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Plenary lecture

26A1
CIREN's strategy and results for Neurological Restoration and Stereotactic Neurosurgery during its first fifteen years
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During this last fifteen years, the International Center for Neurological Restoration have been developing novel focus in the way to treat neurodegenerative diseases and sequels of neurological disorders. These are based on a program to treat sequels call Neurological Restoration Program and the necessary technology to perform stereotactic neurosurgery. The Neurological Restoration Program is carried out by a multidisciplinary team guided by neurologists. It comprises: the correct diagnosis of disease, incapacity quantification and objective definitions for pharmacological treatment and multidisplinary intensive - personalized rehabilitation. Treatment cycles are organized for periods of 28 days. Functional recovery in the patient neurological conditions is based in neuroplastic changes in the central nervous system organization and processing. These mechanisms had been evaluated in animal models and human being with different tools, like: long-term potentiation, transcranial magnetic stimulation, fRMI, etc. Synaptic changes in learning and memory process, amplification and reorganization of the motor cortical maps and function redistribution between hemispheric cortices are documented. On the other hand, Stereotactic Neurosurgery technology are composed by: a stereotactic frame (Estereoflex), a general computerized planning system for neurosurgery (STASSIS), an electrical deep brain structure recording system (NDRS) and a general team training system. Main characteristics of those components and the accumulated experience transferring these technologies to more than 11 hospitals will be described.

Neurorestorative Treatments

26A2
Chromaffin cells exposed to ELF EMF can be used as transplant material in Parkinson's disease and induce expression of TH positive cells in lateral ventricles
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Cultures of neonatal rat chromaffin cells in presence of Extremely Low Frequency Electromagnetic Fields (ELF EMF) show morphological and ultrastructural changes (Drucker-Colín et al, 1994; Feria-Velasco et al, 1998), different rates of catecholamine release (Verdugo-Díaz et al, 1998), biochemical and electrophysiological modifications (Morgado-Valle et al, 1997). The efficacy of ELF EMF differentiated chromaffin cells transplanted into a Parkinson's disease (PD) patient was tested and neurological, motor and pharmacological changes were determined. A PET-scan study was also done prior to transplant and 7 months after (Drucker-Colin et al,1999). We investigated the effects to applying ELF EMF in vivo into an animal model of PD. Male Wistar rats were subjected to the unilateral destruction of the substantia nigra by applying 6-OHDA and transplanted with neonatal chromaffin cells. The application of ELF EMF (60Hz, 0.7mT) was daily 2 hours in the morning and 2 hours in the afternoon for a period of 2 months. ELF EMF were produced by a pair of Heltzmohtz coils. Chromaffin cells were stained prior to implant with FluoroGold or 5-bromo-2'-deoxyuridine (2 fold daily). The main results obtained in vivo application of ELF EMF were: 1) Improvement in motor deficits and an over expression of Tyrosine Hydroxilase (TH) positive cells in both lateral ventricles of the nigro-striatal lesioned rats with chromaffin cell transplant; 2) No migration of implanted cells and differentiation of progenitor cells of both subventricular zone. In sum, it seems that ELF EMF, can be used as therapy for patients having PD.

26P3
Roles of D1 and D2 receptor subtypes in levodopa-induced dyskinesias in a mouse model of Parkinson disease
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Treatment with L-DOPA is today the most efficacious, non-invasive therapy for Parkinson's Disease. However, chronic treatment with L-DOPA induces in most of the patients the appearance of abnormal involuntary movements known as dyskinesias. The molecular mechanisms underlying these abnormal movements are unknown, although the implication of dopamine receptors as well as other neurotransmitter receptors interacting with the - system is suspected. In the present work, we have studied the contribution of D1 and D2 receptor subtypes in levodopa-induced dyskinesia. In this experiment dyskinesias were induced with intermittent doses of L-DOPA in unilateral 6-OHDA-lesioned mice. Rotational tests were carried out in a rotometer system that counted completed turns (360º) only and the abnormal involuntary movements we have divided in four different types: orofacial, forelimb, locomotive and dystonia, and evaluated. In wild-type animals chronic treatment with L-DOPA induced abnormal involuntary movements that including horizontal or vertical abnormal jaw movements, ballistic movements of the contralateral forelimb and axial dystonia. We have found that inactivation of D1 dopamine receptors completely abolished orofacial dyskinesia, did not affect axial distonia and slightly reduced forelimb dyskinesia. By contrast, knock out mice lacking D2 receptors showed an increase in orofacial dyskinesia after L-DOPA treatment but axial dystonia and forelimb dyskinesia were not present. In summary, our result demonstrate that D1 and D2 receptors play a differential and complementary a role in L-DOPA-induced dyskinesia and that the integrity of the D1 and D2 receptors is critical for different aspects of levodopa-induced dyskinesias

26A4

***Ex vivo* VEGF gene transfer does not increase grafted dopamine neuron survival**

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Specific conditions associated with the post-transplantation interval render grafted mesencephalic dopamine (DA) neurons susceptible to apoptotic and necrotic forms of cell death. Immediately following transplantation, grafted cells are dependent upon diffusion of oxygen and blood-borne materials from the host vasculature until they establish circulation with the host brain. Vascular endothelial growth factor (VEGF) is the primary endogenous endothelial cell mitogen involved in both vasculogenesis and angiogenesis. The present study investigates the ability of ex vivo transduction of mesencephalic reaggregates with a helper virus-free Herpes simplex virus (HSV) amplicon vector encoding VEGF to increase DA neuron survival after transplantation. Mesencephalic reaggregates were generated from E14 F344 rat pups and transduced immediately with either helper virus-free HSV-vegf, HSV-lac (MOI = 1.0 or 2.0) or no vector. Four days post-transduction (PTD4) reaggregates were analyzed for VEGF release to the culture media and levels of VEGF within the aggregates themselves using immunoassay and grafted to the denervated striatum of Fisher 344 rats. On PTD4 HSV-vegf-transduced reaggregates released at least 250 fold more VEGF protein into the culture media and contained at least 130 fold more VEGF protein than HSV-lac or non-transduced control reaggregate cultures. Although these in vitro assays yielded promising results, results of HSV-vegf ex vivo transduction of grafted mesencephalic reaggregates on behavioral and morphological outcome measures were not positive. The present results demonstrate that ex vivo gene transfer of VEGF is not successful in augmenting the survival of mesencephalic grafts. Supported by: AG21546, AG000844, Rochester Nathan Shock Center.

26A5

Administration of different doses of methylprednisolone in adult rats with traumatic spinal cord injury of different intensity and at different spinal cord levels

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After series of preclinical and clinical works, methylprednisolone (MP) became the standard of care in traumatic spinal cord injury (TSCI). However, in some studies MP failed to demonstrate consistent and significant effect on functional outcome. With the aim to test if the injury intensity or the injured level

could affect the response to the MP treatment, adult rats were subjected to mild (30 g/cm), moderate (75 g/cm) or severe (150 g/cm) TSCI at cervical (C6), thoracic (T9) or lumbar (L2) level using a standardized weight-drop contusion model. Groups were divided into subgroups that received vehicle or MP at 15, 30 or 45 mg/kg of body weight. Using the thiobarbituric acid reaction, malondialdehyde (MDA) levels, resulting from lipid peroxidation were obtained. Morphometric studies were done by light and electron microscopy and motor function using the BBB scale. Mild thoracic and mild and moderate lumbar injuries showed motor recovery with MP at 15mg/kg, while 30 and 45 mg/kg were as deleterious as in cervical and lumbar severe injuries. Non motor recovery was observed in moderate cervical and thoracic injuries, where the mortality was increased. In severe thoracic injuries motor recovery was observed with all doses of MP, specially with 30 mg/kg ($p<0.03$). However, in all groups where MP produced motor recovery by protecting axons and myelin sheaths from the secondary injury, it inhibited axonal collateral emission. MDA levels correlated with morphometric parameters and motor recovery. Response to MP treatment after TSCI seams to depend of the intensity and the injury level.

26A6

The administration of two new derivates of xanthines (A15ET and A15BU) reversed the locomotor impairments in rats with dopaminergic lesion

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In Parkinson's disease therapy is symptomatic. The L-dopa like is alternative in this pathology when is administrated by long time. Because of it is necessary to research new drugs about this pathology. One of them are the A2A antagonists that improve some Parkinson motor behavior in patient. In our University new derivates of xanthines like A15Et and A15Bu have been synthesized. The aim of this work was to evaluate the effect of new A2A antagonist (Al5Et and A15Bu) on motor behavior in rats with dopaminergic lesion. One group the rats were injected with 2 ml of 6-OHDA(8mg/ml) in SNc. The lesioned groups were evaluated in the drug induced turning behavior model, and in this condition were administrated A15Et or A15Bu (1mg/kg). The A15Bu was also evaluated in the star case test. Others groups of intact rats were evaluated in locomotors activity in and cataleptic behavior. We found that new A2A antagonist A15Et and A15Bu decreased 50% and 25% the turning behavior 70 and 80 minutes after administration. In the staircase the ability of reach pellets improved in 98%, the catalepsy behavior was reversed by injection of A15Bu 50% and did not modify the locomotor activity in intact rats. These data suggests that A15Et and A15Bu improve the motor function of rats with dopaminergic lesion.

26A7

Calpain inhibitor prevents axonal degeneration

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The ultrastructural change that characterizes the onset of Wallerian degeneration is the disintegration of axoplasmic microtubules and neurofilaments, followed by myelin breakdown. The mechanism underlying such processes is an increase in the amount of intracellular calcium, leading to activation of proteases called calpains. The aim of this study is to evaluate whether nerve fibers can be preserved by the use of calpain inhibitor, after optic nerve crush. The left optic nerve of eight opossums (Didelphis aurita) was crushed (Group A) and four of them received the calpain inhibitor-2 that remained in the crushed area (Group B). Right optic nerves were used as control. After 96 hrs the nerves were dissected and processed for electron microscopy. Group A presented degenerating fibers, besides disorganization of the optic nerve structure. Group B maintained the structure of the optic nerve, which was organized in fascicles, thus preventing the dispersion of the fibers. The quantitative analysis showed that the Group B presented more normal fibers (25.36 ± 7.83) than Group A (21.47 ± 7.27), $p<0.05$, and less degenerating fibers (7.65 ± 2.80) compared to group A (10.22 ± 4.33), $p<0.001$). We also calculated the G ratio (axonal area/fiber area), which showed that the Group B presented G ratio (0.45 ± 0.29), close to normal values (0.44 ± 0.19). However Group A presented the largest G ratio (0.85 ± 13.57), when compared to the other two groups ($p<0.01$). In conclusion, our findings suggest that calpain inhibitor is capable to provide neuroprotection after a crush lesion.

26A8

Striatal trophic factor pleiotrophin augments dopamine neuron survival and neurite outgrowth

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Transplantation of embryonic ventral mesencephalic (VM) tissue is an experimental therapy for Parkinson's disease. Both survival of grafted neurons and reinnervation of the striatum are essential for functional recovery. Our aim was to identify genes/factors that are upregulated during time points critical to nigrostriatal development and synaptogenesis. We utilized a microarray to profile gene expression in the rat E15 lateral ganglionic eminence, P1 and adult striatum. We identified genes that are upregulated during development, and tested their ability to promote dopamine neuron survival and neurite outgrowth in culture. Microisland cultures of E14 rat VM were exposed to pleiotrophin. On day 4 in vitro, cells were processed for tyrosine hydroxylase immunoreactivity (THir). Cell counts of THir neurons yielded 114.7 ± 8.0, 113.9 ± 11.0 and 134.3 ± 4.5% of control for cells treated with 10, 50 and 100 ng/ml pleiotrophin, respectively. Furthermore, neurite outgrowth was significantly increased in pleiotrophin treated cultures, 158.5 ± 21.3, 150.2 ± 18.1, 180.2 ± 20.1% of control for cells treated with 10, 50 and 100 ng/ml, respectively ($p<0.05$). Pleiotrophin may be an important cue in the establishment of nigrostriatal circuitry. Grafting of embryonic dopamine neurons in conjunction with pleiotrophin may promote reinnervation and functional recovery in Parkinson's disease.

Molecular mechanisms of neurodegeneration

26A9

Parkin and Ariadne share redundant functions

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Parkinson's Disease is characterized by the presence of Lewy Bodies and the loss of dopaminergic neurons. Long thought to be a causative factor in neurodegeneration, Lewy bodies may in fact serve a protective role. Patients with Autosomal Recessive Juvenile Parkinsonism (AR□JP) display an early onset of symptoms and the absence of LB formation. Many of these individuals carry germline mutations in the ubiquitin E3 ligase Parkin. We have found that Ariadne, the closest structural homolog to Parkin, can substitute for Parkin in many cellular functions. Both Parkin and Ariadne bind to the same substrates in vitro, and both can support the formation of Lewy body-like aggresomes in cultured cells. The aggresomes they produce are indistinguishable and are characterized by: centrosomal localization, high concentrations of ubiquitinated proteins, □-synuclein sequestration, and a dependence on intact microtubules. In parallel studies, we are examining the role of Parkin and Ariadne in neuropathology using the fruit fly Drosophila as a model. Working with wild-type and Parkin null flies, we are assessing the ability of wild-type and mutant human Parkin and Ariadne to rescue cellular defects. Ultimately, we hope to understand why dopaminergic neurons are selectively compromised in AR-JP.

26A10

Effects of 6-hydroxydopamine lesion on glutamate and GABA release in the pedunculopontine nucleus

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The pedunculopontine nucleus (PPN), co-localized with the mesencephalic locomotor region, has been proposed as a key structure in the physiopathology of Parkinson's Disease (PD). The goal of the present study was to assess if the amino acid neurotransmitter release in the PPN is modified by the degeneration of dopaminergic cells, from substantia nigra pars compacta (SNc) in 6-hydroxidopamine (6-OHDA)-lesioned rats. Simultaneously it was studied the amino acid neurotransmitter release in the PPN of rats with lesion of the subthalamic nucleus by quino-

linic acid (100nM) intracerebral injection. The extracellular concentrations of glutamic acid (GLU) and gamma-aminobutyric acid (GABA) were determined by brain microdialysis and high performance liquid chromatography (HPLC). Rats were assigned to five groups: SNc lesioned (n=11), Sham-operated (n=7), STN lesioned (n=7), Double lesion SNc+STN (n=9), and untreated rats (n=13). The extracellular concentration of GLU in 6-OHDA lesioned rats, was significantly increased in comparison with the others groups ($F(4, 42) = 16.35$ $p<0.001$). Extracellular GABA levels exhibited a significantly increase in all lesioned groups (SNc, STN, SNc+STN) in comparison with untreated and Sham operated rats ($F(4, 40) = 12.81$ $p<0.001$). The infusion of artificial cerebrospinal fluid with higher potassium (10mM) induced an increase in the GLU and GABA concentrations in all groups, which confirm the neuronal origin of the extracellular content. These results are in agreement with the current model of basal ganglia functioning and suggest the role of STN-PPN projection in the physiopathology of PD.

26A11

An animal model of ALS-PDC based on consumption of cycad toxins mimics the Human Disorder

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ALS-parkinsonism dementia complex is a complex neurodegenerative disorder of the island of guam which can express as classical ALS, as a form of Alzheimer's dementia with strong parkinsonism features, or as some combination. Epidemiological data of Kurland and colleagues linked the disorder to the consumption of neurotoxins contained in the flour of seeds of the local cycad palm, a traditional food source. We have duplicated the disease in an animal model by feeding male laboratory CD-1 mice a diet containing cycad flour. Exposed mice show both behavioural abnormalities of motor, cognitive, and olfactory function, in addition to neurodegeneration in corresponding neural subsets, including cortex, hippocampus, substantia nigra, and olfactory bulb. Biochemically, the same areas show profound decreases in EAAT2 glutamate transporter expression, elevated protein kinase C, CDK5, and other protein kinases, and a loss of tyrosine hydroxylase in striatum. Affected regions show the presence of activated astrocytes. MRI analysis shows volume changes in these areas. These features of abnormal neural function and morphology are found in various other mouse strains, but can be attenuated or potentiated by various genetic alterations. Apo E wild type mice are as profoundly affected by cycad feeding as CD-1 mice, but knockout Apo E mice appear to be largely neuroprotected. In contrast, mSOD1 G93A mice show enhanced neural degeneration following cycad exposure. These results support the notion that cycad is a key factor of ALS-PDC. The isolation of the putative toxin, a sterol glucoside, suggests that similar molecules may contribute to related age-dependent neurological disorders elsewhere.

26A12

Protective actions of S-allylcysteine on quinolinate- and b-amyloid peptide-induced oxidative neurotoxicity in rats

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We investigated the effects of S-allylcysteine (SAC), an aged garlic extract compound with well-known antioxidant properties, on the in vivo oxidative neurotoxicities produced by the intrastriatal injection of quinolinate (QUIN) and the intrahippocampal injection of amyloid-β peptide 25-35 (Abeta(25-35)) in rats, as experimental models of Huntington's (HD) and Alzheimer's diseases, respectively. QUIN is an excitotoxin acting at the N-methyl-D-aspartate receptors, whereas Abeta(25-35) is the toxic fragment of the amyloid-β peptide accumulated in Alzheimer's brains. Reactive oxygen species (ROS), lipid peroxidation (LP) and activities of the antioxidant enzymes superoxide dismutase (SOD) and glutathione peroxidase, were evaluated in striatum and hippocampus 120 min after QUIN (240 nmol/µl) and Abeta(25-35) (100 µM) injections. Both QUIN and Abeta(25-35) significantly increased ROS and LP, whereas pretreatment with SAC (300 mg/kg, i.p.) decreased these markers in both models when administered 30 min before the lesions were done. Except for the significant recovery of the QUIN-induced decrease in

Cu,Zn-SOD activity after SAC treatment, all other enzyme activities were found unchanged in both models after SAC or toxins administrations. In addition, SAC significantly reduced the QUIN-induced circling behavior in rats, an specific marker of striatal neurotoxicity. In summary, SAC ameliorated the in vivo QUIN- and Abeta(25-35)-induced oxidative toxicities by mechanisms related to its ability to scavenge free radicals, decreasing oxidative stress and preventing cell damage in striatum and hippocampus, respectively. For the HD model, the preservation of the striatal activity of Cu/Zn-SOD also seems to account for neuronal protection. SAC is likely to be a promising therapeutic agent.

26A13

Effects of the chronic administration of L-dopa on learning, spatial memory and malonyldialdehide levels in rat with dopaminergic lesion

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L-3-4-dihydroxyphenylalanine (L-Dopa) has been administered for long periods of time in Parkinson disease (PD) to alleviates the symptom such as motor functions. Unfortunately, many problems such as dyskinesias, wearing-off and on- phenomenon arise over the years. This chronic administration can be associated with cognitive deficits, and the L-Dopa metabolism to contribute to disease progression through free radicals (FR) generates. Another markers of stress oxidative such as malonyldialdehide are present too. In this work we evaluate, the effect of chronic administration of L-Dopa on spatial learning and memory in water maze were studied. After that we measured malonyldialdehide levels in rats with 6-hydroxydopamine (6-OHDA) lesion into sustantia nigra pars compacta (SNpc) was studied. The control group was administered SSI and the experimental group received L-Dopa/Carbidopa (200 mg/kg) for 60 days. Under these conditions, the spatial learning and memory was evaluated in both groups. After that malonyldialdehide levels were also measured from striatum and cortex by tiobarbituric method. We found that learning and spatial memory decreased 50% and 20% respectively. The malonyldialdehide levels decrease 93%, 65% and 90% in the striatum, frontal and temporoparietal cortex of the rat with L-Dopa. This facts suggest that there are relation between stress oxidative and deficits on learning and memory by chronic administration of L-Dopa.

26A14

Glutathione depletion by buthionine sulfoximine potentiates cerebral oxidative stress

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Oxidative damage to biomolecules has been postulated as a common molecular mechanism underlying brain aging and neurodegeneration. A marked brain glutathione deficiency by buthionine sulfoximine (BSO), an irreversible inhibitor of glutathione synthesis, provoke an imbalance in the cellular redox state towards the pro-oxidant status causing lipid peroxidation, protein oxidation and DNA damage. The toxicity of BSO to the brain has not been extensively studied, but appears to be chiefly related to its effect on cerebral oxidative metabolism.
The activities of the enzymes superoxide dismutase, catalase, glutathione peroxidase, glutathione and malondialdehyde content were studied in several rat brain areas following the intracerebroventricularly (icv) BSO lesion. The animals were assigned to both experimental groups: icv BSO lesioned 24 and 48 hours, control groups: icv saline lesioned 24 and 48 hours and intact groups. The SOD and CAT activity levels in the BSO lesioned group were higher than the values detected in saline lesioned and intact animals in 24 and 48 hours. Concerning CAT activity showed an increase, non-significant, with regard to the saline lesioned group in 24 hours. We found both, SOD and CAT activity, the saline lesioned group exhibited higher levels than the intact animals in 24 hours, in contrast, the saline lesioned group showed a slight increase, non-significant, with regard to the intact group in 48 hours. In addition the increment of SOD activity in the BSO lesioned groups in 24 hours with regard 48 hours was statistical significant but in the CAT activity only showed a non-significant tendency.

26A15

Mechanism of ethanol-induced glial apoptosis. Site of trophic protection

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We have previously shown that GDNF protects glial cells in culture from ethanol induced apoptosis. The aim of the present work is to investigate the mechanisms involved in ethanol-induced glial cell death and in trophic mediated glioprotection. Briefly, B92 glial cells were plated over glass coverslips with 100 ml D-MEM at 30,000 cells/cm2. After 24 h medium was replaced by treatment medium with 86, 172 mM EtOH, during 1 or 2 h, alone or supplemented with GDNF (30 ng/ml). After fixation, cells were prepared for immunochemistry, cytosqueleton kit detection, and for DAPI nuclear staining to identify apoptotic nuclei. We observed that active JNK (pJNK), a MAP kinase involved in apoptotic signal transduction, is unusually placed as stress fibers, and co-localized with actin filaments. After ethanol exposure cells lose their stellated form and acquire circular morphology. They exhibit a significantly higher amount of ring-formed actin cells, and a more diffuse organization of actin filaments. In the meantime, pJNK can be observed in the nucleus and perinuclearly. This data suggest that cytosqueleton may play a protective role abducting pJNK and thus, ethanol noxious effects may be drived by the disorganization of actin cytosqueleton through the release of pro-apoptotic actin associated pJNK. In turn, GDNF protective treatment fails to prevent actin disorganization indicating that it may be involved into an alternative mechanism of glioprotection.ngcarri@imbice.org/UNESCO 02-2000 and CONICET PIP-2580 Grants.

Posters

26P1

Evaluation of the neurorestorative effects of the murine beta-nerve growth factor infusions in old rat with cognitive deficit

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Nerve Growth Factor (NGF) is known to participate in the regulation of the expression levels and activity of the choline acetyltransferase (ChAT) in the Nervous System. This enzyme is sensitive to the degenerative changes found in Alzheimer's disease. We compared the effectiveness of intraparenchymal and intracerebroventricular administration of the murine b-NGF (b-NGFm) purified in our laboratories, through the evaluation of ChAT expression levels by reverse transcription and polymerase chain reaction (RT-PCR), the determination of ChAT activity by a radiochemical method, and through the evaluation of spatial memory and learning of aged rats with cognitive deficit in the Morris water maze tasks. Our results indicate that intracerebroventricular infusion of b-NGFm stimulates the expression levels of ChAT gene in the striatum of old rats. Remarkable losses in the ChAT activity was observed in the septum and striatum of old rats. b-NGFm infusions produced significant increases of ChAT activity in these brain regions differentially according to the administration pathway. The molecular and biochemical changes observed in the expression levels and activity of ChAT after b-NGFm infusions is related with the significant reversion of the memory deficiency. The results of the behavioral test suggest that the intraparechymal pathway offers the best results for a neurorestorative treatment.

26P2

Evaluation of bone marrow mononuclear cells surviving when are transplanted in rats injured with quinolinic acid

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The transplant of bone marrow mononuclear cells is one of the novel alternative therapeutic options for the treatment of neurodegenerative diseases, and its aim is to achieve a substitution of neural cells lost during the development of the disease. The objective of this work was to study the capacity of BMMC to survive the transplant and to look for a method that allow in vivo detection of implanted cells. BMMC were extracted from rat's femur using a Ficoll - Hypaque gradient. These cells were genetically modified with an adenovirus, which expresses the Green Fluorescent Protein (GFP), or they were labelled with Hoechst reagent. Labelled cells were implanted in the

striatum of rats with lesions caused by quinolinic acid. The viability of genetically modified cells was low, while the viability of the labelled cells with Hoechst reagent was bigger than 90%. Implanted cells survived, at least one month, after transplant and they were dispersed from the entrance place toward corpus callosum and cortex in the brain. In conclusion, BMSC has characteristics, which allow them to be considered as novel cellular source for transplantation. In our conditions, we consider more advantageous the use of Hoechst reagent for in vivo detection of these cells.

26P3

Comparison of fresh and hibernated rat ventral mesencephalon cells transplanted in a rat model of Parkinson's disease

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Despite the therapeutic potential of such transplants, there remain practical difficulties for widespread adoption of this promising therapy. One approach to overcome some of these constraints is to develop tissue storage procedures, which also have several further advantages. To evaluate whether hibernation of rat ventral mesencephalon cells influences graft survival and function in vivo, we transplanted either freshly and prepared or hibernated cells suspension into the striatum of 6-hydroxydopamine-lesioned rats. Fragments of rat ventral mesencephalon were stored in hibernation medium at 4°C for 3 and 7 days. The cells suspension was prepared and implanted in lesioned animals. To monitor graft function amphetamine-induced rotation was measured. After sacrifice, histological methods were used to compare fresh cell and hibernated cell transplants with respect to graft survival, differentiation and integration. Hibernated cells were founded to be either equivalent to fresh cells with respect to rotational correction, graft survival, total graft volume, total cell number (TH+), neuronal diameter and neuronal area. There was no significant difference between fresh and hibernated grafts ($F(2,28) = 2.96$ $p > 0.05$ n.s.). There were significant differences ($p < 0.05$, U Mann Whitney) between neuronal density in fresh and hibernated 7 days grafts, showing an increase of neuronal density at 7 days of hibernation. In conclusion, these results indicate that it is feasible to hibernate rat ventral mesencephalon cells for a week prior to transplantation in animal model of Parkinson's disease without a loss of their survival and functionality.

26P4

***In vitro* survival of dopaminergic neurons hibernated for 7 days**

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The use of fresh tissue in neural transplantation presents considerable logistical difficulties and limits their clinical applicability. One approach to overcome some of these problems is to develop tissue storage protocols that did not affect the viability and survival of dopaminergic cells after transplantation. In this study we examined the influence of hibernation for 7 days on in vitro survival of mesencephalic tissue compared with fresh tissue. Fragments of rat ventral mesencephalon were stored in hibernation medium at 4°C for 1, 3, 5 and 7 days. We determined the TH+ cells in fresh as well as in hibernated cultures. Comparison of hibernated with fresh ventral mesencephalon cell suspensions showed no significant difference with respect to cell viability. The morphology of cultured dopaminergic neurons after hibernation was very similar to that of fresh cells. There was no significant difference between the TH+ immunoreactive cells at 1, 3 and 5 days of hibernation. The lower survival was observed at 7 day of hibernation. There were significant differences between the TH+ cells in fresh and hibernated tissue. Despite the significant differences founded when compared fresh and hibernated tissue, this procedure guaranty the in vitro survival of TH+ neurons at first 5 days of hibernation. This method could be considered a useful procedure for conserving neural tissue to be used in clinical transplantation. Moreover, further research is needed on survival and functionality of hibernated cells after being transplanted into animal models, in order to evaluate their application in the neurorrestorative therapy.

26P5

Rat bone marrow stromal cells produces NGF and GDNF

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Bone marrow stromal cells (BMSC) have attracted interest through their possible use for cell therapy in neurological diseases. Recent reports demonstrated that these cells are able to migrate and have potential for neuronal differentiation after transplantation into brain parenchyma. The objective of this work was determine whether rat BMSC express NGF and GDNF, in order to study its potential application for treatment of neurodegenerative diseases. BMSC were harvested from male rats and cultured in DMEM supplemented with 20 % fetal bovine serum. At passage 6 the total RNA was isolated using TriZol reactive. RT-PCR reactions to evaluate the expression of NGF and GDNF using specific primers were carried out. The PCR reaction products were run in an agarose gel and compared with DNA molecular weight markers. Ours results indicate that rat BMSC have potential to produce NGF and GDNF. The production of NGF by these cells was reported in the literature; nevertheless, we have not found any report in favor of GDNF production by rat BMSC. Whether rat BMSC could produce CNTF, IGF-1 and BDNF is currently under research.

26P6

Bone Marrow stromal cells cultured in N2-supplemented medium

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Generation of brain cells from adult bone marrow stromal cells (MSCs) has evidenced their great plasticity and potential usefulness for cell therapy in the nervous system. Most of the culture system for in vitro maintenance and neural differentiation of MSCs use synthetic media supplemented with 10 or 20% fetal bovine serum. Serum, however, is comprised of unknown quantities of undefined substances, which could interfere the effect of exogenous substances on neural differentiation of MSCs. Here we describe survival of MSCs cultured in culture conditions where serum was reduced at 0.5 and 1 % using Bottenstein and Sato´s N2 formula (1979) and poly-L-lysine (PLL)-coated substrate. Survival of MSCs cultured in N2 supplement was reduced at about 40% of that observed in 10% FBS containing medium. Under these conditions cell morphology was also affected. However, when N2 containing medium was supplemented with FBS at 0.5 or 1% a significant increase of survival with respect to that observed in N2- supplemented cultures was observed. Cells seeded on PLL -coated surface increased their survival by contrast with their homologous cultures seeded on uncoated surface. This culture system, which combines N2 formula with FBS 1% and PLL-coated surface, is useful for the maintenance of MSCs. We speculate that these conditions could offer advantages for the study of neural differentiation of these cells. Currently, experiments aimed to evaluate the effect of EGF and FGF on MSCs using this culture system are being carried out.

26P7

Transplantation of cultured fetal human brain cells into injured spinal cord of adult rats

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We examined the survival ability of in vitro-expanded human neural stem/progenitor cells transplanted into damaged spinal cord of adult rats. Experimental group was undergone mechanical injury at the spinal cord level T-8-9 and bilateral injection of 6 ml suspension (300000 cells/ml) fetal cells expanded in culture during 14 days and control group was undergone damage only. Grafts were investigated after 7, 15, 30 and 60 days following the surgery by histology and immunohistochemistry. The control animals had damage zone with necrosis and forming cysts and glial scar. In experimental group human nuclei-immunopositive grafted cells located alone or by groups and migrated along white matter fiber and blood capillaries. Double immunostaining for nestin and human nuclei revealed that part of transplanted cells maintained non-differential phenotype. Double immunostaining for human nuclei and GFAP and immunostaining for β-III-tubulin revealed glial and neuronal differentiation. In this group we did not observe forming cysts. There was glial reaction in the damage zone, but glial scar was absent. Thus, our

results show that human neural stem/progenitor cell grafted into damaged adult rat spinal cord successful survive and positive influence for posttraumatic processes.

26P8

9-O-acetyl ganglioside is expressed by proliferating cells in the subventricular zone of adult rats

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9-O-acetyl GD3 ganglioside is important in migration and neuritogenesis during the development of the nervous system and remains expressed in adult brain SVZ, described as a niche of neurogenesis and from where neural stem cells have been isolated. In this work we are trying to characterize SVZ cells by the expression of known markers and 9-O-acGD3. To identify proliferating cells in the CNS, adult rats were treated with BrdU. The brains were sliced or the tissue was dissociated into single cells. After immunocytochemistry we were able to observe BrdU incorporation and 9-O-acGD3 expression in situ and in single cells and that both are present preferentially on the same regions of the lateral ventricles. By confocal microscopy, we could detect colocalization of these antigens. To characterize 9-O-acGD3 positive cells, we performed immunocytochemistry reactions for antigens present in SVZ cells, like GFAP, nestin and PSA-NCAM and for the ganglioside. By confocal microscopy, some 9-O-acGD3 positive cells were also positive for those antigens. In this work, we could observe that the expression of 9-O-acGD3 occurs at the same regions of high cell proliferation in adult brain. The colocalization of the ganglioside and BrdU shows that it is expressed by proliferating cells in the SVZ. The co-expression of 9-O-acGD3 and GFAP or nestin suggests that it could be present in the cells described as neural stem in the adult brain and may remain expressed by neuroblasts as some was positive for PSA-NCAM. At the moment, we are quantifying all those populations by flow citometry.

26P9

Effect of swim stress on 5-HT1A receptor density in different mouse brain regions

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Several stressful agents induce synthesis and expression of 5-HT1A receptor; for example, forced swimming-induced stress produces changes in RNAm synthesis, as well as modifications in 5-HT1A binding in the hippocampus rat. In the present work we have studied the effect of an acute swim stress session on 5-HT1A receptors in amygdala, dorsal and ventral raphe nuclei, hippocampus, hypothalamus and thalamus. Swiss Webster male mice were used. The stressful session consisted on putting each mouse into a cylinder filled with water at 25ºC. Mice were divided in two groups; one of them was forced to swim for 15 min and 24 hr after, sacrificed by cervical dislocation. A non-stressed second group was used as a control. The brains of all animals were removed and immediately frozen. Slices measuring 20 µm were obtained in a -20oC cryostat. Quantitative autoradiography experiments were carried out labeling the 5-HT1A receptor of the above mentioned regions with [3H]8-OH-DPAT. An increase in density of 5-HT1A receptors in hypothalamus, thalamus and amygdala was observed in stressed animals, accompanied by a diminution of this subtype receptor in raphe nuclei and hippocampus. These findings can be interpreted as a compensatory mechanism of the diminution in the serotonin levels observed after stressing. Furthermore, it has been reported that stress induces an increase in corticosteroids brain levels, which diminishes the synthesis of 5-HT1A receptor in hippocampus rat. Taken together, these evidences show that some aversive agents such as forced swimming-induced stress are able to induce synaptic changes in the central nervous system. This work was supported by CGPI and COFAA-I.P.N.

26P10

Pinacidil reduces neuropathic pain by activation of different potassium channels

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Previous studies have shown that peripheral administration of pinacidil reduces carragenin- and prostaglandin E2-induced mechanical hyperalgesia in the rat. Besides, spinal or supraspinal administration of pinacidil produces antinociception in mice. It is be-

lieved that pinacidil-induced antinociception is produced only by activation of ATP-sensitive K+ channels. However, it is likely that other K+ channels could participate in its antiallodynic effect. In this work we assessed the effect of different K+ channel blockers on pinacidil-induced antiallodynia. L5 and L6 left spinal nerves were ligated to female Wistar rats and fifteen days later animals were anesthetized to insert a spinal catheter. Five days after surgery, withdrawal threshold was assessed (with von Frey filaments) as a measure of allodynia. Reduction of withdrawal threshold was considered as the antiallodynic effect. Spinal administration of pinacidil (1-10 µg) reduced withdrawal threshold in a dose-dependent manner in neuropathic rats. Glibenclamide (50 µg, ATP-sensitive K+ channel blocker), apamin (3 ng) and charybdotoxin (1 ng, small- and large-conductance Ca2+-activated K+ channel blocker, respectively), but not margatoxin (10 ng, voltage-gated K+ channel blocker), partially reversed spinal pinacidil-induced antiallodynia. K+ channel blockers, by themselves, were not able to modify neuropathic pain. In conclusion, data suggest that the antiallodynic effect of pinacidil could be produced by opening of ATP-sensitive, small- and large-conductance Ca2+-activated, but not voltage-gated, K+ channels. In addition, K+ channel openers could be useful to treat neuropathic pain in humans.

26P11

Synergistic interaction between spinal gabapentin and oral B vitamins in a neuropathic pain model

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Experiments in animals have shown that vitamins B1 (thiamin), B6 (pyridoxine) and B12 (cyanocobalamin) and their combination have antinociceptive activity against chemical- and heat-induced pain. The mixture of B vitamins is often used in neuropathic pain, however, there is no evidence about the efficacy of this preparation in this kind of pain. Therefore, the purpose of this study was to assess the analgesic activity of B vitamins (B1, B6 and B12), gabapentin and the co-administration of gabapentin and B vitamins in a neuropathic pain model. Rats were submitted to the ligation of the left L5 and L6 spinal nerves. Tactile allodynia was assessed daily by von Frey testing on the injured paw. B vitamins (75-600 mg/kg, p.o.) and gabapentin (25-200 µg, i.t.) produced a dose-dependent reduction of tactile allodynia. However, the antiallodynic effect of gabapentin was significantly higher than that produced by B vitamins. The co-administration of gabapentin and B vitamins also produced a dose-dependent reduction in allodynia. Isobolographic analyses revealed a synergistic interaction between spinal gabapentin and oral B vitamins, suggesting that this combination could be useful to relive neuropathic pain in humans.

26P12

Participation of peripheral and spinal cox-1 in the inflammatory pain

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Formalin produce a biphasic nocifensive response of the injected paw. Whilst peripheral inflammation following formalin injection is evident. Nonsteroidal anti-inflammatory drugs (NSAIDs), when administered systemically or intrathecally, fail to affect the first phase of the formalin response, but attenuate the second phase. It is not clear whether this is peripherally or centrally-mediated. The aim of the present study was to improve the understanding the contribution of peripheral and spinal ciclooxigenases 1 and 2 (COX-1 and COX-2) to the development of inflammatory pain. Female Wistar rats aged 6-8 weeks were used in this study. All experiments followed the IASP guidelines for investigation of pain in animals. 50 µl, 1% formalin was injected into the dorsal surface of right hind paw. Local injection of the selective COX-1 inhibitor, resveratrol and the non-selective COX inhibitor, diclofenac produced antinociception, while the selective COX-2 inhibitor celecoxib was ineffective. Inthrathecal injection of COX-1 or COX-2 inhibitors produced antinociception as well as the non-selective COX inhibitor. In summary, these data suggest that the participation of COX-1 rather than COX-2 is important at peripheral level, whilst, both COX participate at spinal level. The analgesic effect of conventional NSAIDs is not accounted for solely by COX-2 inhibition and requires the inhibition of both COX-1 y COX-2.

26P13

B vitamins increase the anti-allodynic effect of dexamethasone in neurophatic rats

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In this work we evaluated the antiallodynic effect of dexamethasone and B vitamins in a neuropathic pain model in female Wistar rats (Chung Model). Neuropathy was produced by tight ligation of L5 and L6 left spinal nerves. Twelve days after surgery, the withdrawal threshold was assessed (with von Frey filaments) as a measure of allodynia. Reduction of withdrawal threshold was considered as an antiallodynic effect. Subcutaneous administration of dexamethasone (4-32 mg/kg), vitamin B1 (75-600 mg/kg) and vitamin B12 (0.75-12 mg/kg), but not vitamin B6 (75-600 mg/kg), significantly reduced in a dose-dependent manner withdrawal threshold in neuropathic rats. Doses necessary to produce a 30% of reduction of allodynia (ED30) were 5.41 ± 1.2, 178.4 ± 20.1 and 1.26 ± 0.0 mg/kg for dexamethasone, vitamin B1 and vitamin B12, respectively. In addition, co-administration of dexamethasone and either vitamin B1 or B12 reduced in a dose-dependent manner mechanical allodynia. Experimental ED30 for the dexamethasone-vitamin B1 and dexamethasone-vitamin B12 combinations were (50.1 ± 3.4 and 1.8 ± 0.0 mg/kg, respectively) significantly lower than theoretical ED30 (91.9 ± 10.1 and 3.7 ± 0.6 mg/kg, respectively), thus suggesting a functional synergism between these drugs to reduce allodynia. In conclusion, our results suggest that these combinations could be useful to treat neuropathic pain in humans.

26P14

Abstract not available

26P15

Neural plasticity in the MPTP-treated parkinsonian monkey: dissociated responses of cognitive and motor performances

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Evidence of dissociation in cognitive and motor performances was found in three groups of adult Cebus apella monkeys: females (Group1: N=3), males (Group2: N=4; Group3: N=3). A spatial delayed response task (SDR) was administered at A (pre-MPTP), B (post-MPTP) and C (post- surgery) stages. Performance was recorded until reaching the maximum possible delay (<1, 2, 4, 6, 8, 10 seconds). Before B all groups received MPTP hydrochloride (0.5 mg/kg i.m. per day; total dose: 21 mg). After B astroglial or "sham" transplants into the neostriatum were performed [Group 1: unilateral; Group 2: bilateral (N=2) and "sham" (N=2); Group 3 with no surgical intervention and two series of testing in A]. All monkeys performed efficiently in SDR with delays of up to 8-10 seconds in A. Non spontaneous motor recovery was observed [6 to 10 points in Smith et al. (1993) scale of parkinsonism]. Efficiency was severely altered in Groups 1 and 2 in B. The "sham" individuals did not modify this performance. Animals from Groups 1 and 2 receiving transplants improved their performance nearly reaching the levels of delay observed in A. No statistical differences were observed between groups in the number of sessions and trials received in A. Mesencephalic sections showed significant reduction of TH-immunoreactivity in all MPTP-treated cases. Residual plasticity in system(s) subserving cognitive performances was apparent in MPTP-treated monkeys expressing a full fledged motor parkinsonism. Results encourage the possibility of cognitive improvement in clinical parkinsonism, in which a combination of interventions could be applied. Acknowledgements. Emprendimientos San Jorge, Chevron-Texaco, Fundación Conectar, FONCYT (PICT # 01-03465), Fundación René Barón.

26P16

Neurogenesis and gliogenesis in the spinal cord of juvenile turtles : A multidisciplinary study

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Since the 60' it has been demonstrated postnatal neurogenesis at several brain regions of vertebrates. However few are known about spinal cord postnatal neurogenesis. Studies in turtles have provided novel evidences of postnatal neurogenesis at the spinal cord level. We have recently demonstrated by the use of " in vivo" BrdU injections that proliferating neural cells are present both in the gray and white matter along the spinal cord. Larger densities of BrdU- labeled- nuclei occurred in the so-called central gelatinosa (CG).Different methods have been applied to know the cellular composition of CG. Two morphological types can be recognized by mean of Golgi technique that could correspond to different stages of differentiation of neuronal or glial lineages. Electron microscopy studies demonstrated synaptic contacts

on putative Golgi-stained neuroblast. Immunohistochemical labeling allowed us to clearly confirm that S-100 positive cells (early glial marker) and Huc/d positive cells (early neuronal marker) are intimately associated in the ependymal epithelium of spinal cord. Double-labeling experiments indicated that BrdU labeled cells expressed S-100 in animals fixed 1-hour post injection, however the BrdU labeled cells only expressed Huc/d 30 to 60 days after. Double labeling immunocytochemical studies revealed GABAergic and serononinergic botouns making contact with Huc/d positive somas. Whole cell patch clamp recording from CG showed three different electrophysiological phenotypes: 1) cells without signs of membrane active properties (putative glial or stem cells); 2) cells with high input resistance and outward rectification that did not generate spikes (putative neuroblast) and 3) cells that generate action potential (neurons).

Epidemilogy, accelerators and risk factors in AD

26B1

The primary pathogenetic role of vascular hypoperfusion, mitochondria failure and oxidative stress in Alzheimer disease

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Vascular insufficiency, with concomitant chronic hypoxia/hypoperfusion, may play a key part in the initiation of Alzheimer disease (AD). However, the role of vascular abnormalities and their participation as pathogenic factors during the development and maturation of AD is controversial. Adding to this complexity are the mechanisms by which reactive oxygen species (ROS) participate in the development of vascular insufficiency-induced chronic hypoxia/hypoperfusion, which also may play an important role in the pathogenesis of AD. We studied the cellular and subcellular features of vascular lesions and mitochondria in brain vascular wall cells from human AD brain biopsies, human short postmortem brain tissues, yeast artificial chromosome (YAC) and C57B6/SJL transgenic positive (Tg+) mice overexpressing amyloid beta precursor protein (AbPP) and in aged rats given selective mitochondrial antioxidants (Lipoic Acid and ALCAIR). In situ hybridization, using mitochondrial DNA (mtDNA) probes for human wild type, 5kb deleted and mouse mtDNA, was performed in conjunction with immunocytochemistry using antibodies against AbPP, 8-hydroxyguanosine (8OHG) and cytochrome c oxidase (COX). We found a higher degree of amyloid deposition in the cerebrovascular walls in the human AD cases, YAC and C57B6/SJL Tg (+) mice when compared to aged-matched controls. In addition, vessels with more severe lesions showed immunopositive staining for AbPP and possessed large, lipid-laden vacuoles in the cytoplasm of endothelial cells. Significantly more mitochondrial abnormalities were seen in microvessels, where lesions occurred, in human AD specimens, YAC and C57B6/SJL Tg (+) mice and old aged rats without treatment. However, the animals that received treatment showed an absence of any cellular or subcellular abnormality in brain cellular compartments. In situ hybridization, using wild type and chimera (recognizing mtDNA with the 5 kB deletion) mtDNA probes, revealed positive signals in the damaged mitochondria from the vascular endothelium and in perivascular cells of lesioned microvessels in human AD, YAC and C57B6/SJL Tg (+) mouse tissues. This damage was proximal to regions of large amyloid deposition. Interestingly, these features were absent in undamaged regions of human AD tissues, YAC and C57B6/SJL Tg (+) mouse tissues and in aged-matched control subjects. In addition, vessels with atherosclerotic lesions revealed endothelium and perivascular cells, which stained positively and in clusters when probed with wild and deleted mtDNA probes. These mtDNA deletions were associated with increased amounts of immunoreactive AbPP, 8OHG and COX in the same cellular and subcellular compartments. The mtDNA deletion and expression of oxidative stress markers in vascular wall cells of the AD brain indicate that energy deficiency and oxidative stress, in AD, selectively affects the brain vascular tree and whole populations of vulnerable neurons. We hypothesize that vascular abnormalities, especially mitochondrial lesions and increased oxidative stress, in the cellular and subcellular compartment are responsible for regional blood flow alterations. Further, this alteration can lead to blood brain barrier failure and breakage during the development of AD. We theorize that by using selective pharmacological agents to block the underlying oxidative

stress stimuli and damage that it will be possible to normalize the actions of the endogenous antioxidant systems in vascular wall cells. We theorize also that similar stimuli-blocking intervention strategies will help to normalize the antioxidant systems in AD patients and in aged individuals. Future studies, which examine the importance of mitochondrial pathophysiology in different cellular compartments may provide important insight not only into neurodegenerative and/or cerebrovascular disease pathobiology but may provide targets for treatment approaches in these conditions.

26B2

The Cuban Dementia and Alzheimer's Study Playa (EDAP)

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Background and Objectives: Cuba is a developing country, with a health profile similar to that of developed countries. With a population of 12 million people Cuba will become the second oldest country in Latin America by the year 2020, when those aged 60 years and over will account for 25% of the population. The Cuban Dementia and Alzheimer's Study Playa is a multicenter, population-based study with a sample of 18 351 people over the 65 years. It constitutes one of the most extensive prevalence studies in Cuba and Latin American. The core objectives were to know the prevalence of Cognitive disorders, the dementia syndrome and its different causes in people over 65 in Playa municipality, Havana City, as well as risk factors including the genetic factors and the impact that these dementia syndromes cause in families. Methodology: A door to door study was carried out, in which 18 351 people over 65 were studied by means of the application of the Mini Mental State Examination (MMSE), the Clinical Dementia Rating Scale (CDR) and an interview based on risk factors. Different criteria such as: the DSM-IV, the NINCDS-ADRDA, the NINCDS-AIREN and others established for specific dementias were used in the diagnosis of dementia syndrome. Conclusions: The prevalence of dementia syndrome was 9,25/100 people over 65. Alzheimer's disease followed by vascular dementia were the most frequent causes. Stroke, Parkinson disease, advanced age, occupation, family history of dementia, depression, the antecedent of cranial trauma, and the low school level were the factors that mostly influenced on the appearance of the dementia syndrome.

26B3

A rat model of MCI upregulates hippocampal nitric oxide and precedes memory loss and Ab 1-40 accumulation after chronic brain hypoperfusion

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Chronic brain hypoperfusion (CBH) using permanent occlusion of both common carotid arteries in an aging rat model, has been shown by us to mimic human mild cognitive impairment (MCI), an acknowledged transition stage that often converts to Alzheimer's disease. Purpose: An aging rat model was used to determine whether hippocampal nitric oxide (NO) is abnormally expressed following CBH for 2 or 8 weeks. At each time point, spatial memory, hippocampal A$ 1-40/1-42 and amperometric measures of constitutive NO were measured. Results: Two weeks after CBH, NO hippocampal levels were upregulated nearly 4-fold when compared to non-occluded rats but no alteration in spatial memory or A$ products were observed at this time point. By contrast, NO concentration had returned to control levels by 8 weeks but spatial memory was significantly impaired and A$ 1-40 (but not A$ 1-42) had increased in the CBH group when compared to control non-CBH rats. Since changes in shear stress are known to upregulate eNOS but generally not nNOS, these results suggest that shear stress induced by CBH hyperactivated vascular NO derived from eNOS in the first 2 weeks as a reaction by the capillary endothelium to maintain homeostasis of local cerebral blood flow. The return of vascular NO to basal levels after 2 weeks of CBH may have triggered metabolic changes within hippocampal cells resulting in spatial memory impairment and accumulation of A$ 1-40 peptide. These findings support the notion that CBH in aging rats mimics human MCI and may explain, at least in part, some of the molecular events that can trigger memory impairment at a pre-clinical stage to Alzheimer's disease.

26B4

Role of reactive oxygen species in brain ageing

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There are more than 300 theories to explain the aging phenomenon. Many of them originate from the study of changes that accumulate with time. Among all the theories, the free radical theory of aging, postulated first by Harman, is the most popular and widely tested, and is based on the chemical nature and ubiquitous presence of free radicals. Tight linkage between aging and oxidative stress is indicated by the observations that reactive oxygen species generated under various conditions of oxidative stress are able to oxidize nucleic acids, proteins, and lipids and that aging is associated with the accumulation of oxidized forms of cellular constituents, and also by the fact that there is an inverse relationship between the maximum life span of organisms and the age-related accumulation of oxidative damage. Nevertheless, validity of the oxidative stress hypothesis of aging is questioned by (i) the failure to establish a causal relationship between aging and oxidative damage and (ii) lack of a consistent correlation between the accumulation of oxidative damage and aging. The present discussion is focused on the complexity of the aging process and suggests that discrepancies between various studies in this area are likely due to the fact that aging is not a single process and that the lack of consistent experimental results is partly explained by individual variations. Even so, there is overwhelming support for a dominant role of oxidative stress in the aging of some individuals.

26B5

Aluminum-triggered structural modifications and aggregation of b-amyloid

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Amyloid b-peptides, as insoluble fibril deposits, is the major component of the senile plaques that characterize Alzheimer's disease brain [Behl (1999) Progress Neurobiology 57: 301] The conformational changes induced by several cations (Cu2+, Zn2+, Al3+, Mn2+, Ca2+) on the □-amyloid (Ab) fragments 1-40 and 1-42 have been studied at physiological pH, with the aim to get clues into the modality of metal binding. As probes of conformation we used the variations of the intrinsic tyrosine (Tyr) fluorescence and the fluorescence quenching by acrylamide. Ca2+ and Mn2+ did not affect the amyloid conformation. Cu2+, Zn2+, though binding to the same hydrophilic N-terminal domain [Miura et al., (2000) Biochemistry 39: 7024] caused, respectively, a burial and a high degree of exposure of Tyr residues. The most relevant effects on the peptides conformation were found upon binding of Al3. Amyloids 1-40 and 1-42 were also tested for their hydrophobicity and aggregation properties by following the increase of the fluorescence intensity of 8-anilino-1-naphthalene sulfonic acid (ANS) and Thioflavin-T (ThT), respectively. The surface hydrophobicity and the assembly process were more pronounced for the 1-42 peptide, as compared to 1-40, and Al3+ was the most efficient cation in inducing aggregation. Electron microscopy experiments ascertained that only Zn2+ and Al3+-induced Ab1-42 aggregates led to formation of fibrils with Al3+ promoting the process at much lower concentration than Zn2+. The conformational and aggregational effects of Al3+ were specifically abolished in the presence of desferoxamine mesylate, a trivalent metal ion chelator used in therapy to treat toxic Fe3+ and Al3+ overload conditions.

26B6

Excitotoxicity and oxidative stress induce activation of cell-cycle proteins and DNA repair systems in primary neurons

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The possible link between excitotoxicity, oxidative stress and the induction of cell cycle-related factors has been matter of extensive investigation during the last 5-10 years and it is now supported by several in vivo and in vitro data offering significant answers in the AD ethiopathogenic mechanisms. In particular, in vitro studies have elucidated the role of p53 in apoptosis induced by excitatory amino acids (EAA). Exposure of primary cultures of cerebellar granule neurons to neurotoxic concentrations of glutamate was found to induce a significant, short-lasting increase of p53 expression (Uberti et al. 1998; Grilli and Memo, 1999). Transcriptional activity of the over-expressed p53 was demonstrated by an increased p53 DNA binding activity and the concomitant enhancement of waf1/cip1 kinase inhibitor p21. The direct correlation

between p53 expression and glutamate-induced apoptosis in cerebellar granule cells, has been suggested by the finding that under the same experimental conditions, a p53 specific antisense oligonucleotide prevented both glutamate-induced p53 expression and apoptosis. We have recently further extended this concept by demonstrating the induction of p53 and Gadd45 in primary cortical neurons exposed to NMDA. The mechanism(s) by which glutamate induces activation of cell cycle related factors and apoptosis is not clear. We hypothesize that overstimulation of ionotropic glutamate receptors, possibly by generating oxygen free radicals (ROS), may induce DNA damage. A single and/or double-strand DNA breaks caused by excitotoxicity has indeed been suggested by numerous studies (Didier et al., 1996, Liu et al., 1996, Chen et al., 1997). In summary, we suggest that, similarly to proliferating cells, postmitotic neurons may respond to (EAA-induced) DNA damage by activating a cascade of events involving DNA damage sensors and repairing factors. In this regard, we have found that the expression of the DNA mismatch repair factor MSH2, which is a p53 downstream gene functioning in recognition and repair of a several types of DNA damage, is significantly increased in primary cultures of cerebellar granule cells after glutamate exposure as well as in CA3 hippocampal neurons after kainate treatment.

Challenging views of AD therapy I

26B7

Current status and future development of pharmacological treatment of AD: Strategies towards disease modifying therapy

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Most approved drugs for treatment of mild to moderately severe Alzheimer's disease (AD) are cholinesterase inhibitors, showing modest but reproducible improvement of cognitive performance, global function, and activities of daily living. Their effect size is similar, but they differ in the side effect profile. Expectations about long term effects were not fulfilled. The new choline-esterase inhibitors Phenserine induces decrease of APP expression by direct interaction with the 5'UTR on translational level, lowering Aß 1-42 and Aß 1-40. The ongoing clinical program is designed to investigate, if this results in fast cognitive improvement and slowing of disease progression. Memantine modulating NMDA signalling has been recently approved by FDA for treatment of severe AD patients. Targeting amyloid metabolism, new compounds to block activity of gamma- or beta-secretase are under development. The enthusiasm about the anti-amyloid vaccination cooled down after occurrence of severe side effects in the phase II clinical study. Approaches for safer vaccination are under investigation, stimulated by reports about cognitive effects in the initial clinical trial. Passive immunisation is explored as safe alternative. Cholesterol lowering and modulating drugs are addressing Aß-production and aggregation. Recent drug developments are investigating inhibitors of GSK-3ß to prevent tau hyperphosphorylation. Substances interfering with formation of paired helical filaments and stimulators of phosphatases are also discussed. These developments are promising because cytoskeletal pathology shows good correlation to disease severity. Enormous efforts of basic research and industrial drug development give raise to the hope that in the near future efficacious therapy of AD might be available.

26B8

Neural stem cell survival is compromised in the aged brain

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Most research investigating the competence of neural stem cells to differentiate and the capacity of the brain to support their survival and differentiation has been conducted in neonatal or young adult brain. However most patients likely to benefit from structural repair by neural stem cells require therapy for stroke or neurodegenerative disease would be in the sixth decade of life or older. Little is known of the capacity of the aged brain to support either endogenous or grafted stem cells. We examined the rate of neurogenesis by confocal stereology and investigated the ability of this region to support the survival and differentiation of grafted young neural progenitor cells. Aging profoundly impairs neurogenesis in the olfactory bulb with a 70% decline in new cells. Over 90% of newly generated cells differentiate into mature neurons in both young and aged animals suggesting that differentiation signals remain intact. We grafted neural progenitor cells derived from young adult animals into the aged bulb and hippocampus to determine if these regions could support their differ-

entiation. In contrast to robust neuronal differentiation in young adult recipients, few cells survived in the aged brain and differentiated into astrocytes. These results suggest that it is not only the competence of the stem cell, but the environment in which that cell is placed that must be considered for the development of structural brain repair strategies. The aged brain may require environmental enhancement before use of neural stem cells for brain repair will be possible. Supported by: NIH-AG20047.

26B9

Restoring complex circuits and functional recovery with cell replacement and environmental manipulation in aging and disease: A unifying hypothesis

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Neurodegenerative diseases, including Parkinson's disease and Alzheimer's disease exhibit a selective loss/dystrophy of specific subsets of neuronal populations whose underlying causes are not clear but they are key features to the impaired condition. Over most of the past century, it was thought that the adult brain was completely incapable of generating new neurons. New research showing that (i) neurogenesis is not restricted to embryonic development, but normally also occurs in limited regions of the adult mammalian brain (ii) that there are significant numbers of multipotent neural precursors in many parts of the adult mammalian brain (iii) that it is possible to induce functional recovery even in the aged brain, via manipulation of endogenous multipotent precursors in situ with complex stimulus i.e. housing environment complexity and; (iv) that non neural stem cells can survive and differentiate to neurons after grafting. Results from motor/cognitive impaired aged rats as recipient of bone marrow stem cells (BMSCs) grafting and/or long term housing in complex environment in relation to biochemical, functional and behavioral concerns (Submitted Ann NY Acad. Sci). Our hypothesis attempts to explain, at least in part, the observed results after two different neurorestoration modalities evidencing that age, oxidative damage, and altered neuroimmunotrophic signaling contribute to the age-associated functional impairments which can be reversed after direct/indirect manipulation of affected neuronal populations, demonstrating that the aged brain still has appreciable plasticity in terms of functional recovery. The hypothesis contribute to novel concepts and programs in prevention/reduction both, incidence/severity and outcome of age-associated neurodegenerative

26B10

Neuroprotection of adult human sensory neurons against prolonged anoxia and trauma

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CNS injury due to trauma, anoxia, and disease leads to unpredictable and unpreventable neurological deficits. Ischemia and trauma kill neurons immediately, while over the subsequent 48 hours secondary causes related to the trauma and ischemia kill an even greater number of neurons. To minimize ischemia/trauma-induced immediate and long-term neurological losses, the number of neurons killed during ischemia and reperfusion must be reduced. Clinical attempts to reduce neuron death have focused on decreasing the energy requirements of spinal cord neurons using protective agents such as hypothermia, barbiturates, and antioxidants. However, none are so successful as to become the standard of care. Work on animal and in vitro models have found that alkalinization, calcium channel blockers, and NMDA receptor antagonists also provide neuroprotection. But, most neuroprotective procedures involve only the use of one such agent and still many neurons die. In experiments on isolated intact adult human DRG we found combinations of neuroprotective methods that increase the yield of viable neurons through prolonged ischemia and glutamate insult by more than a 500 fold. The primary neuroprotectors are hypothermia (20oC) and alkalinization (pH 9.3), although together with sodium channel blockers and NMDA receptor blockers neuroprotection is enhanced. Currently we are studying the influences of additional agents, including antioxidants and neurotrophic factors, for their ability to further enhance neuroprtection of adult human neurons, and will begin testing these combinations for their efficacy on the adult swine spinal cord model. We believe some of these combinations of agents will also be effective in assisting in recovery from various neurological diseases. Subsequently, successful methods will be tested clinically.

26B11

Zn^{2+} dyshomeostasis and neuronal injury

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Zn2+ is potently neurotoxic "in vitro" and "in vivo" trans-synaptic movement of Zn2+ from pre- to post-synaptic neurons contributes to ischemic neural injury. Zn2+ can enter neurons through NMDA channels, voltage sensitive calcium channels (VSCC), and AMPA/kainate channels (Ca-A/K channels). Mechanisms by which Zn2+ exerts its potent neurotoxic effects are still largely unknown. We have recently suggested that an important factor could be the Zn2+ dependent disruption of mitochondrial function. Neuronal mitochondria play an important role in restoring Zn2+i homeostasis but this Zn2+ uptake leads also to prolonged mitochondrial depolarization and free radicals generation. These injurious and likely necrotic effects are particularly evident upon the large and rapid Zn2+i rises (D[Zn2+]i) resulting from Zn2+ entry via the Ca-A/K channels. Interestingly, more moderate D[Zn2+]i, triggered by Zn2+ entry via VSCC, promote release of pro-apoptotic factors such as cytochrome-C or Apoptosis Inducing Factor, suggesting that different degrees of cytosolic D[Zn2+]i might activate distinct injurious pathways. In addition to roles in acute injury, Zn2+ might play roles in the selective neurodegeneration associated with aging and and Alzheimer's disease (AD). Indeed, cumulative effects of repeated Zn2+ exposures could contribute to the oxidative damage and mitochondrial dysfunction seen in AD. Moreover, recent studies have suggested that the cation promotes the aggregated state of b-amyloid peptide. Zn2+ is in fact found in high concentrations in mature amyloid plaques in human tissue, and its chelation favors the disaggregation and dissolution of the plaques. A better understanding of the mechanisms involved in neuronal Zn2+ homeostastasis seems therefore highly desirable.

26B12

Reversal of symptoms of Alzheimer disease following omentum transposition to the brain

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Objective: To show that patients who have Alzheimer's disease (AD) can have their cognitive and neurological symptoms reversed by placing the omentum directly on the brain Method: The omentum is separated from the transverse colon and from the proximal portion of the stomach leaving the gastroepiploic vessels in the omental apron. The omentum is surgically lengthened and then brought up through a subcutaneous tunnel developed along the chest and neck and behind the ear. A craniotomy is performed, the dura opened and the omentum laid on the brain. Results: Alzheimer patients can have their symptoms reversed most probably because of increased CBF following omental transposition (OT) to the brain. It is theorized that improvement in cognitive symptoms results from increased vascular and biochemical substances originating from the omentum which allow viable but deteriorating neurons to be "rescued" by augmenting neuronal energy (ATP production) that leads to cognitive improvement. Conclusion: It is possible to reverse cognitive and neurological symptoms of biopsy-proven AD patients as a result of OT to the brain.

vessels in the omental apron. The omentum is surgically lengthened and then brought up through a subcutaneous tunnel developed along the chest and neck and behind the ear. A craniotomy is performed, the dura opened and the omentum laid on the brain. Results: Alzheimer patients can have their symptoms reversed most probably because of increased CBF following omental transposition (OT) to the brain. It is theorized that improvement in cognitive symptoms results from increased vascular and biochemical substances originating from the omentum which allow viable but deteriorating neurons to be "rescued" by augmenting neuronal energy (ATP production) that leads to cognitive improvement. Conclusion: It is possible to reverse cognitive and neurological symptoms of biopsy-proven AD patients as a result of OT to the brain.

Posters

26P17

CDK5 and GSK3 are key factors in tau aggregation and tangle formation in vivo

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Cdk5 and GSK3 are implicated in tau hyperphosphorylation and pathogenesis. To examine whether phosphorylation impacts tauopathy in vivo, transgenic mice over-expressing the cdk5 activator, p25, were crossed with the JNPL3 line that over-expresses mutant (P301L) tau. JNPL3 mice accumulate insoluble, somatodendritic tau in several brain regions and develop tangles, mainly in the brainstem and spinal cord. P25/JNPL3 double transgenics showed significantly enhanced pathogenic tau formation, including an increased number of argyrophilic neurons in the brainstem and cortex relative to matched JNPL3 controls. This suggests that overactive cdk5 enhances tau aggregation and tangle formation in mice with abnormal tau. We then examined the effect of lithium-mediated GSK3 inhibition on pathogenic tau formation in the JNPL3 line. Mice with moderate tauopathy treated with LiCl for one month showed a dramatic reduction in insoluble tau, whereas younger mice with milder pathology treated for the same time showed an increase in insoluble tau. Interestingly, LiCl treatment of younger mice resulted in induced cdk5 activity and as tau in younger JNPL3 mice is more axonally distributed compared to older mice, the combination of axonal tau under the influence of enhanced cdk5 may explain the unexpected increase in insoluble tau in these animals. These results suggest that kinases such as cdk5 and GSK3 are involved in pathogenic tau formation, but other factors (tau distribution, conformational or aggregation status, or the action of other modulating agents) may impact the outcome. These findings may have significant implications for the timing of administration of kinase inhibitors for therapeutic use.

26P18

Caloric restriction in primates and practical implications for aging and age-related disease

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If the dozen major causes of death in developed countries were eliminated today, the gain in mean lifespan would only be about fifteen years. Moreover, since the quality of life in those extra years is equally, if not more, important than the quantity, it will be necessary to attack both the diseases/disabilities of aging and the underlying mechanisms. For many years, our own research focus has been on dietary caloric restriction (CR), the ONLY intervention conclusively shown to slow aging and maintain health and vitality. CR studies have spanned the evolutionary scale of experimental animal models from invertebrates to primates. Most recently, optimistic researchers have extrapolated from this work to include the possibility of CR benefits for humans. In theory, at least, there is much to be said for lowering the risk of diabetes, cardiovascular disease, cognitive deterioration, and cancers, all of which can be reduced by CR. However, in practical terms, it would be very difficult for most people to adopt the thirty to forty percent reduction in caloric intake necessary for optimal health and life prolongation effects in animals. For this reason, we introduced the concept of CR mimetics in 1998. These agents, which include potential pharmaceuticals, nutraceuticals, and other dietary supplements, exert many of the same beneficial effects as CR (including anti-disease effects such as neuroprotection and reduction in circulating insulin levels), but WITHOUT limiting food consumption.....in essence, "having one's cake and eating it too." The race to develop CR mimetics for human use has recently become extremely competitive, with many academic, government, and industrial laboratories now actively pursuing this quest. The history and current status of the field will be critically reviewed and prospects for the future realistically assessed.

26P19

New evidences on the role of cyclooxygenase isoenzymes in oxidative stress and neuronal injury following cerebral ischemia

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Three cyclooxygenase isoenzymes (COX-1, COX-2, and a recently-identified COX-1 splice variant termed COX-3) are involved in the biosynthesis of prostaglandins and thromboxanes from arachidonic acid. Brain is one of the few tissues that constitutively express COX-2 under normal conditions and several evidences suggest that COX-2 expression is related to synaptic function. Unlike COX-1, COX-2 has been shown to be rapidly and significantly increased within neurons and vascular cells after cerebral ischemia and other insults that result in neurodegeneration. COX-2 mediates ischemic brain injury by producing reactive oxygen species and toxic eicosanoids, supporting and sustaining the inflammatory response after cerebral ischemia. We emphasize the most recent findings linking COX-2 activity to increased oxidative stress and neuronal death following cerebral ischemia. A summary of the main results obtained by our research group is discussed. In addi-

tion, the role of the constitutive isoform COX-1 on ischemic cerebral damage is also discussed. A clearer understanding on the precise role of each COX isoform in cerebral ischemia could potentially influence treatment choices and care of patients suffering from stroke.

26P20

Transplantation of human neural stem cells into rat brain after hypoxy: approach to the vascular dementia and stroke treatment

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The goal of study was to reveal the possibility of human neural stem cells (HNSC) survival in the brain of rats submitted to acute hypoxic hypoxia, and their effect on recipient cognitive functions. Four animal groups passed experiments: hypoxia; hypoxia + HNSC transplantation; hypoxia + physiological solution; and the norm. Next day HNSCs, initially cultured 65 days in vitro, were transplanted into hippocampal region (volume about 3 µl, containing 1.5 x 105 cells/µl). All rats were conditioned to bilateral escape (BEC) on 4, 9 and 23 days after hypoxy. On the 27th day cryosections of rat brain were investigated by immunohistochemically. Results demonstrated that transplanted HNSCs survived in all cases. They were found in the cortex, hippocampus and partially in thalamic structures by stain with human nuclear antibodies. Expression of nestin, ß–tubulin III and vimentin had been observed in them. Transplants did not resolve from recipient tissue by glial scar. In some cases migration of HNSCs in cortex and hippocampus was observed. Behaviour tests demonstrate that HNSC transplantation does not affect activity of rats submitted to hypoxia, and significantly normalizes conditioning to BEC. HNSCs transplantation may provide a cell source to treat stroke and vascular dementia.

26P21

Abstract not available

26P22

Effects of nutritional supplementation on the aging mammalian brain: in vivo magnetic resonance spectroscopy of brain mitochondrial metabolism

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Mitochondrial decay in tissues and organs, including the human brain, can impair the cellular processes of detoxification, DNA replication and repair, osmotic balance, and the capacity to generate ATP. Despite the critical role of mitochondria in the aging process, there currently exists no protocol for non-invasive in vivo assessment of mitochondrial metabolism in the mammalian brain. With recent advances in large bore high field nuclear magnetic resonance (NMR) hardware and instrumentation, it is now possible to monitor in vivo brain metabolites with high spatial and temporal resolution. Concentrations of key mitochondrial metabolites (ATP, ADP, phosphocreatine, and inorganic phosphate) contain phosphorous (31P) and are indicators of normal or abnormal mitochondrial function. 31P and proton (1H) NMR spectroscopy at a field strength 3 Tesla will allow researchers to non-invasively acquire information on the immediate and long term changes in brain mitochondrial metabolism after ingestion of the mitochondrial cofactors alpha-lipoic acid and acetyl-l-carnitine. A dual-tuned volume coil has been custom built in order to acquire both 1H-decoupled 31P NMR spectra and high-resolution 1H and 31P NMR images. This hardware enables the registration of changes in mitochondrial function localized within brain substructures and with a temporal resolution of approximately 30 minutes. Current progress in the performance testing of the coil and preliminary results obtained from subject and control rats will be presented. After testing in rats, a similar protocol will be used with populations of healthy aging primates and humans.

Restoration of motor function in adult patients

26C1

Reorganization of cortical motor function in patients after stroke

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Changes in cortical maps are related to motor recovery in patients after stroke as an expression of neuronal plasticity, and physical rehabilitation can modulate some of these changes. To find out which are the effects of a neurological rehabilitation program in cortical motor maps in patients after stroke, we studied 2 groups of patients who suffered a cerebral ischemic stroke 1-3 years ago, with partial recovery of their motor function (Barthel index >85, modified Rankin scale =<2); all of them gave their written informed consent. One group of 5 patients was evaluated twice without any treatment; and another group of 15 was included in an intensive and integral rehabilitation program 10 hours a day for 28 days, and were evaluated before and after treatment. Besides clinical evaluation, we carried out a motor mapping procedure with transcranial magnetic stimulation (TMS) of the resting first dorsal interoseus muscle in all of them. Enlargement of motor cortical map with displacement of its center in the affected hemisphere was the most frequent finding in patients; ipsilateral motor responses to TMS was observed only in three patients. After treatment significant changes in motor area determined by TMS were seen in both hemispheres (affected and not affected (non affected: $Z=2.36$, $p=0.017$; affected: $Z=2.66$, $p=0.007$) in the group of treated patients. No significant differences were detected in the non-treated group between evaluation 1 and 2($p>0.05$). In conclusion motor recovery in patients after stroke in response to therapy is related to an enlargement of motor responses area.

26C2
Multidisciplinary approach to stroke sequels: Evaluation of efficacy of the Neurological Restorative Program

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Introduction: Stroke is a main source for impairment disability and handicap for patients. Motor sequels and speech disturbances are the most common consequences, which are liable to change, based on the brain plasticity properties. An intensive, multidisciplinary and personalized therapy program has been developed at our hospital in the last ten years to improve disability, handicap, motor and language performance in chronic stages of stroke, this program was called Neurological Restorative Program (NRP). Patient and Methods: A pilot open-label and controlled clinical trial in 29 patients with chronic sequels of stroke was conducted to assess the efficacy. This assessment included Barthel Index (BI) and Scandinavian Stroke Scale (SSS) at the beginning and after 4 weeks of treatment. The data obtained were analyzed by descriptive statistic; match pairs test and correlations variables. Results: The mean of age was 56±14.4, the mean of the disease was 2±2.43, and 72% of the patients have severe and moderate disability. Average improvement was 15% for the BI and 10% for SSS after 4 weeks of treatment. The patients with severe and moderate disability obtained the most important benefit, which was dependent of a bigger recovery of the walk. The patients with lesions of dominant hemisphere and non-hemisphere showed a bigger improvement in the SSS (16%) that was dependent of a bigger recovery of the language and capability of walk.

Round table: Restoration in neuro pediatrics

26C3
Integral approach to pervasive development disorders

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Pervasive development disorders include interesting and numerous conditions. Autism and autism/like behavior were under research in the last ten years. Based on the demonstrated concept of neuroplasticity, we applied in our clinic an integral, personalized an intensive program called Neurorestoration program. In PDD we include the diet therapy (gluten and casein-free foods), pharmacological therapy for symptoms (hyperactivity, repetitive movements and so on), a TEACH method and a speech therapy and kinesiologic therapy. We show the preliminary results of 9 children under this program.

26C4
Integral management of cerebral palsy
Gabriel Rodríguez García, Carlos Maragoto Rizo, Andrés Garcia Cruz, Lilia Esther Dulzaides, Verónica Morales, Nayoy Rodríguez Verde
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Cerebral palsy is one of the most common causes of disability in children. Two to 5 of 1000 children at school age have motor disability. Several evidence support the concept of neuroplasticity in children. In our clinic we develop a strategy that help to recover function in this patients, called Restoration Program. We discuss the step and explain how can we manage these patients. Neurorestorative program have 2 steps: evaluation according to neurological sequels and application of standard scale, the second is the pharmacological, neurosurgical and neurorehabilitation of the patients. Besides, we expose preliminary results of a blind and controlled study of 18 patients treated with this program. Further studies will tray to demonstrate this fact.

26C5
Integral Handling of Dystonia in physical rehabilitation
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Dystonia is a neurological syndrome characterized by involuntary, sustained muscle contractions that provoke trunk repetitive muscular contractions or abnormal postures. Dystonic movements can affect various muscular groups, are present at rest, and can be enhanced during voluntary movements (action dystonia). Dystonia fluctuates and its clinical expression can be modified by diverse sensorial stimuli, being frequently associated to tremor. Local or distal pain is usually associated, being one of the principal causes of discapacity. Objective: To present our experience and results with dystonic patients assisted at CIREN´s Neurology Clinic for Children. Patients and methods: A retrospective study was performed on 15 cases with the same diagnosis, which were evaluated using motor tests (gross motor) at the beginning and the end of treatment. Results: In all cases, positive changes were observed in socializing, on gross motor and in quality of life. Conclusions: The results achieved can be considered satisfactory, keeping in mind, the complexity of the disease.

Restauration of motor function in children

26C6
Comprehensive physical therapy management of young children with brain injury
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The purpose of this oral presentation is to describe the comprehensive physical therapy management of the very young child with severe neurological impairment. The subsequent motor sequelae is well documented, however, long-term physical therapy management and intervention are less understood and must be established to ensure optimal outcome and recovery. The cognitive emotional communication and behavioral issues surrounding neurological impairment significantly complicates the role of physical therapy intervention. A comprehensive approach to physical therapy will be presented for infants through adolescents. The objectives of this presentation are to: 1. Demonstrate the impact of motor sequelae on the child's daily life routine, 2. Demonstrate the integral role of the parents or caregivers on motor outcome, 3. Demonstrate various therapeutic interventions including handlign, positioning, casting and recreatonal activities to enhance motor outcomes.

26C7
Integral management of spinal cord lesion in paediatric age
Gabriel Rodríguez García, Carlos Maragoto Rizo, Andrés García Cruz, Maria de los Ángeles Ortega, Ernesto Cossio, Carlos Sánchez
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Spinal cord lesions are relative uncommon in people under 16 years. Several evidence support the concept of neuroplasticity in children. In our clinic we develop a strategy that help to recover function in this patients, called restoration program. We discuss the step and explain how can we manage these patients. Neurorestorative program have 2 steps: evaluation according to neurological sequels and application of standard scale, the second is the pharmacological, neurosurgical and neurorehabilitation of the patients. We presented our experience in 41 patients with spinal cord lesion, 18 of them with mylomeningocele, 12 with traumatic spinal cord lesion. The results of the program were measure throughout ASIA scale,

Barthel index. Further studies will tray to demonstrate this fact.

26C8

Utility of the tizanidine in the treatment of the spasticity in children with cerebral palsy

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Objective: To evaluate the effect of Tizanidine on spasticity of patients with cerebral palsy. Material and Methods: We included for randomized assignation in a double blind study 10 children's treated with Tizadine (1 mg per day) and 30 with placebo for a 6 month period and the same physical and occupational therapy scheme. Both groups were matched in age (p=0.54), weight (p=0.64), height (p=0.81), and gender (p=0.29) with basal p>0.05 in all the depend variables (spasticity Asworth scale, length of lower limbs, posture control scale, reflex scale, contractures, activity of daily living, and liver function test OGT, PGT). Results: From the second through to seventh measurement spasticity in Tizadine group reducing spasticity at 78.85% vs. 7.64% of placebo. (p=0.0001 for differences between groups and p=0.0001 for differences between time of administration) Without reported adverse effects. The liver function test remain normal. Conclusion: Tizanidine produce significant reduction of spasticity in pediatric patients

26C9

Prevalence and incidence rate of the Spinocerebellar Ataxia in Cuba

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The most frequent molecular form in Cuba is the Spinocerebellar Ataxia type 2 (SCA2). The SCA2 is caused by a trinucleotide (CAG) expansion in the coding region of the ataxin 2 gene on chromosome 12q. It is characterized by a dominant autosomic pattern of inheritance. This epidemiological study is aimed at determining the prevalence and incidence of hereditary ataxias in Cuba and comprise a descriptive study of 757 patients suffering from this disease and 7 068 at risk in the country. 1548 non-symptomatic first-degree relatives of SCA2 patients from 101 families with SCA2 were identified by polymerase chain reaction. As a result, it was found out that the rate of prevalence in Cuba is 7 cases per 100 000 inhabitants with one province having the highest rate reaching 43 cases per 100 000 inhabitants, whereas the mean incidence was 4.39 cases per 100 000 inhabitants in Holguin Province and one municipality (Cacocum) has the impressive figure of 18 cases per 100 000 inhabitants. The age group most affected was that between 30-39 years old. The prevalence in this group is about 64 cases / 100 000 inhabitants. Approximately 62 is the rate / 100 000 inhabitants of sick people living in the rural area, practically the double of the rate of prevalence in those living in Urban areas. The most frequent symptoms in the SCA2 are gait ataxia, cerebellar dysarthria, dysmetria and adiadochokinesia

26C10

Cuban national-international cooperative study on clinical, epidemiological, virological and inmunogenetical data in Multiple Sclerosis and demyelinating diseases

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Background: Multiple sclerosis (MS), optic neuromyelitis syndrome (NMO) and inflammatory myelopathies (IM) are one of the most commonly diagnosed disabling neurological disorders of young to middle-aged adults in Cuba. Objectives: To assess the epidemiological, clinical, virological and immunogenetic data of MS, NMO syndrome and IM data in the population of Cuba. Material and methods: The study population consists of patients identified with MS, ONM syndrome and IM in Cuba (11 millions inhabitants). The national health system structure in last years has changed to the organization based on family doctors who are the general practitioners. Patients will be identified from different sources. We will compare the frequency of immunogenetic markers in the patients as well as in two unrelated healthy from de same areas. The diagnostic criteria will be for Multiple Sclerosis, (McDonald et al); NMO (Wingerchuck et al) and for IM according to the primary diseases. A Case Report Form (CRF) will be

used to record the history of each patient: the personal data, ethnicity, family history, date and age at onset, type of onset, symptoms, clinical course, functional systems, the clinical localization & diagnosis, EDSS, complementary tests (blood, CSF, evoked potentials, MRI), final diagnosis and clinical evolution. The genealogical questionnaire will be performed by the genetics and, for the immunogenetical studies, appropriate patients for blood sampling will be choosing, when the family history is known. For the epidemiological study the day of the prevalence will be determinate. Results: The final data will be available by October 2004. Conclusions: This is the most expansively national cooperative study on clinical, epidemiological, immunogetical and virological data on MS and other demyelinating diseases in a Latin-American country

Posters

26P23
Evaluation of the rehabilitation method applied to patient
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The different rehabilitation methods face the challenge of presenting evidences of their effectiveness, in this work a sample of 20 paraplegic patients is presented assisted in the International Center of Health "La Pradera ", which received two months of intensive rehabilitation that it includes a program of integral physical preparation in a personalized way and in group, preparation program and training for the march with ortesis and other auxiliary devices, presports games, psychological attendance, pharmacological modulation and employments of biophysical means as ozone therapy, magneto therapy and electric stimulation, with a frequency of Monday to Friday (6 daily hours). These patients were evaluated with simple and reliable scales as index of Barthel, ambulatory index of Hauser, scale of Ashworth before and after the treatment, with the objective of measuring the effectiveness of the used rehabilitation method. 85% of the patients achieved a functional march that allowed them the independent displacement inside the house and 95% obtained a final qualification in the index of Barthel of more than 60 points, what means that these people are qualified to carry out most of the activities of the daily life

6P24
Qualitative and quantitative analysis of the gait in patient hemiplegics as consequence of cerebrovascular disease
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The work was carried out at the International Center for Neurological Restoration (CIREN) selecting a sample of ninety patients, with the objective of checking the effectiveness of the current program of physical rehabilitation on hemiplegic patients after stroke to promote the recovery of gait, as well as on its qualitative aspects. Patients received two months of physical rehabilitation while two standard evaluation tests were measured at the beginning and at the end of the treatment. The results were statistically processed using the method of two-way ANOVA and MANOVA. A biomechanical study of the gait for using the Movement Analysis System (designed and validated at the ISCF) was also carried out. The cinematic analysis of the gait cycle showed improvements in the quality of gait. The treatment resulted in very significant differences in the measured tests, appreciating an increase of the autovalidism and contributing to the social reincorporation of the patients.

26P25
The use of the Tinetti scale to evaluate the recovery of the gait in patients with static lesions of the nervous system
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This investigation was developed at the Adult Brain Static Lesions Clinic belonging to the International Center for Neurological Restoration (CIREN) in Cuba. We selected 20 patients with static lesions as consequence of stroke to evaluate the recovery gait after applying a physical restoration program designed in our institution. At the beginning and at the end of the treatment (4 weeks) the Tinetti Scale was applied. The results were processed using the Wilcoxon´s non-parametric test to verify the significance of the results. Patients were divided into two groups of ten each. The first group formed with those showing focal motor deficits (hemiplegics) and the other with different sequels (ataxias and paretic disorders). Once the treatment was concluded the effectiveness

of the program of Physical Rehabilitation was evaluated, as well as the sensibility and viability of the Tinetti Scale to evaluate the recovery of the gait and the balance in patients with Static Lesions of the Central Nervous System

26P26

Alternatives for augmenting the mobility and articulatory amplitude of fingers in patients with hemipharesis-like sequel of encephalic static lesions

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In order to achieve one of the objectives of the occupational therapy program at CIREN for treat patients with sequels of encephalic static lesions, we have elaborated a system of activities to accomplish an improvement of amplitude, and articulatory movements of the fingers in the affected hands. These activities were applied to twenty cases with common characteristics: normal intellect, traces of movements, important hemiparesis (as main motor deficit), pain in different levels of fingers and time of evolution from zero to 3 years. Two treatment periods of twenty-four days, six frequencies a week, one hour daily, were applied. Initial goniometric and active final exams were performed at the Psychomotor Integral Evaluation Laboratory (LEIS) measuring: flexion (methacarpophalangical, interphalangical and distal), abduction and adduction to compare the results before and after treatment. The cases studied improved significantly, both quantitatively and qualitatively. The results were analyzed comparing average improvement of each controlled variable using the Wilconxon Matched Pairs non-parametric test to determine the degree of significance of the final results

26P27

Treatment with occupational therapy increase mobility and articulation of shoulders in patients with sequels we to Encephalic Static Lesions

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One of the main objectives included in the program for the treatment with occupational therapy applied to patients with sequels of Encephalic Static Lesions. We elaborate a system of activities to increase the width and mobility to articulate the shoulder. This program was applied to 20 cases with the following characteristics: normal intellect, hemiplegia or hemiparesia, and time of evolution from 0 to 5 years. With this system we carried out an experimental study to demonstrate their influence during two months of treatment. We performed an initial and final goniometrical test for the flexion (L.E.I.S), extension, abduction and adduction of this articulation. The patients improved considerably according to results of statistical comparisons (Wilcoxon Matched Pairs statistical test)

26P28

Treatment with occupational therapy to increase mobility and movement degree of the wrist applied to patients with Sequels of Encephalic Static Lesions

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We present the results of the program for the treatment with occupational therapy to hemiplegics patients bearing motor sequels. A system of activities has been elaborated to increase the movement degree of the wrist. This was applied to 15 patients with common hemiplegic characteristics and motor deficits, but showing normal intellect, between 0-3 years of age. The treatment was applied one hour daily for two months. We performed initial and final goniometrical tests measuring: extension, abduction and adduction of the wrist pain in order to compare results. The patients improved considerably and we results were significant (Wilcoxon Matched Pairs test)

26P29

Training in writing for patient with right hemiparesis as a result of stroke

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Vascular brain diseases are considered to be the most frequent disorders resulting from a primary lesion of brain blood vessels. In most cases, the neurological damage is unilateral, manifesting itself in hemiplegia

or hemiparesis of contra lateral hemibody, with total or partial loss of voluntary motor ability, affecting writing among other abilities. In our work we intend to evaluate the improvement of the writing ability through a training program for the setup and automation of correct patterns of writing in hemiparetic patients due to stroke. The investigation was carried out in a sample of 10 patients between 40 and 60 years. These were subjected to an initial and a final test in writing and evaluated through a quantified scale for writing (created at Ciren's Occupational Therapy Department). During the intermediate period they received an occupational therapy rehabilitation treatment for 35 days of 1 hour daily. The treatment consisted of an initial physical preparation followed by the setting-up and automation for correct patterns of writing. The results obtained showed considerable improvements in the ability to represent basic forms of writing of patients under study, which demonstrate that the activities applied in the study were effective.

26P30

Evidences on the modulating effect of treatment in occupational rehabilitation in the neuroplastic process. A case report

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The recovery of motor functions in the hemiparetic patient through the practice of certain movements, induces plastic changes in the "cortical representation of movement", an aspect of transcendental importance which gives way to the design of therapies, aimed at facilitating the expression of certain processes, and to inhibit others. We present the treatment of a patient at the International Center of Neurological Restoration (CIREN), with a patient suffering from left hemiparesis as a sequel of a brain attack in the right medial cerebral artery territory. The patient received a rehabilitative program for 28 days as part of an intensive multifactorial neurological restoration program that included the strategy of intervention through the development of manual dynamic coordination activities. The influence of this strategy on the recovery of motor functions on patients with cerebral lesion was assesed. The motor mapping using transcranial magnetic stimulation showed positive evidences about the modulatory effect of occupational and physical therapy on the reorganization of the activity from motor function to cortical level

26P31

Kinesiolgic Handling of patients with Cerebral Palsy at CIREN Neurology Clinic for Children

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We can assert that the neurorestorative program used at clinic is valid for the handling Cerebral palsy. This condition is characterized by movement alterations and posture along with other affectations as: epilepsy, mental retardation, motor affections, etc. It is necessary to give the patients a series of activities allow the achievement of habits and motor abilities. Objective: To demonstrate the effectiveness of intensive-integral kinesiologic treatment for patients with Cerebral Palsy. Materials and methods: A sample of 20 children, diagnosed with cerebral palsy, was used. These children received kinesiologic treatment at our clinic for an average period of 84 days. They all received the neurorestorative program developed at our Center for this type of pathology. By using the Motor Gross Functional Evaluation Scale (at the beginning and end of each period) the motor evolution reached by these children was assessed. Results: Positive results were obtained in all the patients included in the sample. Conclusions: This study demonstrates the validity of the intensive and integral rehabilitation program used for therapy of Cerebral Palsy.

26P32

Efficacy in the application of the physical rehabilitation program of CIREN'S neuropediatric clinic of spasticity and increase of the motorial capacity in children with cerebral palsy

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Cerebral palsy (cp) is one of the symptoms that most frequently cause physical or mental limitations among the children's population. Its occurrence varies from 1.5 to 2.5 for 1000 born alive, without the evidence of a tendency to diminish through the years. Spasticity can be defined as a hyper-excitability of the muscular stretching reflex, whose result is an increase of "dependent speed" of the muscular tone or tonic-stretching reflex, with an exaggeration of osteondinosic reflexes. At our center there is an outstanding experience in the treatment of spastic cp. related with reached evidences in the last decade that there are neuroplastic properties during pediatric

ages. and that one of the forms of plasticity is obtained through the treatment of cortical areas; we apply an intensive multifactorial program of physical rehabilitation. To make this work come true we performed a retrospective study of two years' time, on all spastic patients with cp selecting 35 of them. It has as a main objective to evaluate the effects of the program according to their neurological conditions and functional capacities. Scales were applied before starting therapy and after 8 weeks of the rehabilitation program, where there were improvements in each of the evaluated areas. Preliminary results demonstrate that in the evaluated patients there was a diminishing of one point in Asworth's scale and the percentage of improvement increased. In a preliminary way, the efficacy of the physical rehabilitation program applied to children with cp of the spastic quadriparesia and diparetic type can be appreciated.

26P33

Ethiological characterization of a hundred patients with diagnosis of Cerebral Palsy

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The Cerebral Palsy (CP) is a non-progressive overthrough of the muscular tone, the posture and the movement, due to an aggression to the CNS in a period when the maturation and development of the System is not yet finished. A hundred children with this diagnose were studied at the CIREN for an etiological classification. The diagnose of all the patients was confirmed. The etiological agents of this pathology were established through interview to their relatives. EEG and cranial CAT were also done. The frequency distribution and the test x2 according to the used variable were analyzed. It is found that the perinatal etiology was the most frequent. Among the main etiological agents were: premature childbirth (42 cases) and low-born-weight (38 cases). The ephastic diplegia was the more frequent clinical form (56 cases), 46% of the patients presented convulsive crisis, and 36% of them had epilepsy. A significant association between these variables and the different etiological groups were not found (x2=1.611, P=0.4470; x2=0215, P=0.8982 respectively). It is concluded that EEG alterations had a real preponderance in the anterior regions (fronto-temporal) and the tomographic study showed to be a useful diagnostic method in the identification of the structural alterations in children with CP. It was also found that the periventricular leucomalacy and the cortico- subcortical atrophy are the more frequent in the newborn etiological group. It is recommended to do a correct etiological characterization of the patients with CP and a careful search of the etiological agents mainly in the patients that come to the Health Tourism Centers. These results were compared with the one reported in a national research done in Cuba in the year 2002-2003 showing similar results with those reported in this work.

26P34

Occupational Therapy Treatment for Children with Cerebral Palsy after the use of Botulinic Toxin Type-A

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Cerebral palsy (CP) is defined as “a movement and posture disorder due to a defect or lesion of the immature brain”. According to its clinical manifestations it is classified in: spastic, of cerebellose basal ganglia-type, or mixed. The application of Botulinic Toxin type-A on these patients is supposed to have therapeutic advantages over other treatments, as it permits to act directly on affected muscles without repercussion over the patients’ general status. Objective: To demonstrate the effectiveness of the use of Botulinic Toxin Type-A for allowing occupational therapy treatment. Material and Method: We performed a retrospective study where all clinical and defectologic records of the patients hospitalized at the International Center of Neurologic Restoration at the Neurology Clinic for Children, at Havana, Cuba, were revised. The sample was composed of 13 patients (8 males and 5 females) diagnosed with Spastic Cerebral Palsy. Their ages ranged from 2 to 10 years that received treatment for a period of 3 months. At the beginning and end of treatment, the modified Asworth’s Scale and Susana Matas’ Early Intervention Forms were used to evaluate the degree of spasticity. Conclusion: We appreciate a favorable evaluation as to the variation in the muscular tone and the development of new manipulative abilities. The patients with Spastic CP were benefited with the application of Botulinic Toxin Type-A and occupational therapy rehabilitation treatment, which comprises an Early Stimulation Program.

26P35

Neurophysiological Markers for the identification of modifiers genes and other factors of the clinical expression of the SCA2

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The SCA2 is a dominantly inherited cerebellar ataxia. It has a prevalence of 43 per 100 000 inhabitants in Holguín province, which is the highest one reported worldwide. 202 patients from 56 families with SCA2 and Fifty-five non- symptomatic first-degree relatives of SCA2 patients were identified by polymerase chain reaction and sequenced. First-degree relatives (sons) were studied 5 times over a period of 17 years. The Peripheral and Central Nervous System of these patients were subject to clinical studies and electrophysiological evaluation. Correlation analysis were made between the CAG repeat and various electrophysiological parameters. In 188 of them, ataxia of the gait was the first symptom of the disease, while gait ataxia with cerebellar dysarthria was present in 12 patients. All patients had ataxic gait, cerebellar dysarthria, dysmethria and dysdiadochokinesia. The main abnormality found in the patients and presymptomatic relatives was a reduction of sensory action potential as well as increase in the latency of the P40 component. The severity of these electrophysiological changes was found to be related to the CAG repeat. Our electrophysiological results agree with the loss of ganglion cells in the dorsal root ganglia. This studies have proved that while the number of CAG repetitions increase, bigger electrophysiological alterations are produced in patients, until they get to total blockade of the afferent conduction as a sign of severe neurodegeneration. It is speculated that a rise in CAG repeat might lead to increased toxicity of the SCA2 gene product which subsequently accounts for more neuronal loss in the Peripheral and Central Nervous System.

26P36

Phenotipical characterization of the Cuban SCA2

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Autosomal Dominant Cerebellar Ataxias are a heterogeneous group of neurodegenerative disorders characterized by varying degrees of brainstem and cerebellar pathology and dysfunction. Translated CAG repeat expansions encoding polyglutamine tracts are found in the six genes: SCA1, SCA2, SCA3, SCA6, SCA7 and SCA17. The Cuban SCA2 is the highest prevalence in the world. The study was performed in 553 patients from 101 families with a molecular diagnosis of SCA2. This group of patients was composed by 284 male and 269 female, onset age mean 32,75 (range 2-75). The mean time of evolution was of 14.6 years. The studied included clinical, biochemical studies and electrophysiological evaluation. All patients were gait ataxia, cerebellar dysarthria, dysmetria, adiadochokinesia, tremor, hypotonia, abnormal reflexes and slowed and limited eye movements. No patients had optic atrophy, spasticity, pigmentary retinal degeneration and endocrine dysfunctions. In patients with severe disability there was involvement of the peripheral and central nervous system regulating autonomic function, such as vasomotor disorders, constipation, urinary and rectal incontinence, tachycardia at rest, exocrine gland disorders, and a syndrome of cachexia with bulimia and sleep disorders. Biochemical finding demonstrated oxidative stress. The main abnormality found in the experimental group was the reduction of the sensitive potential amplitude, in all studied sensitive nerves. This electrophysiological characteristic continues evolving and it is more accentuated in the patients with the longer evolution time in the disease. The increase in the sensitive potential latency and the slowing of the sensitive conduction velocity were the other two abnormal characteristics also seen in this group of subjects. The analysis of the changes in the variability of the heart rhythm demonstrated a hyperfuntion of the Simpatetic Nervous System with slight hypofuntion of the Parasimpatetic.

26P37

Multidisciplinary Approach to Cerebellar Ataxias: Preliminary Report

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Cerebellar Ataxia is the second most frequent movement disorder in our Clinic. This syndrome is associated with impaired locomotion, manipulation, and communication as well as severe disability. Non-pharmacological or surgical approaches are useful to control the motor impairments or to improve functional capabilities. Conventional physical therapy,

training of gait by different techniques and isolated speech therapy has demonstrated transitory improvement but there is no report describing the effect of combined techniques to train motor performance. From June 2002 to June 2003 we conducted and open, uncontrolled, clinical trial to assess the efficacy of a multidisciplinary therapy, structured in periods of 4 weeks. The study includes 23 patients with this motor disorder. The follow up protocol define the same battery of evaluation, i.e.: the International Cerebellar Ataxia Rating Score (ICARS, WHO, 1999), the subtest for coordination and gait from an standard system for motor performance (LEIS), the Bartell Index and the SF-36 Questionnaire to asses both functional state and quality of life, at baseline and after ending each cycle of treatment. The preliminary results show an average improvement of motor performance of 31,6% in the group with higher degree of reduction in the ICARS total value for most handicapped patients and better results for the patients who extend the training for more than two periods. Bartell Index improves in about 20 %and the Qlo (Sf-36) do not reach statistical significance. In conclusion, multidisciplinary therapy can improve both motor performance and functional capabilities but further studies with more patients should be done.

26P38

Use of the International Cooperative Ataxia Rating Scale to evaluate the recovery of movement of upper limbs in patients with ataxia as a result of neurodegenerative disorders

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Ataxia is a common landmark for a group of degenerative diseases. These illnesses can have a progressive course, however, some symptoms can be alleviated by a skilled and rational treatment. This investigation has the objective of checking the effectiveness of the International Cooperative Ataxia Rating Scale, ICAR (World Neurology Federation) to measure the evolution of ataxic patients after being subjected to rehabilitation treatment. A sample of 12 patients, were treated with occupational therapy (one daily hour) for 45 days. We applied ICAR scale to evaluate movement in superior limbs. A comparison was carried out between results with this scale and coordinative capacities tests performed at the Psychomotor Integral Evaluation Laboratory (LEIS). Indicators of manual skills as: dismetry, tremor, and irregularity of movements were measured. The decrease of the punctuation of these indicators coincides with the decrease in the number of errors (evaluation indicator) of the coordinative capacities tests (LEIS). Both evaluations showed 52,9 and 27,2% of improvement respectively, with regard to initial evaluations. ICAR scale supplemented our information about the evolution of the ataxic patient.

26P39

A comparative study on the physiatric treatments of bell´s peripheral facial paralysis

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A descriptive-retrospective study was made in patients assisted at the Military Central Hospital Dr: "Luis Díaz Soto" referred by neurological services in order to evaluate the physiatric treatment effectiveness in those who underwent a 1-year-long-peripheral facial paralysis. Two groups of patients were treated; in the first one prevailed 20-year-old males (66.6%), while in the second one there were 11 individuals within 30 to 39 accounting for (36.6%). Hyperesthesia was present in 20 patients (66.6%) following retro-auricular pain and hyperacusis present in 18 and 17 cases in each age group, as major neurological signs related to the hemiface damaged. Whilst lip and eye orbicular muscles were seriously damaged in (100%) of the cases, the (90%) of them did not show muscular contraction at the beginning of the physiatric treatment, however, at the end of it (46.6%) of the cases presented "normal" contractions and only 7 individuals (23.33%) had a "poor" muscular contraction level. Ultra-frequency treatment; electric stimulus, facial massage and mimicry exercises exerted optimal effects (46.6%), while the other treatment reached only (36.6%) of effectiveness. The healing process was evident in 20 patients (66.67%) being 14 cases under the first group and only 6 in the second one. 5 patients (16.6%) of the first group and 4 of the second one were grouped under the middle-level healing process. The latter proved to have the worst diagnosis as permanent sequels occurred.

26P40

Congenital Multiple Arthogriposis. A case presentation

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Congenital Multiple Arthogriposis (CMA) is a term that defines the presence of contractures in the articulations at a child's firth. The objective of our work is the presentation of a clinical case. Material and Method. A case under pediatric age with a Congenital Multiple Arthogriposis diagnosis is presented. We applied the evaluation of motor function (at the beginning and end of neurorestorative treatment). A 4 year old female patient at nine months of pregnancy, the mother had a delayed birth work, delayed crying of the baby after birth, cyanosis and low weigh of only 2800 grams, remaining in an incubator for 10 days. The patient presented an evolutive retardation in psychomotor development in all the spheres of neurodevelopment. At the moment, the child presents significant disorders is her self-validism, especially in gross and fine motor functions, language and its psychopedagogig learning. At the physical exam, retardation in the maturation and language requisition was observed. She did not sit up; sedestation and standing up biped station were impossible. A 28-day cycle of the Neurorestorative Program was performed. She obtained some improvement of the muscular strength and superior limbs (scapular waist) and improvement of the articular amplitude of limbs and the child remains seated without support. Conclusions. The evaluation of function initially showed a 10,5% level and a final 15,2%, for a 5,3% increase in only one cycle of rehabilitative treatment.

26P41

Gait evaluation at the integral psychimotor evaluation lab on patients with motoric sequels due to cranioencephalic trauma

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Nature and environment expose us to multiple situations that can cause cranioencephalic trauma. Gait alterations are often derived from accidents, which also can hinder the normal capacities to develop motor skills impairing the patient's social life. The fundamental objective of this work was to evaluate patients with gait motor sequels caused by encephalic trauma. These evaluations were carried out in a sample of 52 patients assisted at CIREN. We have collected numerical evaluations of the patients gait problems. These evaluations were performed at the initial state and after evolution in their rehabilitation. Evaluated tests on gait were: amplitude of average steps and frequency of steps in 10 meters (amount of steps and frequency of performance). Of the 52 evaluated patients, 38 changed their gait amplitude.

26P42

Inflammation and multiple sclerosis. An integral survey from intratecal immunity and antioxidant activity

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Inflammation and oxidative stress are refereed as biological markers from different fluids in ME, looking for some evidences helping to a more integral understanding of the course of the disease. CSF analysis is a main tool in the study of these biological markers; nevertheless, no less important markers from peripheral fluids add information on the pathological events of the disease. We show an integral result of the immune-inflammatory response and oxidative stress in-patients with the diagnosis of ME and control subjects. The analysis included the evaluation of intrathecal immune response using Reibergram program, the quantitative determination of cytokines (IL 1b, TNFa) following ELISA method as well as the quantitative estimation of antioxidant activity referred to the evaluation of variables relatives to oxidative (GPX) and nitrative (ON) stress. The probable interaction between all this parameters was analyzed too. A differential Reibergram pattern of oligoclonal intrathecal fraction was observed while the antibody polyspecific response to neurotrophic viruses showed an increased AI with a differential frequency of combination to each patient. Also, ME patients showed a significant difference to TNF a and GPX activity ($p<0.05$) as well as some interaction level with the former with antioxidant nitrative activity The results underline the inflammatory mechanism in ME and tag the reactive oxygen species as cellular messenger instead a simple pathogenic agents to the disease, in add to their potentiality to evaluate the progression/ activity of the disease.

26P43

Acupuncture treatment for neurologic restoration

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Introduction: Asian Traditional Medicine (ATM) and within it Acupuncture is a diagnosis and treatment system approved by WHO and promoted by our National Public Health System. There is a growing interest on ATM efficacy in chronic affections of the CNS, as its use has been reflected in the clinical practice, and in the increasing number of investigation on this issue. Our center is one of the pioneers in incorporating this source of knowledge so much in attention care as in investigation. Objective: to describe and analyze the diagnostic, the therapeutic strategy, and the patient s´ evolution in some of the more frequent neurological affections at our Center. Development: The bases for ATM are described here, so much as to the traditional conception as from the results of present-day investigations. The diagnosis process is described here, the design of the therapeutic strategy and treatment as well as evolution of different affections are explained in detail in relation with encephalic static lesions due to occlusive cerebrovascular disease. Conclusions: Acupuncture implies an individualized and therapeutic approach based on diagnosis. there are investigation in which acupuncture seems to have a neuroprotective action and its use favor recovery of patient neurological affections. Basing ourselves on our experience, we can assert the value of its integration to the Intensive Multifactorial Rehabilitation Program.

26P44
Risk factors and carotid steno-occlusive lesions

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Cerebro – vascular disease is one of the most frequent issues of urgent neurological assistance, which constitutes a serious problem for public health. According to World Health Organization, Cerebro – vascular disease is the third cause of death and the first of disability in adults. Aterotrombosis stroke due to carotidean ateromatosis is a frequent form of presentation of such disease. We performed a prospective study on 60 patients hospitalized at the Clinic of Encephalic Static Lesions, all affected with aterotrombotic stroke, to evaluate the behavior of carotid steno – occlusive lesions as a risk factor of ictus recurrence, as well as those factors that condition this type of lesion. Data were conformed according to the medical exam practiced on these patients and other complementary studies, including carotid Doppler study of the Duplex – type. Work was performed on age and sex variables, risk factors, percentage of patients with carotidean lesions and severity of stenosis. We based ourselves on the study performed by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the lineal descriptive method was used for the registering and tabulation of the data. The results showed the presence of steno – occlusive lesions in 58.3 % of studied patients, the greatest amount corresponded to lesions above 50 % and most important risk factors were Essential Arterial Hypertension and hyperuricemia.

26P45
Spirometric alterations in patients with high spinal cord lesions

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Breathing inadequacy is a frequent complication in the medullary lesioned patient. The fundamental objective of this work was to study the results of spirometric evaluations of the Breathing Vital Capacity on patients with high medullar lesions. We use a sample of 30 medullary-lesioned patients assisted at CIREN. Tests to evaluate the breathing capacity (vital strength capacity by using a Multispiro Sensor with an international scale: ECCS). Results. After initial and final evaluations, we verified the majority of cases were not able to vary their category as to restrictions (severe, moderate, slight) of the breathing capacity, however we observed positive modifications in all cases after receiving breathing therapy.

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Response to the breathing therapy in the cervical medullary injured patient

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Objective: to Demonstrate the utility of the logopaedic therapy on the recovery of patients with Cervical Medullar Lesions. Material and method: We use a sample of 20 patients with cervical medullar lesions, assisted in the Raquimedullar Clinic in our center

during the year 2000. Patients received from 1 to 4 treatment cycles (28 days each), with a frequency of a daily hour. An initial study was carried out that included chronometric, inspirometry, numeric count, spirometry, vocalizations during an espiration and the evaluation of the possibility of coughing, to expectorate and to sneeze. DiscussioN: It was possible to establish the appropriate breathing type (costodiafragmatic). The inhaling exercises and exhaling resulted in the increase of the breathing capacity in an average of 300 cc and the appropriate coordination. The exercises for the dosage of the air during verbal emission contributed to normalize the vocal emission in 100% of the cases. The whole group of procedures allowed the variation of the rest of the controlled vital functions: 50% achieved expectoration without help; 45% achieved audible cough. Conclusion: Improved the quality of life of the patients with cervical medullary lesions can be achieved with our therapeutic program.

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Determination of the antigen HLA-DR2 15 in patients with multiple sclerosis

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The Multiple sclerosis (MS) is an inflammatory demyelinating disease of the nervous central system (SNC), characterized generally for an initial boss of exasperations and cyclical references, evolving to a chronic progressive course. Even that the MS is one of the most common neurological diseases, it is an entity of which, the reason and the pathogenesis are unknown. Is observed with major frequency in persons that carry the antigen HLA-DR2-15, by which there is presumed that the persons who carry this antigen are more capable of suffering MS. The aim of this work was to determine the above mentioned antigen in hybrid Mexicans with diagnosis of clinical MS and by magnetic resonance. Material and Methods: one determined the antigen HLA-DR, 15 with PCR (Polymerase Chain Reaction) in 8 subjects with MS. Also it was determined: age, sex, place of birth and time of residence, personal precedents of sufferings, family precedents of sufferings, nourishing habits, alcoholism, nicotine poisoning, current place of residence, trips, education, profession, socioeconomic status, anomalies of the sexual function and if they live together or not with animals. Result: The analyzed patients are 6 women(wives) and 2 men, of socioeconomic average way. Nobody has MS's familiar(family) precedents. They all have lived in cities of the country, none lived out of the country during its infancy, and they come from latitudes that do not correspond to the areas of high.