

S101. REGULATION OF EXCITATORY NEUROTRANSMISSION BY NEUROTROPHINS. Ursula Wyneken, Universidad de los Andes

The neurotrophin BDNF, through its cognate receptor TrkB, regulates synaptic excitatory neurotransmission that is relevant to learning and memory, but also to the pathophysiology of depression. However, the underlying mechanisms are poorly understood. In the short term, BDNF regulates glutamate-receptor mediated ionic currents, whereas long term effects are mediated by the endocytosis of BDNF/TrkB.

Our experiments indicate that rapid effects of BDNF are also mediated by the p75^{NTR} neurotrophin receptor, that is activated by all neurotrophins and their precursors. p75^{NTR} is anchored to the excitatory postsynaptic density through an interaction with the scaffolding protein PSD-95, where it acutely and reversibly inhibits NMDA receptor (NMDA-R) currents, opposing the effect of TrkB, that potentiates NMDA-Rs. This system provides bidirectional control of NMDA-Rs that may be relevant to synaptic plasticity. In addition, we have studied long term effects of BDNF/TrkB on excitatory neurotransmission following antidepressant treatments, that stimulate BDNF synthesis. Antidepressants lead to a delayed decrease of total TrkB in postsynaptic densities, but an increase of phosphorylated (i.e. activated) TrkB in intracellular membrane compartments. Our hypothesis is that antidepressants activate synaptic release and endocytosis of BDNF/TrkB with a slow time course, explaining the delayed therapeutic effects of antidepressants. This is supported by biotinylation experiments in cortical synaptosomes, as well as by the isolation of endosomal compartments that carry BDNF/TrkB. Our results provide essential clues on antidepressant-mediated effects of BDNF in the neocortex. The multiplicity of mechanisms activated by BDNF at excitatory synapses may explain why this neurotrophin has been related to such diverse conditions like synaptic plasticity, depression and epilepsy.

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S102. ABSENCE OF HOMEOSTATIC SYNAPTIC PLASTICITY AFTER CHRONIC STRYCHNINE IN DEVELOPING CULTURED MOUSE SPINAL NEURONS.

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Cortical and hippocampal neurons in culture form abundant excitatory, AMPA-mediated networks that contribute to spontaneous synaptic activity and display homeostatic plasticity after chronic CNQX. On the other hand, cortical networks exposed to bicuculline, a GABA_A receptor blocker, responded with an acute increase in activity that returned to control levels after 2 days. In this study, we describe a novel form of anti-homeostatic plasticity produced after culturing spinal neurons with strychnine, but not bicuculline or 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX). Strychnine caused a large increase in network excitability, detected as spontaneous synaptic currents and calcium transients. The calcium transients were associated with action potential firing and activation of γ -aminobutyric acid (GABA_A) and AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors since they were blocked by tetrodotoxin (TTX), bicuculline and CNQX. After chronic blockade of GlyRs, the frequency of synaptic transmission showed a significant enhancement demonstrating the phenomenon of anti-homeostatic plasticity. Spontaneous inhibitory glycinergic currents (sIPSCs) in treated cells showed a 4-fold increase in frequency (from 0.55 to 2.4 Hz) and a 184% increase in average peak amplitude compared to control. Furthermore, the augmentation in excitability accelerated the decay time constant of mIPSCs. Strychnine caused an increase in GlyR current density, without changes in the apparent affinity. These findings support the idea of a postsynaptic action that partly explains the increase in synaptic transmission. This phenomenon of synaptic plasticity was blocked by TTX, an antibody against brain-derived neurotrophic factor (BDNF) and K252a suggesting the involvement of the neuronal activity-dependent BDNF-TrkB signaling pathway. These results show that the properties of GlyRs are regulated by the degree of neuronal activity in the developing network.

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S103. TRAFFICKING AND FUNCTION OF NMDA-RECEPTORS Andres Barriá

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The calcium permeant NMDA-type glutamate receptor (NMDA-R) plays a critical role during induction of synaptic plasticity, brain development, and various neurological and psychiatric pathologies. The receptor is an obligated heteromultimer composed of NR1 subunits and one or more of the NR2 subunits (A-D). NR2 subunits control trafficking of the receptor into synapses and can regulate synaptic function by conferring different electrophysiological properties to the channel and interacting with scaffolding and signaling proteins in a subunit specific manner. During development the subunit composition of NMDA-Rs changes from NR2B-containing receptors to NR2A-containing receptors in a process that requires synaptic activity. The role and mechanisms of NR2 subunits in controlling synaptic incorporation of NMDA-Rs and regulation of synaptic plasticity will be discussed.

S104. BIOPHYSICAL PROPERTIES OF HEMICHANNELS. Michael V.L. Bennett. Dept. of Neuroscience, Albert Einstein College of Medicine, NY, USA.

Gap junction hemichannels are hexamers formed in intracellular membranes and then transported in vesicles that are inserted into surface membrane. They diffuse in the surface to dock with hemichannels in an apposed membrane to form cell-cell channels. Surface but nonjunctional hemichannels open rarely, as would be expected for large non-selective channels and the requirement for cell homeostasis, but opening is increased by various treatments including low divalent ion solutions, inside positive potentials and metabolic inhibition ("chemical ischemia"). Hemichannel opening is identified by recording of single channel conductance about twice that of the cell-cell channels and by increase in dye uptake that is restricted to molecules that permeate gap junctions. If cell-cell channels have a substate, that substate can be recorded in hemichannels. Finally, differing time courses of gating between states in cell-cell channels are observed in corresponding gating transitions in hemichannels. Both hemichannel opening and dye uptake can be prevented by gap junction blockers (of varying specificity), which generally are membrane permeant, and La^{3+} when applied to the extracellular side. Low pH also closes hemichannels, and the binding site is on the intracellular side of the "pH gate". Certain binding sites relevant to gating, such as C-terminal cysteines and phosphorylatable serines, are intracellular. Data of these kinds, obtained for a number of connexins, leave no doubt about the reality of hemichannel opening. Ongoing research addresses the role of hemichannel opening under normal conditions and the signaling cascades and covalent modifications that modulate it in both physiological and pathological conditions.

S105. WHO IS A GOOD CANDIDATE FOR THE SURGERY IN PARKINSON DISEASE? Pedro Chaná, Centro de Trastornos del Movimiento, Universidad de Santiago

Numerous factors need to be taken into account in deciding whether a patient with Parkinson's disease (PD) is a candidate for surgery. Patient age, presence of other comorbid disorders, neuropsychological and neuropsychiatry status need to be considered. Other factors related to the PD, as motor status, gait dysfunction, previous medical therapies and adverse effects, diagnosis of Parkinsonism, should be considered.

Main preoperative issues:

1. Levodopa response is the best predictor a good response to surgery.
 2. Dementia should be considered a contraindication for surgery
 3.  Mild cognitive impairment and executive dysfunction in PD might predict incident dementia.
 4. Surgery is directed at treating motor disability, duration and severity of either levodopa-responsive off period akinesia, rigidity, tremor, dystonia and “on” period dyskinesias, or a combination of these.
 5. Non-PD Parkinsonism is generally not sufficiently efficacious to justify surgery.
- For better result in PD surgery is necessary a strong collaboration between neurology and neurosurgery. The neurologist is usually responsible for the selection of patients and the postoperative management of the patient. The neurosurgeon is responsible the perioperative care of the patient, and the management of surgical complications.
- The first step to good result is a best selection.

S106. STRESS EFFECTS ON FEAR PROCESSING IN THE BRAIN AND ITS RELATION WITH THE DEVELOPMENT OF DEPRESSION.

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Stress impairs the limbic system affecting learning and emotional responses. In this study we have investigated whether chronic immobilization stress produces an effect in the acoustic startle response and escape behaviour (unconditioned responses) and the neuronal morphology of the auditory-receiving thalamic nuclei medial geniculate (MG) and posterior (PO), as seen in Golgi preparations. We have found chronic stress did not affect the PO, while the same stress protocol induced a significant dendritic atrophy in the MG which was correlated with an increase of the acoustic startle response and escape behaviour. Furthermore, in the immunohistochemical studies we have found the neurotrophic receptor TrkB is up-regulated by stress in the MG but not in the PO. These results were correlated with the fact that the footshock by itself increased freezing throughout active avoidance conditioning. Our results demonstrate that stress decreased the level of fear threshold activation in the brain and did not affect the processing of unconditioned sensory stimulus. Our results also suggest that freezing to conditioned tone could be processed in part independently of the MG during fear conditioning. TrkB up-regulation in the MG may be a compensatory adaptation to stress. Comparable alterations could be induced by the psychosocial stress in humans and have a role in the development of depression. 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).

S107. ATTENTION MODULATES CORTEX AND COCHLEAR AUDITORY RESPONSES IN MAMMALS ; A POSSIBLE FUNCTION OF THE EFFERENT SYSTEM ?*Paul H. Délano^{1,2}, Pedro E. Maldonado^{1,2} and Luis Robles¹.

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The auditory efferent system has unique anatomical characteristics compared to other sensorial modalities, but its function remains uncertain. One of the functions attributed to this system is to participate in tasks that involve selective attention. The primary objective of this thesis was to study attentional modulations on the neural activity at central and peripheral levels in the mammalian auditory system. We used a chinchilla model of attention based on a two-choice discrimination task, using an intermodal and an intramodal paradigm. In order to assess the neural activity, we performed electrophysiological recordings while the animals discriminated target stimuli (visual or auditory) in the attentional task. We used tetrodes placed in the auditory cortex to record the unitary neuronal activity. At the peripheral level, auditory-nerve compound action potentials (CAP) and cochlear microphonic potentials (CM) were measured with electrodes chronically implanted in the round window of the chinchillas. During the period of visual attention, we found a reduction in amplitude of the auditory-nerve CAP in all studied animals, and a CM increase concomitant to the CAP reduction in two of them. In the auditory cortex, a total of 181 units were recorded in awake and behaving chinchillas. We found that, during the period of higher attentional load, 9.4% of the recorded units had a change in discharge rate, whereas 18.2% of the units showed a change in mean first-spike latency to the auditory stimulus. We concluded that: (1) the responses of about 20% of the units recorded from the auditory cortex of the awake chinchilla can be modulated during the presentation of a visual stimulus in a task that requires attention. (2) The afferent responses from the auditory nerve can be modulated during selective attention to a visual stimulus, and the magnitude of this modulation depends on the attentional load. (3) Selective attention can modulate auditory afferent responses even at the level of sensory transduction, modifying the amplitude of the CM generated by the outer hair cells. (4) The concomitant increase of the CM during the reduction of the CAP suggests that this effect is mediated through the activation of olivocochlear efferent fibers. These results show for the first time in awake animals, that the auditory afferent activity can be modulated, even at the level of sensory transduction, during a task that requires selective attention to a visual cue.

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S108. THE *WNT* SIGNALING PATHWAY AND ITS RELEVANCE TO ALZHEIMER DISEASE. Nibaldo C. Inestrosa. Centro de Regulación Celular y Patología “Joaquín V. Luco” (CRCP), MIFAB, Facultad de Ciencias Biológicas, P. Universidad Católica de Chile.

Previous studies from our lab indicated that the activation of *Wnt* signaling prevents A β neurotoxicity in hippocampal neurons. We have shown that compounds that mimic this signaling cascade may be putative candidates for therapeutic intervention in Alzheimer's patients. We studied the role of the *Wnt* signaling pathway and its implications as a therapeutic target in Alzheimer's Disease. Using agonists of the α_7 nicotinic and m $_1$ muscarinic receptors, PPAR- γ , PPAR- α and PKC we showed that they prevented A β fibril neurotoxicity by a mechanism that implies a cross-talk with the *Wnt* pathway. We have observed that two different *Wnt* ligands control synaptic structure and function. *Wnt-7a* (a canonical ligand) stimulates synaptic vesicle clustering and increases synaptic vesicle recycling in rat hippocampal neurons. On the other hand, *Wnt-5a* (a non-canonical ligand) regulates postsynaptic structure and protein localization, directing the clustering of PSD-95, which in turn, aggregates Frizzled 2 and NMDA receptors. When hippocampal neurons were exposed to A β oligomers a specific decrease of PSD-95 and NMDA receptors was observed, which was prevented by *Wnt-5a*.

These data suggest that synapse formation requires the participation of two different *Wnt* ligands, one for the presynaptic and the other for the postsynaptic compartment; more interesting, the synaptic target of A β oligomers is located at the postsynaptic region. Funded by FONDAP N° 13980001 and MIFAB.

S109. CURRENT CHALLENGES IN THE TREATMENT OF PARKINSON'S DISEASE Carlos Juri C. Departamento de Neurología. Escuela de Medicina. Pontificia Universidad Católica de Chile.

Parkinson's disease (PD) is a neurodegenerative disorder characterized mainly for the death of dopaminergic neurons in the substantia nigra pars compacta. Actual evidence suggests that the onset of neuronal death probably began between 5 and 7 years before symptoms onset. This produces a significant delay in the use of potential neuroprotective therapies.

The actual treatment for the PD is based on dopaminergic replacement therapy. Initially this treatment is very successful; however after 5 years with levodopa, almost 50% of these patients will develop motor complications, mainly in the form of motor fluctuations and dyskinesias.

Both, the presymptomatic diagnosis and the development of motor complications with levodopa therapy, are two of the principal challenges in the study of the PD. In this presentation both situations will be considered and one experimental model for the study of the dyskinesias will be shown.

S110. CELLULAR BASES OF THE ELECTROPHYSIOLOGICAL PROPERTIES OF THE FAST ELECTROSENSORY PATHWAY OF *GYMNOTUS CARAPO*.

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Unveiling the relationship between neural structure and the computational role of neurons is a key challenge in the comprehension of brain function. We addressed this question in a relatively simple neural system, the fast electrosensory pathway of the electric fish *Gymnotus carapo*. Autogenerated pulsatile electric fields generate electric images when interacting with nearby objects. The cells of the fast electrosensory pathway are recruited according to the local field intensity. In this way images are codified as the latency between the spikes of different neurons at the same level of the path. Characteristically, this pathway presents a low responsiveness window after been activated by a single pulse. This phenomenon is implemented at the second order spherical neurons. We used *in vitro* whole cell patch recordings of these neurons to study the cellular mechanisms underlying this phenomenon. We found: a) a single spike at the beginning of a current step regardless of its duration or amplitude, and b) inward and outward rectifications and a prolonged refractory period. Outward rectification and single spike generation can be explained by the activation of a low threshold, non inactivating, potassium current which stabilizes membrane potential near resting values. Slow deactivation of this current might be responsible for the prolonged refractory period. Treatment with 4-aminopiridine partially cancelled the outward rectification and also reduced the long refractory period. However, it does not always turn the onset into a repetitive firing pattern, suggesting the existence of other factors. Given that the electric organ discharge intervals are slightly longer than the duration of the low responsiveness window, we propose that the above cellular mechanism allows the streaming of auto-generated electric images.

S111. HOW METABOLIC INHIBITION INCREASES MEMBRANE PERMEATION THROUGH CX43 HEMICHANNELS M. A. Retamal^{1,2}, K. Schalper^{1,2}, K. Shoji^{1,2}, and J.C. Sáez^{1,2}. ¹Depto-Ciencias Fisiológicas, Pontificia Univ. Católica de Chile and ²Núcleo Milenio Inmunología e Inmunoterapia, Santiago, Chile.

Connexin-based hemichannels (HCs) form cell-cell channels at gap junctions, but are also found in non-junctional membrane where their open probability is low. Metabolic inhibition (MI) increases non-junctional HC opening by increasing the number of surface HCs and their open probability; dithiothreitol (DTT) prevents the latter. To analyze these processes we used HeLa cells transfected with wild-type Cx43 (Cx43-WT), Cx43 truncated at AA 257 (Cx43-257stop) to remove cytoplasmic cysteines, or Cx45-WT, which lacks cytoplasmic cysteines. Surface Cx levels were evaluated by sulfo-NHS-SS-biotin labelling, avidin bead precipitation, and Western blotting. Time lapse imaging of ethidium bromide uptake measured HC permeation. All transfectants exhibited comparable basal uptake greater than that by parental cells. MI (iodoacetate + antimycin A for 60 min) increased surface levels of Cxs and dye uptake in all transfectants but not in parental cells. Increases in surface expression and dye uptake were prevented by BAPTA-AM applied before MI and uptake was prevented by La³⁺, a hemichannel blocker, applied shortly before measurement. DTT applied 30 min after MI blocked MI-induced dye uptake in Cx43-WT but not in Cx43-257stop or Cx45-WT transfectants. We conclude that cytoplasmic cysteines and most of the Cx43 C-terminal are not required for MI-induced increase in surface levels of Cx43 and Cx45; in contrast, cysteine residues are required for block of dye uptake by DTT.

S112. MESENCHYMAL STEM CELLS AND PARKINSON'S DISEASE. Francisco Javier Rubio, Rodrigo Somoza and Paulette Conget. Instituto de Ciencias, Facultad de Medicina, Clínica Alemana-Universidad del Desarrollo, Santiago.Chile.

At the cellular level Parkinson's disease (PD) is characterized by the degeneration of nigrostriatal dopaminergic neurons. Cell replacement therapy for PD is based on restoration of dopaminergic neurotransmission in the striatum. Initially, dopaminergic neurons derived from fetal tissue were used for this purpose. Due to the large quantity of tissue required one approach has been the in vitro generation of large numbers of neurons derived from embryonic stem cells (ESC) and neural progenitor cells or neural stem cells (NSC). However, the origin of the donor tissue (embryon or fetus) poses various ethical concerns and constraints. Therefore, intense efforts are put into research on non-neural cells, such as multipotent mesenchymal stem cells (MSC) derived from adult bone marrow. Importantly, MSC can be expanded in vitro and have the ability to differentiate into cell types of mesenchymal lineage but with the plasticity to generate neural cells. In addition, MSC have hypoimmunogenic and immunosuppressive properties that make them ideal for allogenic cellular therapy.

Our work focuses on in vitro protocols to generate immature neural cells derived from human MSC. By exposition of MSC clones to NSC-expansion medium, we have been trying to characterize the events which stand behind the apparent neural plasticity of MSC. Our findings suggest that adult bone marrow could be an alternative source of neural progenitor-like cells to be eventually used in therapeutic applications for PD.

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S113. OPPOSITE REGULATION OF HEMICHANNELS AND GAP JUNCTION CHANNELS BY HIGH GLUCOSE CONCENTRATIONS. Sáez J.C. Vega N, Sáez P.J., Velarde MV. Departamento de Ciencias Fisiológicas, Pontificia Universidad Católica de Chile, Santiago, Chile.

Rat cortical astrocytes maintained in culture express hemichannels (HCs) and gap junction channels (GJs). Under resting conditions, Cx43 communicate the cytoplasm of cells in contact and HCs remain preferentially inactive. HCs are located in the cellular surface and opening of most HCs so far studied can be promoted with positive membrane potentials or low concentration of extracellular divalent cations. High [glucose] are known to reduce gap junctional communication in several cell types but its possible effect in astrocytes remains unknown. We studied the effects of glucose on the functional state of GJs (dye coupling, Lucifer yellow) and HCs (time lapse measurements of ethidium bromide uptake, EtBr) expressed by cultured rat cortical astrocytes. Astrocytes were cultured in medium containing 5, 16 or 25mM glucose for 72h. Levels of connexin43 forming HCs in the cellular surface were measured by biotinylation of surface proteins, pull-down and immunoblotting. High [glucose] (25mM), but not mannitol (25mM) or low [glucose] (5mM), increased the rate of EtBr uptake ~3.5 folds which was not blocked by dithiothreitol (DTT). On the contrary, DTT caused a further increase in EtBr uptake, suggesting the existence of a gating mechanism that activates HCs already present in the membrane. Accordingly, the increase in dye uptake was not paralleled by an increase in levels of HCs in the cellular surface. The cell-cell communication mediated by GJs dropped ~30% in cells cultured in high [glucose]. These changes in the activity of connexin-based channels might enhance the cellular susceptibility to ischemia-reperfusion during hyperglycemia.

S114. FGF-1 INCREASES MEMBRANE PERMEABILITY THROUGH CX43-HEMICHANNELS: INVOLVEMENT OF INTRACELLULAR Ca^{2+} AND CX43 C-TERMINUS. K.A. Schalper^{1,2}, M.A. Retamal^{1,2}, K.F. Shoji^{1,2}, A.D. Martínez³ y J.C. Sáez^{1,2}. ¹Depto.Ciencias Fisiológicas, Pontificia Universidad Católica de Chile. ²Núcleo Milenio Inmunología e Inmunoterapia. ³Instituto de Neurociencias, Universidad de Valparaíso.

Connexin43 hemichannels (Cx43-HCs) are high conductance plasma membrane pathways with ubiquitous expression that are preferentially closed under resting conditions. In the present study the effect of FGF-1 on membrane permeability mediated by Cx43-HCs and the involvement of $[Ca^{2+}]_i$ and connexin43 C-terminus was studied. We used HeLa cells transfected with wild type Cx26 (HeLa-Cx26WT), Cx45 (HeLa-Cx45WT), Cx43 (HeLa-Cx43WT) or Cx43 truncated in its C-terminus at aa 257 (HeLa-Cx43 Δ 257). Cells were treated for 1-24h with FGF-1 in the presence of extracellular Ca^{2+} and Mg^{2+} . Membrane permeability was measured by time-lapse imaging of ethidium bromide (EtdBr) uptake. The amount of HCs at the cell surface was evaluated by protein biotinylation and immunoblotting. The $[Ca^{2+}]_i$ was measured using Fura2-AM. FGF-1 induced maximal increase in rate of EtdBr uptake at 7h post-treatment. At this time, $[Ca^{2+}]_i$ and levels of Cx-HCs also increased in HeLa-Cx43WT and HeLa-Cx45WT. In HeLa-Cx43WT, the FGF-1 effect was prevented with BAPTA-AM and mimicked by 4-br-A23187. Thus, FGF-1 increases membrane permeability mediated by Cx43-HCs in the presence of extracellular divalent cations which is due, at least in part, to an increase in levels of HCs in the cellular surface. The Cx43-HCs response to FGF-1 is associated to rises in $[Ca^{2+}]_i$ which seems to requires the C-terminus of the protein subunit.

S115. HISTAMINERGIC TUBEROMAMMILLARY NUCLEUS IS ESSENTIAL FOR THE EXPRESSION OF AROUSAL DURING THE APPETITIVE PHASE OF FEEDING. Valdés J.L., Riveros ME. and Torrealba F. Departamento de Fisiología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile

The motivated behaviors where the individual directs efforts to get a reward like food, water or sexual mate, depend on an increase in the arousal state. Spontaneous arousal is commanded by the concerted activity of the ascending arousal system (AAS), which include orexinergic, noradrenergic, cholinergic, serotonergic and histaminergic cells groups. Growing evidence indicate that histamine is essential to display arousal during motivated behavior.

Here we demonstrate that during the appetitive phase of feeding in rats there is an increase of behavioral (locomotion) and vegetative (body core temperature) arousal together with an earlier activation of the histaminergic tuberomammillary nucleus respect to other components of AAS, measured by Fos expression, and a fast hypothalamic histamine release. Additionally a cortical arousal increase was observed, measured by cortical desynchronization (EEG) and Fos expression in the cerebral cortex.

Cell specific lesions directed to histaminergic neurons abolished the behavioral and vegetative arousal and the activation of the AAS and thermoregulatory nuclei during appetitive phase of feeding. In the same way, lesion of the infralimbic cortex, a principal input to the tuberomammillary nucleus and a region that was active during the appetitive behavior abolished the arousal and the activation of relevant nuclei. Our data suggest that the histaminergic system is absolutely necessary to promote arousal during the appetitive phase of a motivated behavior like feeding and that the activation of this system depends of the integrity of infralimbic prefrontal cortex.

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S116. REGULATION OF CONNEXIN43- AND CONNEXIN45-BASED HEMICHANNELS BY FGF-1 IN SPINAL CORD ASTROCYTES. V. Abudara and J.M Garré. Facultad de Medicina, Universidad de la República Oriental del Uruguay, Montevideo, Uruguay

Astrocytes gap junction hemichannels in non-junctional membrane connect the cytoplasm and the extracellular milieu. Spinal cord astrocytes in culture are relatively impermeable to gap junctional tracers such as Lucifer yellow and ethidium bromide. Treatment with FGF-1 activates spinal cord astrocytes and permeabilizes the cells. In FGF-1 treatment, dye uptake occurred first via P2X receptors and then via connexin hemichannels. These pathways were distinguished by differential sensitivity to blocking agents. P2X channels were blocked by purinergic blockers, suramin or oxidized ATP (oATP) and hemichannels were blocked by gap junction blockers, 18 α -glycyrrhetic acid, carbenoxolone or octanol. ATP which is released by activated astrocytes mimicked FGF-1 permeabilization. ATP induced permeabilization was prevented by apyrase, which hydrolyzes ATP, and by the P2X blocker, oATP. Thus, FGF-1-induced permeabilization requires release of endogenous ATP and activation of P2X receptors. Both surface connexin43 and connexin45 were expressed by the astrocyte as determined by Western analysis of biotinylated surface proteins. FGF-1 treatment increased surface levels of connexin45 but not of connexin43. FGF-1 also permeabilized HeLa cells transfected with connexin43 or connexin45 but not parental HeLa cells, demonstrating that the FGF-1 effect is not limited to one connexin or cell type. It is proposed that FGF-1 enhances paracrine cell signaling pathways mediated by P2X channels and connexin hemichannels to coordinate the functioning of reactive astrocytes.