the CNS. Therefore, we studied the effects of tutin, a sesquiterpenoid obtained from *Coriaria ruscifolia*, a native poisonous Chilean plant, on spinal glycine receptors (GlyRs) using patch clamp recordings. In addition, cytosolic Ca^{2+} activity and activation of CREB was also measured in the presence of tutin. Application of tutin inhibited the glycinergic evoked current in a concentration-dependent manner (0.01 to 1 mM), at 0.2 mM tutin reduce it about $44 \pm 11\%$ (n=7). Moreover, the frequency of spontaneous Ca^{2+} spikes (from 0.016 ± 0.005 Hz to 0.040 ± 0.007 Hz, n=14) and spontaneous synaptic activity (AMPAergic events $52.5 \pm 13.67\%$, n=6) was augmented and correlated with an increase in phosphorylated CREB levels, suggesting an enhancement in neuronal excitability. In conclusion, these results may explain the toxic effects of the plant characterized by epileptiform seizures with subsequent coma and death seen in humans and mice.

This study was supported by PBCT inserción de Postdoctorales en la Academia (CONICYT-WORLD BANK) Nro. 7. DIUC 205.033.099-ISP.

C127. IMPLEMENTATION OF A VIRTUAL SPACE FOR THE ENCOUNTER OF PEOPLE INTERESTED IN NEUROSCIENCE Hachi Manzur, Carlos Hammame . Programa de Doctorado , Facultad de Medicina, U de Chile)

It seems clear to us that current questions in Neuroscience cannot be addressed within a single disciplinary field. As the knowledge on this area advances, we realize the need of gathering a number of people from different background in order to address current research problems. In Chile, an increasing number of researchers and post graduate students are interested on Neuroscience as a field of study, while the background of all them seems to be very heterogeneous, including people from the biological sciences, philosophy, mathematics, engineering, etc.

Is in this regard, we think it is necessary an instance for the encounter of such diversity of people. We thought that an important characteristic of this instance is that it should not be restricted at particular times or locations, and therefore must be accessible for everyone interested in the field.

Here we present an early development of a mechanism for meeting and gathering people interested on Neuroscience with the complexity it involves. This instance is embodied on a web site that provides –for the moment- basic principles of the ideas exposed above. This web site includes a home page with statements about de objectives; a forum and a chat for generate communication spaces; a section for downloading some files (books and papers) provided for the community and a section with links of interest. The site is located at <http://complecsity.gigcities.com>. This is a starting point that needs to be improved trough suggestions of the community, while the aim of the authors is to facilitate further enhancement of gentle bridges between people interested on this field.

C128. NICOTINE EFFECTS UPON THE RESPIRATORY RHYTHM OF FETAL MOUSE IN VITRO. Mariqueo, I. Llona, J. Eugenin, Neural Systems Lab., USACH, Santiago, Chile.

Nicotine is a known neuroteratogen and one probable factor linking maternal cigarette smoking during pregnancy with a higher incidence of Sudden Infant Death Syndrome. Perinatal nicotine exposure causes hypoventilation and reduced ventilatory response to hypercarbia in neonatal mice, which is likely due to a dysfunction of the central respiratory chemoreception. During the E17-E19 fetal stages, the respiratory rhythm becomes robust, regular, and acquires characteristics similar to those found in neonates. In this work we assess whether, within this period, the neural network originating the respiratory rhythm shows susceptibility to nicotine.

Nicotine (260 ng ml^{-1}) was administered into the incubation medium in which the isolated brainstem – spinal cord preparation from fetal mice was maintained by 2 days. CF1 mice E17 were obtained by C-section. Their CNS were removed under strict aseptic conditions and incubated in Basal Medium Eagle's supplemented with insulin 1000 units/ml, Kanamycin 0.1 mg/ml, sodium bicarbonate 24mM, D (+) glucose 30mM, Fetal Bovine Serum 0.2%, and Hepes 0.88mM. The medium was equilibrated with 5% CO_2 and 95% O_2 at room temperature (pH 7.4) and changed daily. After 2 days of incubation, spontaneous activity from C3-C5 ventral roots was recorded using suction microelectrodes, while CNS was superfused with artificial cerebrospinal fluid, gassed with 5% CO_2 and 95% O_2 , at 25°C , pH 7.4.

We found that after 2 days of incubation E17 preparations maintained their spontaneous respiratory-like activity either in presence or absence of nicotine. The frequency of the respiratory-like activity was $5.6 \pm 4.4 \text{ min}^{-1}$ (n=6) in controls, and 4.1 ± 0.6 (n=3) in nicotine treated preparations (p= 0.86, Mann-Whitney test). However, the responses to acidification (from pH 7.4 to 7.1) were lower in nicotine treated than that in controls (p=0.035, Mann-Whitney test).

Our results suggest that nicotine does not affect the respiratory-like rhythm in E17 isolated fetal mice CNS incubated by 2 days in vitro. However, nicotine reduces the respiratory response to acidosis. Support Contributed By: Fondecyt 1060110

C129. CONTRIBUTION OF GLUTAMATE RECEPTORS IN THE RETINA OF THE DIURNAL RODENT, OCTODON DEGUS. Pedro Martinez; A.G. Palacios Centro de Neurociencia de Valparaiso, Fac Ciencias, Univ Valparaiso, Chile

The signaling contribution of Glutamate (AMPA, kainate, mGluR6) receptors to the excitatory and inhibitory processes in the retina of the diurnal rodent *Octodon degus* was studied. A conventional patch clamp techniques and DIC optics were used to record in retinal slices the response of different types of bipolar cells (n=47, RS = $45 \pm 11 \text{ M}\Omega$) to brief puffs of glutamate agonists and antagonists. After recording, intracellular filled cells with Lucifer yellow (250 $\mu\text{g/ml}$) establish 9 morphological types of cells that match ON-OFF bipolar type cells classification find in others mammals. One type are, OFF bipolar cells (n= 12), depolarize to kainate (200 μM) and desensitize with a (1-2 minutes) slow response. Their morphology shows a diffuse dendrite three, differing in their axonal terminal. A second type, OFF bipolar cells (n= 8), depolarize to AMPA with fast desensitization (< 100 ms) and were classified as midget cell. A third type, ON (rod and cones) diffuse and midget bipolar cell (n=6), hyperpolarize with AP-4 (300 μM). Taken together, these results support the notion that different excitatory mechanisms operate in the inner plexiform layer. Fondecyt 1040309, PBCT ACT45

C130. INCORPORATION OF SHAKER K⁺ CHANNELS TO THE PLASMA MEMBRANE OF XENOPUS OOCYTES IS REGULATED BY IP₃ SENSITIVE CA⁺² STORE IN THE ENDOPLASMIC RETICULUM. Naranjo D., Gayol S. and Neely A. Centro de Neurociencia de Valparaíso. Universidad de Valparaíso.

To study traffic of Shaker K⁺ channel to the plasma membrane in *Xenopus laevis* oocytes, 6 hrs after the injection of cRNA the surface expression was arrested by incubating the oocytes at 4°C. After 12-24 hrs, arrested oocytes were allowed to resume at room temperature under two-electrode voltage clamp. Surface expression of channels was observed as an increment in K⁺ currents (IK). The channel is arrested presumable at the trans-Golgi network since IK was not blocked by Brefeldin A or Cicloheximide, applied at the end of the arrest period. The stages following the arrest required intracellular Ca⁺², because they were inhibited for BAPTA-AM (but not EGTA-AM), suggesting that the process does not depend on the basal free Ca⁺² but spatial and/or temporally localized increments. IK increments were inhibited by Thapsigargin and could not be restored by intracellular Ca⁺² injections suggesting that intracellular Ca⁺² stores must not be empty. These increments were also inhibited by the incubation with 2-APB, indicating that surface expression requires active IP₃-receptors. The necessary receptor activity proceeds at basal levels of IP₃, since the injections to increase of cytoplasmatic IP₃ do not further increase surface expression of channels. Thus, it is possible that at resting the functional unit sensitive to IP₃ is saturated. Funded by FONDECYT 1030285-1020899 – ACT46

C131. SYNAPTIC PLASTICITY IN OLFACTORY AMYGDALA DURING POSTNATAL DEVELOPMENT. C. A. Oliva¹, J. Bacigalupo², M. Sanhueza². ¹Centro de Neurociencias de Valparaíso, Universidad de Valparaíso; ²Department of Biology and Cell Dynamics and Biotechnology Research Center, Faculty of Sciences, University of Chile.

The amygdala complex is involved in processing of emotionally relevant sensory information. Olfactory inputs have a unique direct access to the cortical amygdala, suggesting it as an integral component of the olfactory system. The major aim of this work is to study the plastic properties at the connectivity between olfactory afferents and the cortical amygdala. We used electrophysiological techniques to record excitatory postsynaptic potentials (EPSPs) from layer I of the anterior cortical (ACo) amygdala, upon stimulation of the afferent olfactory pathway. We found NMDA-dependent synaptic plasticity in ACo. LTP was induced by TBS paradigm and was altered by the NMDAR-antagonist AP-V. We examined the evolution of NMDA-dependent synaptic plasticity during postnatal development. We found that LTP can be observed from P16. The temporal expression of LTP correlates with a differential contribution of the AMPAR/NMDAR ratio during development, reaching a maximal steady state NMDAR contribution at P17. We also found NMDA receptor-dependent long-term depression, but its expression was independent of the developmental stage. Our results represent the first evidence for long-term plasticity in the olfactory projections to the cortical amygdala, revealing a relationship between developmental stages, differential receptor contributions and the expression of LTP. Supported by CONICYT Prog. Bicentenario en Ciencia y Tecnología, ACT-45 to JB, CONICYT graduate fellowship to CO.

C132. N-CADHERIN-DEPENDENT ADHERENS JUNCTIONS PLAY A KEY ROLE IN EPENDYMAL PHYSIOLOGY. Cristian Oliver, Luis Federico Bátiz, César González, Esteban M. Rodríguez. Instituto de Histología y Patología, Facultad de Medicina, Universidad Austral de Chile

Background. The lining of the cerebral ventricles and central canal of the spinal cord is composed of different types of ependymal cells. Ependymal cells are devoid of functional tight junctions and basement membrane and are joined together by adherens junctions. The ependyma plays important barrier and signaling functions between nervous tissue and cerebrospinal fluid (CSF). The physiological role of these cells in central nervous system homeostasis has recently been highlighted by findings in mutant and transgenic mice. The *hyh* mutant mouse carries a point mutation in α -SNAP and develops a fetal-onset neuroepithelium/ependymal denudation that precedes and triggers cortical maldevelopment and hydrocephalus. Evidence from our laboratory suggests that an alteration in the traffic of adhesion proteins is linked to the disruption undergone by this mutant mouse. The aim of the present investigation was twofold: (i) to characterize the intercellular junctions of ependymal cells at molecular level, and (ii) to evaluate the importance of these proteins on ependymal physiology.

Materials and Methods. Explants obtained from adult bovine collicular recess were divided into three groups and exposed to: (1) an specific anti-N-cadherin antibody or a peptide functionally blocking N-cadherin, (2) IgG or a control peptide, and (3) no treatment. All groups were studied by transmission electron microscopy, immunocytochemistry and immunoblotting.

Results. Ependymal cells were joined together by gap junctions and by a set of large and apical adherens junctions. The latter were strongly immunoreactive to anti-N-cadherin. Functional tight junctions were missing. N-cadherin functional blockage, during 24h, leads to (i) changes in N-cadherin immunocytochemical pattern, (ii) ultrastructural modifications and a drastic reduction in the extension of adherens junctions, (iii) increase of the volume of the intercellular space, (iv) severe alterations of the ultrastructure of the ependymal cells not yet detached, and (v) detachment of the ependyma leading to large denuded areas of the explants.

Conclusions. (1) Adherens junctions are important for ependymal physiology; (2) N-cadherin is a major component of these junctions; (3) N-cadherin plays a key role in the stability of the ependymal lining, thus becoming a good candidate molecule to be involved in neuroepithelium/ependymal denudation that triggers hydrocephalus and abnormal neurogenesis in both, rodents and humans.

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C133. RELEASE OF ATP FROM SYMPATHETIC NERVE ENDINGS HIGHLIGHT ITS SYMPATHETIC CO-TRANSMITTER ROLE; EFFECT OF RESERPINE AND GUANETHIDINE ON THE RELEASE PROCESS. M.A Oarrantía, M.V. Donoso and J.P. Huidobro-Toro Centro Regulación Celular y Patología, Instituto MIFAB, Departamento Fisiología, Fac. Ciencias Biológicas, P. Universidad Católica de Chile.

We examined whether the release of extracellular ATP following electrical nerve terminal depolarization is calcium dependent and modified by reserpine and guanethidine, two sympathetic drugs well known to modify NA release by identified presynaptic mechanisms. Methods: The nerve endings of the prostatic half of the rat vas deferens were electrically depolarized (16Hz, 70V, 1 ms during 1 min) in the presence of 1 μ M desipramine to induce co-transmitter release (CoTR), neurochemicals were collected from the superfusion media. Co-transmitters were quantified following HPLC separation procedures: ATP and related purine derivatives were identified by fluorescence after chemical derivatization; NA was quantified by electrochemical detection and NPY by a specific RIA. All Co-TR were assayed from a same buffer aliquot. Results: Electrical nerve terminal depolarization elicited CoTR with a defined time course and in a specific proportion; release was paralleled by an increase in muscular tension. Extracellular calcium was mandatory for the CoTR since tissues incubated in buffer lacking external calcium, the CoTR and tissue tension was obliterated. Three h after 2.5 mM external calcium addition, $\approx$ 50% of the control CoTR and contraction recovered. In reserpinized rats (1 mg/kg i.p. for 48 h) the NA release was annulled (32 ± 12 pmol, $n=9$ vs non-detectable values), while the ATP release ($n=7$) was unaltered; the magnitude of contraction was preserved. 10 μ M guanethidine decreased the release of NA, ATP and its derivatives but not NPY, reducing concomitantly the electrically-evoked twitch tension. TTX annulled CoTR and contraction, indicating the importance of nerve ending depolarization in the release process. Further protocols will examine CoTR in the absence of muscular contraction. Conclusions. The finding that ATP and NA are possibly stored in the same vesicle is supported by guanethidine which in addition did not affect NPY release, raising the hypothesis of at least two types of vesicles, both mobilized, in the nerve ending, by a calcium-dependent mechanism. FONDAP 13980001 and MIFAB fundings.

C134. IN THE HTX MUTANT RAT MALDEVELOPMENT OF THE SUBCOMMISSURAL ORGAN PLAYS A KEY ROLE IN THE DEVELOPMENT OF HYDROCEPHALUS. A Ortloff, K. Vio, S. Rodriguez, EM. Rodríguez. Instituto de Histología y Patología, Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile.

The mutant HTx rat develops a fetal onset hydrocephalus. It is characterized by the obliteration of the Sylvius aqueduct (SA), malformation of the subcommissural organ (SCO) and dilatation of the lateral ventricles. The mechanism leading to aqueductal obliteration occurring during fetal life remains to be elucidated. The aim of the present investigation was to elucidate such a mechanism.

Normal HTx embryos and newborns, and their hydrocephalic littermates were collected at E18-PN1. The brain was processed for scanning electron microscopy and immunocytochemistry, using antibodies reacting with (i) the secretory proteins of the SCO (AFRU), (ii) and the neuroepithelium.

Normal E18 embryos already displayed a fully differentiated and strongly AFRU immunoreactive SCO. The other normal rats studied (E19- PN1) had a SCO strongly immunoreactive and secretory material released into the SA. E18 hydrocephalic embryos had a open SA and a SCO displaying three distinct zones, each one corresponding to about one third of SCO. The rostral and caudal thirds display strongly AFRU immunoreactive cells similar to normal embryos. The middle third, however, was not reactive to AFRU.. At E19, the middle zone of the SCO lacked immunoreactive material and started to fuse with the ventral floor of the SA. The obliteration of the aqueduct was completed at E19. At E20, hydrocephalus started as a moderate expansion of the lateral ventricles. The dorsal wall of these ventricles, corresponding to the pallium (neocortex), had areas devoid of neuroepithelium. Detachment of neuroepithelium started with "denudation center" that expanded radially to form large circular denuded areas. At PN1, the dorsal wall of the lateral ventricle displayed several denuded circles of different diameters.

Conclusions: (i) The SCO is not a homogeneous gland, present three distinct zones; is probably regulated by a different set of genes; (ii) maldevelopment of the middle zone of the SCO (alteration of a select set of genes?) results in the inability of this region to secrete glycoproteins and triggers obliteration of SA and hydrocephalus; (iii) loss of the pallium neuroepithelium appears to be associated to the pathogenesis of hydrocephalus (SCO maldevelopment?) rather than being the consequence of hydrocephalus proper.

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C135. CORRELATION BETWEEN FEATURE MAPS OF NATURAL SCENES AND GAZE POSITION: AN INTER-SPECIES COMPARISON. Jose P. Ossandon, Francisco J. Flores, Cecilia Babul, Pedro E. Maldonado CENI y Programa de Fisiología y Biofísica. Facultad de Medicina, Universidad de Chile

Natural scenes can be decomposed in several feature maps based on the stimulus physical properties such as luminance-contrast, orientation and saliency maps. These feature maps have been extensively used to derive low-level models of gaze control in humans. However, for different species visual fixation behavior can be substantially different due to the cognitive and physiological constraints of each species. We address these questions by comparing the correlation of feature maps and gaze position in two cats and two monkeys, while they freely explore a set of natural images. Ocular fixations were extracted with the use of a scleral search coil. Feature maps were extracted by common algorithm (Itti and Koch, 2000). For both species, we correlated fixation position and feature maps for i) the actual fixations, ii) random fixations, and iii) surrogate fixations. We found significant differences in contrast, orientation and saliency maps for almost all images in both species when comparing actual fixations with a random sample of fixations (Wilcoxon Rank Test, $\alpha = 0.05$). When we compared actual fixations with surrogates, (in order to overcome the bias of animals to fixate in the center of the image), only few images in both animals (monkeys: 4/26 for contrast, 3/26 for orientation, 4/26 for saliency; cats: 5/26 for contrast, 5/26 for orientation and 5/26 for saliency, all differences with an $\alpha = 0.05$) were significantly for the different features. Although there are more images with feature driven fixation in cats, this data cannot support an interspecies difference. Our results are consistent with previous reports showing that fixated points have high values of the different features when they are compared with random points. However, when we use surrogated data we find differences in only a few images of our set, suggesting that monkeys and cats may rely in more high-level cues to control gaze position.

Supported by ICM P04-068-F and Fundación Guillermo Puelma

C136. ACUTE AND LATE EFFECTS OF B-AMYLOID (A β) AGGREGATES ON SYNAPTIC TRANSMISSION IN HIPPOCAMPAL NEURONS. ^{1,2}Parodi, J. Sepúlveda, F.J.

^{1,2}Aguayo, L.G., ¹Department of Physiology, University of Concepción, ²Patagonia Neuroactive Biotech., Concepcion, Chile.

Recent reports have indicated that synaptic dysfunctions in brain might play an important role in Alzheimer's disease (AD). However, the effect of A β on neurotransmission is unknown. Therefore, we examined the effects of low concentrations of aggregated A β ₁₋₄₀ on hippocampal neurons using several techniques.

Acute applications of A β (0.5 μ M) induced a rapid increase in intracellular calcium and in spontaneous synaptic current frequency (1.7 $\pm$ 0.3 to 4.1 $\pm$ 1.2 Hz), without changes in current amplitude (61 $\pm$ 9 pA to 59 $\pm$ 10 pA). This increase was concentration dependent (0.5-5 μ M) and blocked by "0 added" calcium, ruthenium red (100 μ M) and cadmium (20 μ M). Calcium transients were increased in correlation with the synaptic activity (control: 2.4 Hz $\times$ 10⁻³, 0.5 μ M A β : 3.2Hz $\times$ 10⁻³). Acute application of the aggregated induce a destaining of the FM 1-43 in a short time (15 min) indicating an increase in vesicles release number. Interestingly, time course analysis of A β effects showed a biphasic phenomenon. For example, long term treatment (24 hrs) with A β aggregates (0.05 and 10 μ M) caused a significant reduction in spontaneous synaptic transmission. On the other, soluble and reversed A β ₄₀₋₁ peptides, as well as amyloid fibrils, did not affect synaptic parameters. The long-term inhibition was associated to a decrease in the number of intracellular Ca²⁺ transients, FM1-43 staining and SV-2 punctae, a presynaptic marker. The delayed inhibitory effects of A β were blocked by co-culturing the neurons with low extracellular calcium, cadmium and lithium.

In summary, these results indicate that A β ₁₋₄₀, at concentrations without evident neurotoxic effects, induced an acute facilitation in synaptic transmission followed by a late inhibition. The late effects might be relevant for the cognitive impairments associated to AD. We are now searching for small molecules that can antagonize these neurotoxic synaptic effects.

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J.P. is a Conicyt Doctoral Fellow

C137. LONG-TERM REM SLEEP HOMEOSTASIS PARAMETERS AFTER TOTAL OR REM-SELECTIVE SLEEP DEPRIVATION. Sebastián Peña¹ and Adrián Ocampo-Garcés^{1,2}

¹Programa de Fisiología y Biofísica, ICBM, Facultad de Medicina Universidad de Chile, ²Dep. Neurología y Neurocirugía, Hospital Clínico Universidad de Chile.

REM sleep expression is under the regulation of long-term and short-term homeostatic processes. Short intervals without REM sleep, whose duration were similar to the spontaneous sleep cycle, trigger augments in the number of NonREM to REM sleep transitions, whereas longer intervals trigger the consolidation of REM sleep episodes (Ocampo-Garcés & Vivaldi, J.Sleep.Res., 2002). An intermittent REM sleep deprivation protocol (IRD) was applied after two hours of Total or REM-selective sleep deprivation (TSD and RSD respectively). Seven chronically implanted rats under a 12:12 light:dark cycle were subjected after baseline days to: a) 2T2I protocol: 2 hours TSD followed by 2 hours of IRD; (b) 2R2I protocol: 2 hours of RSD followed by 2 hours of IRD. IRD consisted in the alternation, for four successive times, of 10 minutes of spontaneous sleep (REM sleep permission window), and 20 minutes of selective REM sleep deprivation. Protocols and control sessions were started at hour 4 after lights-on. Long-term REM sleep pressure was measured as the consolidation of REM episodes (success rate): the ratio of sustained REM sleep episodes to the total amount of REM sleep transitions observed at 10 minutes-REM sleep permission windows. Time course of success rate differs among protocols. Increase in success rate was delayed in 2T2I respect to 2R2I. REM sleep amount observed at the first hour of recovery doubled that of baseline and control. Our results suggest that total sleep deprivation interferes with consolidation of REM sleep episodes. FONDECYT 1061089

C138. C-ABL TYROSINE KINASE INTERACTS WITH PSD-95 AND REGULATES CO-LOCALIZATION OF SYNAPSIN I AND PSD-95 IN NEURONAL HIPPOCAMPAL CELL CULTURES. Perez de Arce K.^{1,2}, Inestrosa N.C.² and Alvarez A.¹ · ¹Cell Signaling Laboratory and ²Center for Cell Regulation and Pathology “Joaquin V. Luco” (CRCP), Millenium Institute MIFAB. Catholic University of Chile.

The mechanisms that modulate the formation of synaptic connections are pivotal to understand the processes of synaptic plasticity, because they imply remodeling of synaptic structures induced by external morphoregulatory signals. Recently, it has been suggested that c-Abl tyrosine kinase could participate in synapsis formation, since it has been observed that this kinase localizes in pre- and post-synaptic structures and is also required for post-synaptic assembly in neuromuscular junctions. However, it has not been established yet if this kinase would be directly implicated in the synaptogenic process and the c-Abl target proteins which could be mediating its function are still unknown. In this work we had established that c-Abl interacts with PSD-95, a scaffold post-synaptic protein implicated in clustering of NMDA receptor, in 18-21 DIV neuronal hippocampal cell cultures. Additionally, we had observed that this kinase inhibition increases the co-localization of synapsin I (synaptic vesicles associated protein) and PSD-95 in neuronal hippocampal cultures, which has not been previously described. These results support a putative function of c-Abl in synaptic connection formation in hippocampal neurons. Financing: Fondecyt 1040782 / FONDAP 13980001

C139. AGING AND SPATIAL MEMORY IN THE RODENT *OCTODON DEGUS* Ponce Alejandra¹; Cerpa Waldo², Inestrosa Nibaldo², Palacios Adrian¹. ¹Centro de Neurociencia de Valparaíso, Fac de Ciencias, Universidad de Valparaíso. ² Centro de Regulacion Celular y Patología "Joaquin V. Luco" e Instituto Milenio MIFAB, Universidad Católica de Chile

The *Octodon degus* aging brain show important similarities with Alzheimer landmarks diseases (AD) in human. The spatial memory performance during aging was evaluated with a behavioral alternance T-maze task, along with histochemistry methods to visualize (e.g. markers for gliosis, Thioflavin for β -amyloid plaques, β -amyloid peptide) the presence of neurodegenerative land markers find in AD. An alternance T-maze task was applied in base of 10 daily trials, during 12 consecutives days. Four experimental groups differ ring in age: 3m (G₁), 12m (G₂), 24m (G₃) and 36m (G₄) months subjects were use.. The results shows that G₁ need 8.8; G₂ 6.5 and G₃ 7.3 sessions in average to reach an 80% criteria performance, during two consecutives sessions. In G₄ only 2 of 8 subjects reach the learning performance criteria and there was an increment of β -amyloid accumulation in individuals that didn't reach the learning criteria. Other experiments show an increment of gliosis and diminution of body neurons in the hippocampus in animals older than 24 months. We suggest that our *Octodon degus* model shows excellent similarities with neurodegeneratives process and memory decay failures affecting AD patients.

FONDAP, Instituto Milenio, PBCT ACT45.

C140. HEREDITARY PARKINSONISM WITH DEMENTIA IS CAUSED BY MUTATIONS IN A LYSOSOMAL TYPE 5 P-TYPE ATPASE. Ramírez A, Heimbach A, Gründemann J, Stiller B, Dan Hampshire D, Cid LP, Goebel I, Mubaidin AF, Wriekat AL, Roeper J, Al-Din A, Hillmer AM, Karsak M, Liss B, Woods CG, Behrens MI, Kubisch C. Institute of Human Genetics, Institute for Genetics, and Center for Molecular Medicine Cologne, University of Cologne, Institute of Human Genetics and Department of Genomics and Psychiatry, Life & Brain Center, University of Bonn, Institute of Physiology, University of Marburg, Germany, Molecular Medicine Unit, University of Leeds, Department of Neurology, Pinderfields Hospital, Wakefield, Cambridge Institute for Medical Research, Cambridge, UK, Neurology Department, King Hussein Medical Centre, Amman, Jordan, Centro de Estudios Científicos (CECS), Valdivia y Departamento de Neurología and Neurocirugía, Hospital Clínico Universidad de Chile.

Parkinson's (PD) and Alzheimer's disease (AD) are a heterogeneous group of disabling neurodegenerative disorders with motor and cognitive dysfunctions. Their molecular pathophysiology is complex and still largely unknown. However, major progress has been achieved by unravelling the genetic defects in Mendelian forms of these diseases that reveal common pathophysiological pathways. In a Chilean family with an autosomal-recessive early-onset parkinsonism, with pyramidal degeneration and dementia, we excluded the known autosomal recessive PD genes/loci *Parkin*/PARK2, *DJ-1*/PARK7, and *PINK1*/PARK6 by mutation screening or linkage analysis. However, between PARK7 and PARK6 on chromosome 1p36, we found linkage in a 23 cM region bordered by microsatellite markers *D1S2736* and *D1S2644*. Phenotype analysis revealed strong resemblance to a rare juvenile onset hereditary PD of unknown cause called Kufor-Rakeb syndrome (KRS, PARK9), which has been linked to a 9 cM region on chromosome 1p36. The KRS and our locus overlap over a 6.6 cM region between *D1S436* and *D1S2644*. A candidate gene strategy was approached. Direct sequencing of all exons and splice sites of the predicted gene *ATP13A2*, revealed two loss-of-function mutations. *ATP13A2* codes for a novel member of the P-type ATPase superfamily expressed predominantly in neurons. Transient expression revealed that whereas the wild-type protein is located in the lysosome, the unstable truncated mutants are retained in the endoplasmic reticulum and are degraded by the proteasome. Our findings link a novel class of proteins with unknown function and substrate specificity to the protein-networks implicated in severe neurodegeneration and parkinsonism.

C141. HOW AMPHETAMINE DERIVATIVES INHIBIT MONOAMINE OXIDASE: INSIGHTS FROM MOLECULAR MODELING STUDIES.

Miguel Reyes-Parada^{1*}, Angélica Fierro², Mauricio Osorio-Olivares², Silvia Sepúlveda-Boza¹, Dale E. Edmondson³, Bruce K. Cassels⁴. ¹ Facultad de Ciencias Médicas, Universidad de Santiago de Chile *: mreyes@usach.cl ² Facultad de Química y Biología, Universidad de Santiago de Chile ³ Departments of Biochemistry and Chemistry, Emory University, Atlanta, USA ⁴ Facultad de Ciencias, Universidad de Chile

Compounds that inhibit monoamine oxidase (MAO, E.C. 1.4.3.4) have shown therapeutic value in a variety of conditions including affective disorders and neurodegenerative diseases. Several phenylisopropylamine derivatives (often referred to in the literature as “substituted amphetamines”) have been shown by us and others to be potent MAO inhibitors. However, little is known about the binding mode of this class of compounds, in spite of their close structural similarity with endogenous monoaminergic neurotransmitter which are the main physiological substrates of MAO. In this sense, molecular docking is a useful approach since protein-ligand configurations produced by the docking programs, allow a visual analysis of protein-ligand interactions and facilitate an intuitive interpretation and understanding of the binding process at the protein binding site.

In the present study, four *para*-alkylthioamphetamine derivatives were evaluated as MAO inhibitors using the human and rat isoforms of the enzyme. Using the crystal structures of the proteins, molecular dockings were performed in order to gain insights regarding the binding mode of these inhibitors.

All compounds were potent and selective MAO-A inhibitors although a differential rank order of potencies was observed against the enzymes from different species. Two binding modes were determined *in silico* for the interaction of substituted amphetamine derivatives and MAO-A, both of which are consistent with inhibitory properties. Our results demonstrate that some amphetamine derivatives are able to differentially inhibit MAO-A from rat and human, a behavior that can be rationalized on the basis of different binding modes to each enzyme, exhibited by the compounds.

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C142. THE EFFECT OF AGING ON LANGUAGE PROCESSING. AN EXPERIMENTAL STUDY. Bernardo Riffo. Departamento de Español. Facultad de Humanidades y Arte. Universidad de Concepción

The results of 3 psycholinguistic experiments were analysed. In those experiments participated 24 young people (20-25) and 24 elderly people (65-81), who read different kinds of sentence. The time for each word was registered in milliseconds and these data were compared with special attention to age and working memory rates of the participants. The analyses support the hypothesis that the aging process affects some cognitive mechanism (as memory) and (as a consequence of this condition) the language processing capacity.

Expression of synaptic vesicle-related proteins, Rab3A and synapsin I, in substantia nigra in a rat model of presymptomatic Parkinson's disease.

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We have demonstrated an early and dramatic increase in brain-derived neurotrophic factor (BDNF) expression in substantia nigra (SN) in a rat model of presymptomatic Parkinson's disease (PD). These changes could modify, in turn, the expression of vesicle-related proteins in SN, in order to facilitate transmitter release from remaining undamaged cells, following partial dopamine cell population disappearance. Therefore, we have studied the expression of Rab3A and synapsin I in SN of rats in a model of presymptomatic PD.

With immunohistochemical (IHC) techniques, we have detected both proteins, Rab3A and synapsin I, in SN zona reticulata. Rab3A-IR is detected in soma and neuronal processes, whereas synapsin I-IR is detected only in processes. Intrastriatal 6-hydroxydopamine (6-OH-DA) injection was used to partially damage the nigro-striatal DA pathway. After one day of 6-OH-DA injection, a bilateral decrease of Rab3A expression was found in SN. A change in the cellular distribution of Rab3A-IR in SN was also observed. No changes in synapsin I-IR were detected in SN one or four days after 6-OH-DA administration.

Our results suggest that Rab3A expression may be modified at early stages of PD, in a period in which no changes are appreciated as regard to synapsin I expression.

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C143. A TRANSGENIC MOUSE CARRYING A TRANSGENE THAT PREVENTS THE EXPRESSION OF THE TRANSCRIPTION FACTOR RFX4_V3 DISPLAYS AGENESIS OF THE SUBCOMMISSURAL ORGAN AND HYDROCEPHALUS. S. Rodríguez¹, L.F. Bátiz¹, E.M. Rodríguez¹, L.M. DeGraff², J.P. Graves², D.J. Stumpo², P.J. Blackshear² and D.C. Zeldin² ¹Instituto de Histología y Patología, Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile. ²National Institute of Environmental Health Sciences (NIEHS, NIH), USA.

The hypothesis proposed by Overholser et al. in 1954 that a dysfunction of the subcommissural organ (SCO) during ontogenetical development leads to stenosis of the Sylvius aqueduct (SA) and hydrocephalus, has gained strong support from several recent findings including immunological blockage of the SCO secretion and spontaneous and experimental mutations. Blackshear et al. (2003) have developed transgenic mice. These mice develop head swelling, a rapid neurological decline and hydrocephalus. Apparently, formation of the SCO was prevented in these transgenic mice. This possibility has led to collaboration between P. Blackshear's laboratory and ours with aim to investigate the SCO. Heterozygous and wild-type embryos (E12.5- E18.5) and postnatal mice (PN0.5-PN 30.5) were processed for immunocytochemistry. E18.5 heterozygous embryos had normal choroid plexus, pineal gland and SA, but most the SCO was missing. However, the SCO secretory cells overlying the posterior commissure did develop. PN 15.5 wild-type mice had a well developed SCO with secretory activity revealed by its strong immunoreactivity. Choroid plexus, pineal gland, SA and the ciliated ependyma lining the ventricles developed normally. As seen in E18.5 heterozygous embryos, PN 15.5 heterozygous mice lacked most part of the SCO, with only the rostral end being present and with signs of secretory activity. These mice lacked RF. The area normally occupied by the SCO was lined by ciliated ependyma. Although all other epithalamic and periventricular structures were apparently normal, these mice developed hydrocephalus. The findings indicate that (i) the subcommissural portion of the SCO is involved in the secretion and formation of RF; and (ii) the agenesis of this portion of SCO leads to absence of RF and is associated with the development of hydrocephalus. The study of the remaining animal groups, which is in progress, will lead to a better understanding of the role of SCO and RF in the pathogenesis of congenital hydrocephalus. Supported by FONDECYT 1030265 and by the Intramural Program of the NIH, NIEHS.

C144. RESPONSE TO ARGININE-VASOPRESSINE ANALOGUE CHALLENGE IN MAJOR DEPRESSIVE PATIENTS PREDICTS THE LATE RESPONSE TO VENLAFAXINE. ¹P. Rojas, ¹A. Sapag, ²V. Araya, ²R. Fritsch, ²H. Silva, ³L. Herrera, ¹J. Fiedler. ¹Facultad de Ciencias Químicas y Farmacéuticas, ²Hospital Clínico y ³Programa de Genética, Facultad de Medicina. Universidad de Chile, Hosp. ⁴Sótero del Río.

There is a link between stressful life events and development of depression. Also, neuronal atrophy and cell loss in limbic areas are observed in stress and depressive disorder. Probably these changes are consequence of a reduction in the synthesis of BDNF promoted by a sustained increase in cortisol plasma levels. This hormone imbalance is related to an over-activation of the hypothalamic-pituitary-adrenal (HPA) axis. Corticotropin releasing hormone (CRH) activates HPA axis by inducing the secretion of adrenocorticotropin hormone (ACTH), being this release potentiated by vasopressin (AVP). Negative regulation of HPA axis is mediated through the glucocorticoid receptor (GR). Antidepressant treatment normalizes HPA activity, increases GR expression and CREB phosphorylation (P-CREB). This protein regulates BDNF expression probably explaining the higher levels of serum BDNF observed in depressed patients under pharmacological therapy.

Depressive patients were treated with Venlafaxine antidepressant. Late responders to Venlafaxine, when challenged with an AVP analog, showed an augmented ACTH and cortisol secretion compared to early responder patients and healthy subjects. Early and late responder patients had increased serum BDNF after 1 week of treatment; however this effect was no longer observed in late responders. These changes were not correlated with P-CREB level variations in lymphocyte extracts. Also, GR levels were slightly increased during 2 to 3 weeks of treatment in both groups of patients. These evidences suggest that late responder patients are more sensitive to vasopressin, displaying higher levels of cortisol and ACTH. Also in these patients, the pharmacological therapy did not correlate with changes in BDNF.

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C145. SPECIFIC BANDS OF THE SPECTRUM CAN BE SUFFICIENT TO DISCRIMINATE SLANT-FROM-TEXTURE. Rosas, P.¹, Maldonado, P.¹, and Wichmann, F.A.²¹ Centro de Neurociencias Integradas, Facultad de Medicina Universidad de Chile ² Dept. Empirical Inference, Max-Planck Institute for Biological Cybernetics

A prominent monocular cue to depth is texture. There are two main hypotheses for how the visual system uses texture to perceive depth. In one case, it is argued that the visual system identify the texels (or texture primitive elements) of the stimulus and uses the deformation of the texels induced by depth as an indicator of depth. An alternate view that does not rely on texel extraction argues for a mechanism using the spectral changes within an image induced by depth. In this study, we wanted to psychophysically assess the spatial-frequency decomposition on human depth perception by means of masking. We collected data for slant-from-texture discrimination under three conditions: unmasked stimulus, stimulus masked with white noise (flat spectrum), and stimulus masked with noise whose spectrum had a band of spatial-frequency removed (notched noise). As textures, we used two synthetic types: polka-dots (composed of circles) and “leopard-skin” (built with a diffusion algorithm).

Our results show that the notched noise masks affect the slant discrimination performance in a lesser degree than the flat spectrum noise mask, in some cases yielding a performance comparable to that obtained without masking. The critical spectral band for the task was dependent on the texture type and similar across subjects. We interpret our results as suggesting that a mechanism based on the spectral changes within an image can be sufficient for performing slant-from-texture. Funded by Fondecyt Project #3050022

C146. BDNF AND ITS RECEPTOR TRKB ARE INVOLVED IN HOMEOSTATIC PLASTICITY IN THE RAT FOREBRAIN FOLLOWING SEIZURES.

Mauricio Sandoval, Rodrigo Sandoval, Estíbaliz Ampuero, Rodrigo González, Juan José Marengo, Alexies Dagnino, Ursula Wyneken Universidad de los Andes

BDNF and its receptor TrkB, a transmembrane tyrosine kinase, are involved in the pathophysiology of temporal lobe epilepsy (TLE). In acquired TLE, an initial insult triggers synaptic reorganization in the hippocampus during the period of epileptogenesis, leading to increased excitability and the generation of spontaneous seizures that propagate, i.e., epilepsy. An unresolved question is how cortical synapses resist and survive seizure activity that is initiated in the epileptic focus. At excitatory synapses, seizures induce overactivation of NMDA receptors (NMDA-Rs) leading to excessive calcium influx and excitotoxicity, i.e. neuronal damage due to glutamatergic overstimulation.

We studied the role of the neurotrophin BDNF at cortical synapses after kainic acid induced seizures, a model for temporal lobe epilepsy. We found an overall cortical decrease of TrkB levels that is associated with dendritic retraction. However, the TrkB content in a subcellular fraction containing postsynaptic densities, the postsynaptic compartment of excitatory synapses, is increased by 500%. Interestingly, TrkB in postsynaptic densities is not phosphorylated and catalytically inactive. In addition, TrkB inhibits NMDA-R mediated currents by 80%, instead of potentiating them, as it occurs in the normal brain.

Our results suggest that TrkB participates in homeostatic plasticity following seizures by inhibiting NMDA-Rs through a non-canonic mechanism that is independent of its kinase activity. Dendritic retraction as well as the inhibition of NMDA-Rs may counteract seizure propagation in the epileptic brain.

C147. ACUTE MODULATION OF SYNAPTIC ACTIVITY BY β -AMYLOID AGGREGATES INVOLVES CHANGES IN INTRACELLULAR CALCIUM HOMEOSTASIS. Sepúlveda FJ, Parodi J & Aguayo LG. Laboratory of Neurophysiology, Department of Physiology. University of Concepción.

Alzheimer's disease (AD) is associated with the appearance of β -amyloid aggregates ($A\beta_{1-40}$ and $A\beta_{1-42}$) in the central nervous system. It is believed that these aggregates are one of the principal causes of the neurodegeneration found in AD (Selkoe et al, 2003). On the other hand, recent findings suggest that intracellular calcium plays a critical role in the pathogenesis of AD (Mattson et al, 2001). We have recently found that applications (30 min) $A\beta_{1-40}$ 0.5 μ M increased, in calcium-dependent manner, the frequency of synaptic currents. Therefore, in the present study we wanted to examine the role of calcium in the acute effect of $A\beta_{1-40}$ aggregates on cultured hippocampal neurons.

Studies done in the presence of $A\beta$ aggregates using fluorescent indicators for calcium (Fluo-3) and synaptic vesicles (FM1-43) showed parallel increases in calcium transients (0.05 ± 0.01 to 0.14 ± 0.03 Hz, $p < 0.05$) and FM1-43 destaining (0.89 ± 0.03 to 0.61 ± 0.02 $\Delta F_0/F_i$ $p < 0.05$). Experiments done in the presence of cadmium (Cd^{2+} , 20 μ M), a non selective inhibitor of calcium channels, and in the absence of extracellular calcium showed that calcium is critical for $A\beta_{1-40}$ aggregates effects.

Acute applications of $A\beta_{1-40}$ aggregates (0.5, 1 y 5 μ M) produced increases in intracellular calcium, in a concentration-dependent manner. The presence of D-AP5 (50 μ M), CNQX (4 μ M) or a cocktail containing calcium channels blockers did not affect the action of $A\beta_{1-40}$ aggregates. Therefore, the present results indicate that calcium is critical for the early effects of aggregates $A\beta_{1-40}$ on synaptic transmission in brain neurons.

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C148. A COMPARATIVE DEVELOPMENTAL APPROACH OF BRAIN ASYMMETRY IN TELEOSTS.

Signore I.A., Guerrero N., Urbano H., Colombo A., Tello J., Loosli F.¹, Wittbrodt J.¹, and Concha M.L. Programa de Anatomía y Biología del Desarrollo. ICBM. Facultad de Medicina. Universidad de Chile.¹ EMBL, Heidelberg, Alemania

Comparison between related species is a successful approach to uncover conserved and divergent principles of development. Here we studied the developmental mechanisms of brain asymmetry in two teleost species: zebrafish (*Danio rerio*), a well-established model organism for the study of brain asymmetry in vertebrates, and medaka (*Oryzias latipes*). Overall, we found a common developmental pattern of brain asymmetry in both species. However, striking differences were observed in the development of asymmetric connectivity between specific brain nuclei. At early stages, the asymmetrically positioned parapineal organ projects to a dorso-posterior domain of the left habenula in both species. At later stages, parapineal projections remain dorso-posterior in zebrafish but display a turn in 90 degrees to end up in a dorso-anterior domain of the left habenula in medaka. We have begun investigating the role of habenular sub-nuclei organisation as a possible mechanism of differential parapineal connectivity in these species by cloning medaka members of the K^+ Channel Tetramerisation Domain-containing (KCTC) gene family. In zebrafish, KCTC genes such as *leftover*, *right on* and *dexter* label different habenular sub-nuclei. We are currently assessing habenular expression of these genes and investigating the relationship between domains of gene expression and parapineal projection in both species.

Funding: PBCT ACT47 and ICM P04-068-F.

C149. CHRONIC STRESS IMPAIRS THE AUDITORY CORTEX AND INCREASES DISORGANIZATION THE GROOMING IN THE RATS Terreros G.¹, Dagnino A.^{1,2}, Pancetti F.², Díaz-Véliz G.³, Wyneken U.⁴ y Aboitiz F.¹. ¹Depto. de Psiquiatría, CIM, Pontificia Universidad Católica de Chile. ²Laboratorio de Neurofisiología, CEAE, Escuela de Medicina, Universidad Católica del Norte. ³Programa de Farmacología, Facultad de Medicina, Universidad de Chile. ⁴Laboratorio de Neurociencia, Universidad de los Andes.

Stress affects the hippocampus and amygdala leading to impairment in learning and emotional responses. We have recently demonstrated that stress produces an effect in subcortical areas of the subcortical auditory system but not in the visual system. In this study we investigate the stress effects on cell morphology (Golgi) in the auditory and visual cortices. We found that chronic stress induced a significant dendritic atrophy in the basal dendrites of pyramidal neurons from layers II-III of the primary auditory cortex and in the apical dendrites of pyramidal neurons from layers V-VI of the primary auditory cortex and temporal cortices. These results were correlated with an up-regulation of the TrkB expression in the primary auditory cortex. Stress did not affect the neuronal morphology and TrkB expression in the visual cortex, and disorganization of grooming behaviour respect to control animals. We conclude that the morphologic alterations induced by stress in the auditory cortex could affect the cortical and emotional processing of the auditory stimuli. The dendritic atrophy induced by stress in the temporal cortex could affect the emotional processing of the visual stimuli. Disorganization of grooming in the stressed rats indicate increases of anxiety or fear in the stressed rats respect to controls. The stress-related morphological alterations observed in this report might also be induced by the psychosocial stress in humans and have a role in the development of stress-related disorders such as major depression and post traumatic stress disorders.

Funding/support: This study was supported by research grants Núcleo Milenio de Neurociencias Integradas and Proyecto Bicentenario de Inserción de Postdoctorados a la Academia (PSD-11).

C150. CHRONIC STRESS MODULATES PHOSPHO-CRMP-2 LEVELS IN RAT HIPPOCAMPUS WITH NO CHANGES IN MONOAMINES CONTENT IN RAT PREFRONTAL CORTEX. Ulloa JL, Castañeda P, Bravo J, Sotomayor R, Fiedler J
Laboratorio de Neurobioquímica, Facultad de Cs. Químicas y Farmacéuticas Universidad de Chile

Stress is a physiologic mechanism that makes possible an adaptative response. Nervous system (NS) responds to several stimuli modifying its synapses. However, chronic stress produces changes that impair the NS response originating pathologies like depression. It is possible that this impairment be the product of alterations in the proteins that maintain synapses, like the collapsin response protein-2 (CRMP-2). This protein belongs to semaphorine proteins family that modulates the axon pathfinding, turning it in a interesting target of study. It has been reported that the selective serotonin reuptake inhibitors (SSRI) are effective in treatment of depression, however its mechanism is still unknown. In order to investigate the effects of stress and antidepressants we used motion restraint in rats and determined the monoamine levels in prefrontal cortex and CRMP-2 levels in hippocampus.

We observed a little increase in content of serotonin (5-HT) and its metabolite, 5-hydroxyindole acetic acid (5-HIAA) only in the animals with stress and sertraline (a SSRI). In the hippocampus the CRMP-2 levels remain unaltered, but its phosphorylated form was reduced in the stress condition. These results suggest that chronic stress modifies the synaptic efficacy, probably by modulating the phosphorylated state of the CRMP-2, altering the synapse. On the other hand sertraline modifies the 5-HT and 5HIAA levels only when the stress was present. FONDECYT 104093.

C151. DIFFERENTIAL EFFECT OF TGF β 1 ON THE ERK 1/2 PATHWAYS IN HIPPOCAMPAL AND ASTROCYTE CULTURES STIMULATED WITH LPS + INF γ .

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TGF β 1 is a cytokine that modulates cellular reactivity, a trait associated to neuroprotection. Substantial evidence shows differences in the production of TGF β 1 between neuron and astrocyte cultures. However, the mechanisms explaining these differences remain unknown. Extracellular signal-regulated kinases 1 and 2 (ERK 1/2) play an important role in the synthesis of TGF β 1. We will evaluate the production of TGF β 1 in hippocampal (neuron-astrocyte) and astrocyte cultures, and its association with ERK 1/2 activity. In hippocampal and astrocyte cultures, pro-inflammatory conditions LPS + INF- γ (LI), decreased intracellular LapTGF β 1 (TGF β 1 precursor) by 40% and 25% respectively. In contrast, extracellular LapTGF β 1 increased by 60% in both cultures. Whereas TGF β bioactivity in hippocampal cultures increased by 550%, it only increased by 85% in astrocyte cultures. Previous to the increase of TGF β activity, in hippocampal cells stimulated with LI, phospho-ERK 1/2 increased by 3-3.5 fold. TGF β 1 also could self-induce its synthesis, associated with an increase of ERK 1/2 activity. Nevertheless, astrocyte cells showed a decrease of ERK 1/2 activity, that depended on the concentration of recombinant TGF β 1 they were exposed to. This modulation was inverted when exposed to conditioned media of hippocampal cultures. Our results suggest that soluble factors, secreted in response to the interaction between neurons and astrocyte, could induce stimulation of the ERK 1/2 pathway and in consequence, a greater production of TGF β 1.

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C152. CALCIUM SIGNALS IN NFAT ACTIVATION IN SKELETAL MUSCLE FIBERS.

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Mammalian skeletal muscle consists of fast and slow contracting muscle fibers. The muscle fiber type is controlled by neuronal input. It has been shown that crossing the nerves innervating fast or slow twitch fibers result in a gradual transformation of the muscles to the opposite fiber type, the same result is obtained using direct electrical stimulation that mimics the firing pattern of the motor neuron. Skeletal muscle fibers adapt to different patterns of motor nerve activity modifying the gene expression of proteins involved in specific aspect of contraction, metabolism and muscle mass (muscle plasticity). The signaling pathways regulating fiber type gene expression are beginning to be elucidated.

Skeletal muscle activity involves calcium release from internal stores which activates several calcium dependent pathways, for example, the. Calcineurin activation followed by dephosphorylation and subsequent nuclear translocation of NFATc1, has been suggested to be an important step in the signaling pathway to switch from fast to slow twitch fiber type. However, the source of calcium pool required to activate NFATc1 translocation and permanency in the nucleus has not been identified. The aim of this work is to study the contribution of the calcium pools originated from RYR or by IP3R for NFAT activation. Using a fluorescent calcium indicator and NFATc1 translocation analysis in culture mouse fibers, monitored after different protocols of electrical stimulation in the presence or absence of 50 uM Ryanodine (RyR inhibitor) or 50 uM Xestospongine C (IP3R inhibitor), we determined that RyR-mediated calcium release is playing a role in NFATc1 translocation.

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C153. AICD/C-ABL/FE65 COMPLEX MEDIATES GENIC TRANSCRIPTION DEPENDENT ON C-ABL KINASE AND γ -SECRETASE ACTIVITIES. Vázquez, M.C.^{1,2}, Alvarez, A.R.¹. & Inestrosa, N.C.^{1,2}. ¹Cell Signaling Laboratory, Cellular and Molecular Biology Department and ²Center for Cell Regulation and Pathology “Joaquín V. Luco” (CRCP), Millennium Institute MIFAB, Biological Sciences Faculty, P. Catholic University of Chile.

γ -secretase dependent processing of APP releases an intracellular fragment named AICD, which has been implicated on gene transcription modulation. However, it is still unknown the mechanisms that regulate AICD dependent transcription and which are *in vivo* target genes. It has been showed that c-Abl and Fe65 could interact with APP C-terminal domain.

In order to study the AICD dependent transcription we used Neuro2a-human APP clones. We observed that these clones express high levels of AICD fragment and also a consistent increase in Neprilysin expression levels, a putative AICD target gene. In other hand, we performed co-immunoprecipitation and immunofluorescence assays of their components, in conditions of stimulation or inhibition of c-Abl kinase and γ -secretase inhibitors. Recent reference indicates that p53 would be a target gene for AICD. In this context, we studied the expression of p73, a p53 homolog, by transiently co-transfection of luciferase reporter constructions for promoter regions of TA (*full-length*) and Δ N p73 isoforms, observing an increase in proapoptotic isoform expression.

Our results suggest that TA p73 could be a new AICD target gene and, AICD/c-Abl/Fe65 complex formation could modulates, on Neuro2A clones, the transcriptional activity dependent on APP processing mediated by γ -secretase.

Financing: FONDECYT Project 1040782, FONDAP-MIFAB-13980001.

C154. AUDITORY FREQUENCY DIFFERENCE LIMEN IN CHINCHILLAS María José Velásquez, Katherina Villa, Beatriz Villanueva, Paul H. Delano and Luis Robles. Programa de Fisiología y Biofísica, ICBM, Facultad de Medicina, Universidad de Chile.

Although chinchillas (*Chinchilla laniger*) have been widely used in psychoacoustic studies, their frequency-difference limen (just noticeable difference between two tones of different frequencies) is still controversial. We trained three chinchillas in an auditory frequency two-choice discrimination task. Each chinchilla was trained every day for seven months, using reference tones of different frequencies (450, 1000, 2000 Hz) at about 70 dB sound pressure level. Operant cage, stimuli presentation and data acquisition were controlled by a custom made digital interface and computer program. Behavioral performance was assessed by measuring: correct and incorrect responses, latencies (1 ms resolution) and omissions. At the beginning of training, target tones differed by about 1 octave from reference tones. When chinchillas reached an accuracy of discrimination ($[\text{correct responses} / (\text{correct} + \text{incorrect responses})] * 100$) above 70 %, we reduced the frequency difference between reference and target tones. We determined the frequency-difference limen using as criterion the minimum frequency difference between target and reference tone at which chinchillas had an accuracy above 70%. The Weber ratios ($[(\text{target frequency} - \text{reference frequency}) / \text{reference frequency}] * 100$) corresponding to the observed limens varied between 4-5.5 %. These results show that auditory frequency-discrimination limens in chinchilla are smaller than previously reported in similar discrimination tasks and are closer to those of humans.

Supported by Fundación Puelma.

C155. VISUAL SENSITIVITY IN THE SUBTERRANEAN RODENT *CTENOMYS MAGELLANICUS* Vielma A¹, Bozinovic F², Palacios AG¹. ¹ Centro de Neurociencias de Valparaíso, Fac de Ciencias, Universidad de Valparaíso. ² CASEB. Dept. Ecología, Universidad Católica de Chile.

Subterranean mammals are normally considered to have reduced vision as a convergent adaptation to their underground microhabitat. The *Ctenomys* genus is exclusively subterranean; however some species display diurnal habits and others nocturnal. We have studied the prospect of vision in the South America subterranean *Ctenomys magellanicus* (*Tuco-tuco*), the southernmost species of the group living in Tierra del Fuego. We report here the study of the optical and spectral properties of the eye, through the electroretinogram (ERG), the electrical light response of the retina under different light adaptations conditions. In the range of 300-700 nm the ERG of *Ctenomys magellanicus* (n=5) shows two regions of high spectral sensitivity between 460 and 520 nm (blue-green) and 340 nm (UV). The eye ocular media shows a significant level of absorption, however light transmittance is possible from 320-700 nm. Those results suggest a well developed diurnal or photopic visual system in Tuco-tuco. The behavioral, ecological and evolutionary meaning of such diurnal retinal specialization is under further experiments.

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C156. THE VISUAL SYSTEM OF CHILEAN ROCKY-SHORE MARINE FISHES: *AUCHENIONCHUS MICROCIRRHS* AND *SCARTICHTYS VIRIDIS*. Vielma A¹, Herrera G¹, Pizarro J¹, Ardiles AO¹, Rojas JM², Schmachtenberg O¹, Palacios AG¹. ¹Centro de Neurociencia, Facultad de Ciencias, Universidad de Valparaíso ²CASEB, Departamento de Ecología, Facultad de Ciencias Biológicas, Universidad Católica de Chile

Coastal fishes are confronted to a diversity of microhabitats, including variations in light distribution. Visual signals are important for interspecies communication, depredation, and sexual behavior. We measured body reflectance under different light adaptive conditions, as well as the reflectance spectra of objects belonging to the microhabitat of these species. Furthermore, we studied the eye response to different wavelengths and intensities by electroretinogram (ERG) and the retinal cells morphology in two representative rocky-shore marine fishes, *Scartichthys viridis* (Blenniidae), a herbivore, and *Auchenionchus microcirrhys* (Lambrisomidae) a carnivore. The spectral sensitivity for both species shows a maximum of sensitivity (λ_{max}) between 460 and 560 nm, and lower but significant responses in the ultraviolet (UV) region. In addition, the ocular transmission (spectacle, cornea and lens) presents important light absorption under 400 nm, suggesting UV protection. On the other hand, body reflectance is dominant in the UV region, with a λ_{max} near the 350 nm. These results suggest a visual system well adapted to photopic conditions, in which the UV light could play an important role in the visual behavior of these fishes within their microhabitat.

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C157. THE CEREBROSPINAL FLUID OF THE HYDROCEPHALIC HTX RAT DISPLAYS ABNORMAL FORMS AND CONCENTRATIONS OF THE PROTEINS SECRETED BY THE SUBCOMMISSURAL ORGAN. Vio K, Ortloff A, Rodríguez EM.

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The subcommissural organ (SCO) is a brain gland located at the entrance of the Sylvius aqueduct (SA); it releases glycoproteins to the cerebrospinal fluid (CSF) flowing through SA. A evidence indicates that SCO is involved in the pathogenesis of hydrocephalus. A colony of HTx rats developing hydrocephalus is being bred in our lab. This has allowed, for the first time, to investigate the CSF-soluble proteins secreted by the SCO of normal Sprague Dalwey rat (SD) and hydrocephalic HTx rats, at different stages of development. The CSF samples were processed for immunoblotting using antibodies against secretory proteins of the SCO. Results obtained were: (i) CSF collected from the cisterna magna of E18 embryos displayed several immunoreactive bands ranging between 25 and 190 kDa. These glycoproteins were also found at PN1 and PN7; at PN30, only three of these compounds (190, 63, 50 kDa) were detected. (ii) The ventricular CSF of HTx hydrocephalic rats (PN1, PN7) displayed one different pattern of secretory proteins than the corresponding CSF of the normal HTx rats. Furthermore, the CSF concentration of some of these proteins was higher in the hydrocephalic CSF. (iii) When ventricular and cisternal CSF samples were obtained from the same hydrocephalic rat, it became clear the different pattern of secretory proteins present in both CSF compartment. The presence study in the hydrocephalic CSF of abnormal forms and quantity of SCO secretory proteins, even at fetal stages, suggests that: (i) there is a defect in the intracellular and/or post-release processing of the SCO secretory proteins; (ii) this is a primary defect of the SCO being expressed prior to onset of hydrocephalus; (iii) obliteration of SA prevents the SCO secretions to reach the subarachnoidal CSF and the pial surface of the developing cerebral cortex. This latter abnormality might be related to the abnormal corticogenesis reported for the HTx rat.

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C158. INHIBITORY EFFECTS OF B AMYLOID AGGREGATES LABELLED WITH GOLD NANOPARTICLES ON SYNAPTIC TRANSMISSION. ¹Wandersleben, G., ¹Parodi, J., ²Boussert, S., ³Kogan, MJ, ¹Roa, J., ¹Opazo, C., ¹Aguayo, L.G. ¹Departamento de Fisiología, ²Parc Cientific de Barcelona (Spain), ³Departamento de Química Farmacológica y Toxicológica, ¹Universidad de Concepción, ²Universidad de Chile.

The Alzheimer's disease (AD) is a cognitive disorder caused by the accumulation of senile plaques and neurofibrillary tangles. The histopatologic landmark of AD is the β amyloid ($A\beta$) peptide, which was recently showed to be deposited in the synapse.

In this study, we have used a methodology to mark $A\beta$ aggregates and to determinate its ultrastructural localization. Monomers of $A\beta$ were conjugated to gold (Au) nanoparticles (10 nm) forming the $A\beta$ Au conjugates and mixed with control $A\beta$ monomers. These mixtures underwent an aggregation protocol consisting of different unmarked/marked monomer ratios (1:2, 1:3 and 2:3). The result was the generation of complexes (F-Au) between the conjugates $A\beta$ -Au and the amyloid fibres. Following this protocol, several samples were photographed under electronic microscopy. Analysis of the length, revealed the presence of two main species formed by $A\beta$ -Au and $A\beta$ (100-200 nm and 600-800 nm). In addition, the control $A\beta$ fibres and F-Au species presented a main group having a length near 800 nm. Treatment of neurons with $A\beta$ and $A\beta$ -Au showed that miniature synaptic currents were reduced from 1.75 ± 0.1 Hz to 0.6 ± 0.05 Hz and to 0.8 ± 0.12 Hz, respectively. The presence of SV2, a marker for synaptic vesicle, was also reduced by treatment with $A\beta$ and $A\beta$ -Au. Experiments using cultured neurons to localize $A\beta$ -Au are now under way.

Therefore, these studies will allow to localize $A\beta$ -Au in the neuronal ultrastructure and relate its localization to the neurotoxic effects of the peptide in synaptic transmission.

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C159. AMYLOID- β OLIGOMERS DEPRESSED SYNAPTIC TRANSMISSION: POSTSYNAPTIC SITE PARTICIPATION. Cerpa W¹, Molina C², Bonansco C², e Inestrosa NC¹.

¹ Centro de Regulación Celular y Patología “Joaquín V. Luco” (CRCP), MIFAB, Facultad de Ciencias Biológicas, P. Universidad Católica de Chile, Santiago, Chile ² Departamento de Fisiología, Facultad de Ciencias, Universidad de Valparaíso, Valparaíso, Chile. Alzheimer’s Disease (AD) is a progressive neurodegenerative disorder which major molecular characteristic is the presence of amyloid- β (A β) deposits. Synaptic dysfunction is increasingly viewed as an early AD manifestation, but the cellular mechanism by which A β affects synapses remains unclear. It has been shown that A β oligomers target synapses in cultured rat hippocampal neurons, suggesting that they play a role in the regulation of synaptic function. We study the glutamatergic synaptic transmission of the Schaffer collateral excitatory synapses onto CA1 pyramidal cells recorded in 3-4 week old rat hippocampal slices. We analyze the amplitude of excitatory postsynaptic currents (EPSCs) and paired-pulse facilitation (PPF). Field recording of CA1 pyramidal cells treated with A β fibrils did not show any effect on EPSCs amplitude or PPF, under our experimental conditions. Similar results were observed with intracellular recording. However, when the A β oligomers were used, a clear decrease in the evoked response over 50% recording was observed, and no change in the PPF was found with the A β oligomers. The analysis of the facilitation ratios suggest that A β oligomers effect is produced by a mechanism depending of the postsynaptic site. A postsynaptic effect over glutamate receptors may be related to desensitization or alternatively to the removal of receptors from the postsynaptic membrane. We think the second possibility is more likely, because A β oligomers treatment reduces PSD-95, a macromolecule primary involved with postsynaptic glutamate receptors. Taken together, our results suggest that A β oligomers decrease the amplitude of synaptic responses by affecting the postsynaptic region.

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