

Wednesday 25 February 2004

Plenary lecture

25A1

Growth Factor Gene Therapy in the Central Nervous System

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Growth factors influence nervous system development, functional plasticity, and responses to injury. The neurotrophin family of growth factors (NGF, BDNF, NT-3 and NT-4/5) is the most extensively characterized of nervous system growth factors. NGF prevents injury-induced and age-related degeneration of basal forebrain cholinergic neurons in rodents and primates, ameliorates spatial memory decline in rodents, and reverses declines in cholinergic systems in a mutant mouse model of amyloid overexpression. Satisfactory means of delivering neurotrophins to focal brain regions, without exposing non-targeted neurons to growth factors, is required for the practical implementation of growth factor delivery in the clinic. Gene delivery is one means of potentially meeting growth factor delivery requirements to the brain. Based upon extensive efficacy and safety data in primates, we have begun a clinical trial of growth factor gene delivery in Alzheimer's disease (AD) to test the hypotheses that 1) NGF delivery will prevent cholinergic neuronal decline in AD, and 2) that reducing the extent of cholinergic neuronal degeneration will ameliorate cognitive decline in AD.

Neuroplasticity and brain repair

25A2

Extensive cortical rewiring following brain injury

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In a previous publication, we showed that the ventral premotor cortex (PMV) underwent neurophysiological remodeling when examined a few months after injury to the primary motor cortex (M1). In the present study, we examined cortical connections of the reorganized PMV. We provide evidence that PMV substantially increased its connections with the primary somatosensory cortex (S1). These results support the hypothesis that following a cortical injury, as might occur in stroke, cortical areas distant from the injury undergo major neuronatomical reorganization, involving sprouting of corticocortical axons over long distances. Cortical rewiring over such distances has not been demonstrated previously in adult subjects, and is likely to contribute to behavioral recovery after stroke.

25A3

Motivational consolidation of LTP. Mechanisms and effects of aging

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Long-term potentiation (LTP) is a form of synaptic plasticity expressed in excitatory synapses in form of an activity-dependent increase in synaptic efficacy, which might be involved in learning, and rehabilitation. It has been shown that LTP can be modulated in its duration by emotional/motivational factors (motivational consolidation, MC). However, the mechanisms involved in such interaction are not known. We have studied this issue, and the consequences of aging on motivational reinforcement of LTP in the dentate gyrus, combining behavioral, electrophysiological, pharmacological, and biochemical methods. Results show that the amygdala is a key structure in MC. Its stimulation mimics the effect of behavioral reinforcers and its temporal or permanent inactivation blocks MC. This effect seemed to require the mediation of septal afferents. Lesioning the fimbria-fornix abolishes MC while stimulating the septum mimics the effect of behavioral reinforcers. The pharmacological studies indicate a role for noradrenergic systems. Antagonists (propranolol) block MC, while agonists (norepinephrine) cause a similar reinforcing effect. A role for cholinergic systems have also been

shown, but resulted controversial in pharmacological experiments using antagonists (atropine) or agonists (oxotremorine). MC requires protein synthesis as is completely blocked by anisomycin. Microdialysis-biochemical studies have shown an increase in acetylcholine and a reduction in norepinephrine and serotonin release at the dentate gyrus after amygdala stimulation; while behavioral reinforcing paradigms showed changes in glutamate and glycine, suggesting that different sub-systems might mediate different forms of reinforcement. Finally we have shown that aging, associated with cognitive impairments have a profound effect impairing mechanisms of motivational consolidation, induced both by a behavioral reinforce or the stimulation of the amygdala

25A4

The contribution of the basal forebrain cholinergic system to cortical plasticity associated with normal learning and functional recovery following brain injury

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Cortical plasticity, and the reorganization of cortical sensorimotor representations, has been proposed as a substrate for normal learning and recovery of function following brain injury. The physiological and cellular mechanisms responsible for cortical reorganization have not been fully elucidated. In our recent studies, we investigated the contribution of the basal forebrain cholinergic system in modulating plasticity associated with cortical motor representations. We first investigated the effects of specific basal forebrain cholinergic lesions upon cortical reorganization associated with learning a skilled motor task and addressed the functional/behavioral consequences of blocking cortical map reorganization. Results from this study demonstrate that disrupting basal forebrain cholinergic function significantly impairs, but does not abolish, acquisition of a new motor skill. Electrophysiological mapping techniques indicated that skilled motor learning was associated with a significant $30.3 \pm 7.7\%$ expansion of the caudal forelimb representation in the cortex controlling the trained limb. In animals with selective lesions of the basal forebrain cholinergic system, the expected expansion is completely blocked. Additional experiments demonstrated that the basal forebrain cholinergic lesions did not lead to deficits in i) global attention associated with performing the reaching task, ii) other forms of learning such as associative

fear conditioning or iii) general sensorimotor function. Taken together, these results support the hypothesis that the basal forebrain cholinergic system may be specifically implicated in forms of learning requiring plasticity of cortical representations.

25A5

The development and function of mammalian motoneurons following their rescue from programmed cell death by deletion of the pro-apoptotic gene Bax

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Genetic deletion of the pro-apoptotic gene Bax (Bax KO), a member of the Bcl-2 family, permanently rescues many populations of developing neurons, including motoneurons (MNs) from apoptotic programmed cell death (PCD). Because normally 50-60% of all post-mitotic embryonic MNs undergo PCD, Bax deletion results in the survival of thousands of excess neurons into postnatal and adult stages. Although this sub-population of "undead" MNs initially differentiate normally and innervate peripheral muscle targets, by perinatal/early postnatal stages, two populations of MNs can be identified: approximately one-half of all MNs appear cytologically normal and maintain innervation of target muscles, whereas the remaining sub-population ("undead" cells) have small atrophied cell bodies and peripheral axons that appear to reach no further than the ventral root or proximal sciatic nerve. We reasoned that the failure of the sub-population of "undead" MNs to grow normally and sustain muscle innervation may be due to limiting amounts of target-derived neurotrophic factors (NTFs). To test this idea, we have provided Bax KO mice with excess amounts of one potent NTF, GDNF, during either embryonic, postnatal or adult stages. GDNF but not BDNF treatment was able to prevent the atrophy and loss of innervation in Bax KO mice when available to the embryo and reversed the atrophy and denervation of the "undead" MNs when GDNF treatment occurred postnatally or in the adult. Preliminary studies suggest that following postnatal treatment with GDNF, the rescued "undead" MNs in the Bax KO mice may contribute to motor behavior. Studies are in progress to examine disease progression in a mouse model of ALS (the SOD1 mutant) when crossed with the Bax

KO (i.e. will Bax deletion or Bax deletion plus GDNF rescue the disease phenotype).

25A6

Involvement of DNA damage and repair systems in neurodegenerative process

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Preservation of genomic stability is an essential biological function. Cells engage very efficiently mechanisms involving DNA surveillance/repair proteins that work to maintaining inherited nucleotide sequence of genomic DNA over time. After DNA damage, that can arise during duplication or after genotoxic stimuli, cells activate intracellular pathways which are able to recognize the damage, to arrest cell cycle, to recruit DNA repair factors, to repair the damage or induce apoptosis. This definitely relevant process is finalized to prevent the generation and the persistence of impaired cells which may ultimately be detrimental to the organism. Very little is known about the role of DNA damage sensors and repair factors in terminally differentiated, not proliferating cells, like neurons. It is well recognized that mutation of genes related with DNA damage repair are associated with specific cancer-prone syndromes. Interestingly, many human pathological conditions with genetic defects in DNA damage responses are also characterized by neurological deficits. These neurological deficits can manifest themselves during many stages of development, suggesting an important role for DNA repair during the development and maintenance of the brain. Here I will present recent data from my group underlining the contribution to neurodegeneration of at least two transcription factors known to be involved in DNA damage sensing and repairing: the tumour suppressor gene p53 and the component of the DNA repair system MSH2. Both proteins participate in the cancer prevention machinery for the body as well as in the neurodegenerative process. Moreover, they interact with each others to orchestrate DNA repair functions.

25A7

The injection of the fraction 25-35 of amyloid- β into hippocampus of neonatal rats produces changes on cognitive, morphological and biochemical tests

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In Alzheimer's disease (AD), the neuropathological hallmarks includes extracellular deposits of β -amyloid in senile plaques, reactive astrocytes and intracellular deposits formation of neurofibrillary tangles, the loss of neuronal cells and synapses. Histopathological, behavioral and biochemical research suggest that the amyloid- β protein produce a toxic effect and start the injuries. It's unclear how or when this protein is aggregated into hippocampus and cortex. The aim of this work were evaluated the effect of 25-35 fraction A β injected into neonatal hippocampus and cortex, on learning, memory, histopathological and biochemical test. The animals used, were PD7 male and female Wistar rats pups. The pups were treated uni and bilateral with 1 μ L of 25-35A β (100 μ M) into hippocampus by stereotaxic surgery (AP=+1.5, L= \pm 2.3, P=-2.0). After twelve and fourteen weeks were evaluated spatial learning and memory in the radial maze, respectively. The program was (number trial /number opportunities. 1st day 3/8, 3/7 y 3/6, 2nd day 1/6, 3/5, 3/4 y 2/3, 3rd day 3/5, 3/4, 3/3, and for memory test 8/3. We found in female rats deficits 18% and 32% uni-bilateral lesion on spatial memory, respectively. In the hie, PASS and Bielschowsky stained we found a decrease 40% in the neuron number in CA1 region. We found until 25% reactivity antibodies to GFAP. Moreover, we found a 23% of increase for NO levels at four hours after deposit the 25-35 fraction A β . However, we didn't found amyloid deposits using the antibody to A β . Those results suggest that 25-35 A β fraction produce neurotoxicity in CA1 neuron of hippocampus and decrease the spatial memory since neonatal stage, maybe NO way.

25A8

Cerebellar and pontine norepinephrine contents after motor recovery in rats

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Motor cortex ablation induce motor deficits such as hemiplegia in rats. A spontaneous recovery that can be enhanced by either cerebellar infusion of norepinephrine (NE) or administration of NE agonists has been reported. These suggest that cerebellum (C) and pons (P), that contains the NEergic locus coeruleus, can play an important role in the recovery after motor brain injury. However, there are not data that relate directly the cerebellar and pontine NE contents with motor recovery. In order to assess the status of the NE contents in P and C after functional recovery, we trained 21 male wistar rats (280-320 g) to obtain their basal gait prints. Then animals were allocated into two groups: sham operated (n=10) and injured by right motor cortex ablation (n=11). After 6 hours post-surgery, gait prints were recorded every 6 hours during 48 hours. Subsequently, animals were decapitated and the left and right hemispheres of P and C were processed for NE extraction and HPLC analysis. The remained brain was fixed in formalin-buffer 10% in order to be stained with Nissl's method to verify the extension of the lesion. Length, width and angle were measured in the gait prints. Results showed that gait parameters were fully recovered 48 hours after performance of the lesion, while NE contents were increased in left and right P and decreased in left and right C. We conclude that recovery observed could be a result of a reorganization in the NE pathways, which also could involve to other cerebral structures.

25A9

Proechimys guyannensis rat: an animal model of resistance to epilepsy

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The potential interest of *Proechimys Guyannensis* (PG), a spiny rat living in the Amazonian region, as an animal model of anti-convulsant mechanisms prompted the investigation of the susceptibility of PG to different epileptogenic paradigms. The findings pointed out a remarkable resistance of these animals to different models of experimental epilepsy: 1) Amygdala kindling development – *Proechimys* animals demonstrated a striking resistance to reach the stage 5 of kindling. From 43 *Proechimys* rats submitted to the kindling process only 3 animals reached the stage 5. From 40 animals that did not reach the kindled state, 16 did not extended beyond stage 1, 15 from stage 2, 7 from stage 3 and 3 from stage 4. Amygdala electrical stimulations were followed by very long after-discharges, mainly in stages 1-4. 2)

Intrahippocampal kainic acid (KA) – A remarkable sensibility to intrahippocampal KA was noticed in PG. One-tenth of the KA dose usually used in Wistar rats elicited self-sustained electrographic status epilepticus in PG animals which lasted for more than 48h with increased mortality rate. On the other hand, none of the surviving animals presented spontaneous seizures in the long-term observation period (up to 120 days). Neuropathological examinations of the hippocampus of *Proechimys* animals after KA injection showed a complete neuronal destruction at the injected hippocampal formation, more pronounced in CA1/CA3 areas, and with less marked changes in the contralateral hippocampus. 3) Pilocarpine – Pilocarpine (350-380 mg/kg – doses regularly used in Wistar rats), when administered to PG induced severe tonic seizures followed by death of all animals. Dose slightly lower (300 mg/kg) than those previously mentioned was able to induce repetitive electrographic and behavioural seizures that culminated in status epilepticus 20-30 min following pilocarpine. However, pilocarpine-induced SE in PG had a shorter duration, rarely exceeding 2 hours, clearly in contrast to the 8-12 h long SE in the Wistar rat. From 60 animals injected with pilocarpine, 48 presented SE and only 2 presented some spontaneous seizures (approximately 1/week for 8 weeks) after silent periods of 60 and 66 days. The histological analysis of the brain of these 2 animals revealed neuronal loss in the CA3 area, in the hilus of the dentate gyrus (DG) and mossy fibers sprouting in the supragranular layer of DG and in the stratum radiatum of CA3. Altogether these data indicate that PG, although extremely sensitive to chemical convulsants (ie, KA and pilocarpine) and presented longer afterdischarge following electrical stimulation of the amygdala, is unable to establish a circuitry appropriated to the elaboration of spontaneous seizures, ie, epilepsy. In other terms, it seems probable that limbic circuitries, such as those found in the amygdala or the hippocampus, is highly affected by excitatory stimulation. However some "external factors" such as inputs originating in extralimbic areas seem to prevent or inhibit the formation of a true epileptic focus. Some behavioural aspects observed in PG during the 3 experimental situations described above could give some hints to justify this hypothesis. During amygdala kindling stimulation and also during the seizures observed after systemic pilocarpine or intrahippocampal KA, a cataleptic behaviour was clearly observed in PG animals characterized by opisthotonus and S tail suggesting the participation of the opiate system in this process. These findings indicate that PG rats may have natural en-

dogenuous antiepileptic mechanisms and further investigations (anatomical, biochemical, etc) need to be carried out to clarify this phenomenon.

25A10

Subacute electrical stimulation of parahippocampus and gaba system of patients with temporal lobe epilepsy

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We previously reported that subacute electrical stimulation of the parahippocampal cortex (PHC) reduces electrographic and clinical seizures in patients with intractable mesial temporal lobe epilepsy (MTLE). The present study was carried out to evaluate the GABA system and neuronal loss in PHC of patients with MTLE who received subacute electrical stimulation and presented antiepileptic effects. GABA tissue content, GABAA and benzodiazepine (BDZ) receptor levels as well as cell density were determined in PHC of patients with MTLE who received subacute electrical stimulation (130 Hz, 450 μ s, 200-400 μ A, continuously during 16-20 days) in this brain area and demonstrated a significant decrease of interictal spikes and seizures (ESAE group, n=5). Values were compared with those obtained from patients with MTLE plus electrical stimulation but without antiepileptic effects (ESWAE group, n=4) and those with MTLE in whom no electrical stimulation was applied (MTLE group, n=4). Autopsy material acquired from subjects without history of epilepsy was considered control PHC (C group, n=4 obtained from 3 subjects). ESAE group demonstrated high GABA tissue levels (219%), as well as a significantly higher cell count (58.5%) when compared with the MTLE group. Both the MTLE and ESAE groups demonstrated decreased GABAA receptor values compared to controls with no significant differences in BDZ receptor values. The present results suggest that subacute electrical stimulation of PHC electrical stimulation is more effective in patients with less severe epilepsy, and effect associated with a high GABA tissue content and a low rate of cell loss.

25A11

Localization of the epileptogenic zone in temporal lobe epilepsy by ictal V-EEG compressed spectral arrays analysis

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Objective: Localizing the seizure onset and temporal evolution of ictally dominant frequencies in patients with temporal lobe epilepsy submitted to successful Standard Anterior Lobectomy and evaluate the role of this methodology in lateralization diagnosis when Resonance Magnetic Imaging shows normal or bilateral abnormalities. Methods: The onset of the ictally dominant frequency and its temporal evolution was studied in eight patients using Compressed Spectral Arrays Analysis. Five clinically and electroencephalographic representative seizures were selected, the time period chosen was 20 s before and 16s after the electroencephalographic seizure onset. Sources of EEG activity were determined with an inverse solution method called Variable Resolution Electrical Tomography (VARETA), which provided a spline-distributed solution. We also compared the lateralization diagnosis provided by this methodology with the information showed by neurofunctional techniques. Results: In all patient an ictally dominant and consistent frequency of 5.90 ± 1.31 Hz could be determined, however in 6 of 8 patients a second dominant frequency peak between 4.24-8 Hz was found. The use of linear inverse solution will allow to control that the analyzed frequency is generated approximately within the brain region whose resection rendered all patients seizure free. The lateralization and localization of the main dominant frequency during the evaluated period around the ictal EEG onset corresponds well with the lateralization proposed by other neuroimaging techniques such a interictal/ictal SPECT, and Cho/Cr ratio measured by MRS ($x2(18)=42.5$ $p=0.009$). Conclusions: Our data suggest, that the ictally dominant frequency analysis and inverse solutions can be reliably used to detect ictal seizures onset arising in mesial temporal lobe epilepsy. Combination of ictal EEG using spectral analysis, SPECT and ERM improved the reliability of the localization and lateralization diagnosis in Temporal Lobe Epilepsy patients much more important when the Resonance Magnetic Imaging shows normal or bilateral abnormalities.

25A12

Excitatory Amino Acid Transporter Activity and Oxidative Stress

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The activity of high-affinity, sodium-dependent, glutamate transporters (EAAT 1-5) terminates synaptic transmission, prevents extracellular glutamate (Glu) from reaching excitotoxic levels, and controls synaptic spillover. EAAT regulation is rather complex involving phosphorylation/dephosphorylation states, internalization/surface expression and redox status. The possible reversal of EAAT activity has been the focus of the last decade. However such approach is impractical as it would require precise knowledge of EAAT status in order to be of therapeutic use. In addition to excessive Glu receptors activation, elevated [Glu] levels are likely to interfere with the cystine-glutamate exchange interfering with glutathione homeostasis. Riluzole, used for amyotrophic lateral sclerosis (ALS) directly increases EAAT activity and partially prevents veratridine-induced EAAT inhibition. Moreover, chlorphed, a cystine-glutamate exchange inhibitor, significantly increases EAAT activity in rat hippocampal slices in the presence of 50 μ M Glu and partially prevents the inhibitory effects of veratridine on EAAT activity. These results suggest that modulation of EAAT activity may be accomplished by separate mechanisms; directly as with riluzole and indirectly via cystine-glutamate exchange (and glutathione) dynamics.

25A13

Post-traumatic epilepsy

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Objectives: to evaluate the frequency, the clinical presentations and the therapeutic management of post traumatic seizures and post traumatic epilepsy. **Methods:** we analysed and compared the recent studies concerning early post traumatic seizures and late post traumatic epilepsy in children and adults. **Results:** Early seizures were more prevalent among subjects 0-15 years of age with severe head trauma than among individuals over 15 years of age. A majority of early seizures are focal and of those 75 % are partial motor seizures. The fits may be single or repetitive. Status epilepticus or acute repetitive seizures are more common in children than in adults. The occurrence of early seizures is an indication for repeating imaging even in case of mild head injury. EEG plays only a limited role in the evaluation of early seizures.

The incidence of late post traumatic seizures differs largely with age, type of trauma, neurological or neuroradiological signs attesting the severity of the trauma. Incidence varies from 7 % in civilian injuries to 35 % in military injuries. Conversely to early seizures, late seizures are less common and more delayed in children than in adults. The spectrum of all types of partial seizures as well as generalised seizures can be observed except bilateral myoclonias and absences. The issue of using antiepileptic drugs (AEDs) to prevent post traumatic seizures remains very controversial. Phenytoin remains the drug of choice for preventing and treating early post traumatic seizures because its efficacy and the possibility to use intravenous administration. All other AEDs can be used in treating late seizures.

25A14

Preliminary study of the anticonvulsant and anxiolytic like effects of GABA-amides derivated from n-GABA-3-(R-fenil)-2-E-propenamide in mice

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Both etiology and treatment of anxiety and epilepsy have been associated with the GABAergic system. It is well known that GABA can not cross the blood-brain barrier. A direct substitution therapy in neurological diseases attendant on GABA deficiency is therefore not possible. This report concerns the relationship between ten GABA-AMIDES synthesized from GABA and R-propenamide group in order to get major liposolubility as a fundamental strategy to develop therapeutic alternatives as anticonvulsant and anxiolytic drugs. Taconic mice maintained at standard conditions were used. GABA-AMIDES were obtained by synthesis and diazepam was tested as positive drug. Mice were injected with pentylenetetrazol, strychnine and 4-aminopyridine to record occurrence of the first episode of clonic or tonic seizures and mortality. Anxiolytic like effect was carried out on an exploration model. Effects on the coordination motor and miorelaxation were also assayed. The R-propenamide group increased liposolubility of GABA, important factor to produce effect on the central nervous system, but not a determinant factor to

produce anxiolytic like effect, because it was not observed a direct relation between pharmacological effect and log P data. Number and position of constituents appears to play an interesting roll in these pharmacological properties. It is because, two GABA-AMIDES with the chemical group metoxi on positions 2,4 or 3,4 were the most active. Agree with LD50 data, all active GABA-AMIDES were no toxic. One of them showed anticonvulsant activity. These results suggest that GABA-AMIDES have anxiolytic like effects without adverse effects, it is an advantage over drugs clinically used. Differential effect of these GABA-AMIDES could involve different mechanism of action to the GABAergic system.

25A15

CaM kinase II-Mediated Modulation of GABAA Receptor Phosphorylation in Status Epilepticus

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Calmodulin-dependent kinase II (CaM kinase II) activation has been shown to positively modulate both agonist and allosteric modulator binding, and agonist-induced anion currents. Prolonged status epilepticus (SE) has been shown to result in both inhibition of CaM kinase II activity and loss of γ -amino butyric acid (GABA) receptor function. This study was designed to determine if the SE-induced inhibition of CaM kinase II activity also resulted in loss of GABAA receptor phosphorylation. The pilocarpine rat model of SE was utilized, and SE level was determined both behaviorally and by EEG measurements by surface electrodes. Following SE or sham treatments, animals were decapitated, and crude synaptic membrane fractions isolated by differential centrifugation. Standard CaM kinase II assays were performed, GABAA receptor subunits isolated away from synaptic proteins by detergent solubilization, immunoprecipitation and resolution onto SDS-PAGE. Phosphate incorporation into GABAA receptor subunits was quantified by direct counting of resolved protein bands on either SDS-PAGE or western blots (Instant Imager, Packard Instruments). There was poor correlation between behavioral seizures and loss of kinase activity. However, all animals that progressed into continuous seizure activity measured by EEG recordings, displayed a significant loss of

kinase activity in brain fraction homogenates. In crude synaptic membrane fractions SE resulted in an approximate 41% inhibition of CaM kinase II activity towards exogenously added substrates (Autocamide 3, Calbiochem). In parallel reactions, SE resulted in approximately 40% inhibition of CaM kinase II-mediated phosphorylation of GABAA receptor $\alpha 1$ subunit (27.8 vs. 16.6 amol/mm²/min). Furthermore, SE resulted in approximately 37% inhibition of GABAA receptor $\beta 2/3$ subunits that co-precipitated with $\alpha 1$ subunit protein. Since CaM kinase II activation has been shown augment both GABAA receptor agonist and allosteric modulator binding and agonist-induced current, the data suggest a mechanism whereby SE results in loss of GABAA receptor operation. RO1-NS39970, P50-NS25630

25A16

The hyperthermia induced seizures produce transient gabaergic cell death in the hippocampus of the rat

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The febrile seizure is the most prevalent age-specific seizures in infant and young children. Whether they result in long term sequels such neuronal lost and lobe epilepsy, it is controversial. Some studies of human febrile seizure have found no adverse effects on the developing brain. However, adults with temporal lobe epilepsy have a history of prolonged febrile seizures in early life. This study is aimed to know if hyperthermia-induced seizures produced neuronal death in infant and developing brain. Infant rats were subject to hyperthermic seizures (a model of prolonged febrile seizure). Neuronal death was assessed in sections of forebrain, stained by DAPI nuclear stain, in situ terminal deoxynucleotidyl transferase dTUP nick-end labeling (TUNEL stain), annexin V antibody and electronic microscopy. We used two neuron marker, NeuN antibody by neurons and GAD65/67 antibody by GABAergic cells. The studies were carried at 24 hrs after the seizure and 5, 15, 20 and 30 days after seizures. The results showed TUNEL and annexin positive cells in hippocampal formation mainly in the CA1, CA3, and dentate

gyrus, 24 hrs after seizures and few TUNEL and annexin positive cells at 5, 15 and 20 days after seizures. The 100% tunnel positive cells, 30% colocalized with GAD65/67 positive cells and 20% colocalized with NeuN positive cells. The electronic pictures showed some apoptotic neurons with dispersed chromatin and some neurons with necrotic characteristics. These results showed the prolonged febrile seizures resulted in transient neuronal death in immature hippocampus involved death of GABAergic neurons. The loss of these neurons could be enhanced susceptibility to further limbic seizures.

25A17

Anticonvulsant valproic acid induces differentiation in human neuroblastoma cells

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Valproic acid (vpa, 2-propylpentanoic acid) is an established drug in the long-term therapy of epilepsy. During the past years, it has become evident that vPA is also associated with anti-cancer activity. The present study was aimed at evaluating the effect of sodium valproate on differentiation and proliferation in the human neuroblastoma cell lines AF8 and TS12. Neuronal differentiation was assessed by means of morphological and cytochemical parameters, i.e. neurite outgrowth and acetylcholinesterase specific activity. Growth curves and colony-forming assay were performed in order to determine cell growth inhibition. Sodium valproate induced inhibition of cell growth (demonstrated by growth curves) and reduced the colony forming ability in a dose dependent manner in both cell lines. Inhibition of cell proliferation was accompanied by morphological features of neuronal differentiation: on both cell lines valproate induced neuritogenesis in a dose dependent fashion. Biochemical differentiation was demonstrated by the increase in the acetylcholinesterase specific activity, an enzyme widely used as biochemical marker for neuronal differentiation in neuroblastoma cells. These results underline the role of HDACs inhibitors as new cancer drugs and suggest the evaluation of sodium valproate for cytodifferentiation therapy in the treatment of neuroblastoma.

Posters

25P1

Subacute electrical stimulation with antiepileptic effects modifies GABAergic system in patients with intractable temporal lobe seizures

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Experimental studies demonstrated that high frequency stimulation (HFS) of cerebral regions reduces seizures in patients with refractory temporal lobe epilepsy (TLE). We suggest that HFS in these patients induces the activation of GABAergic system. Methods: Tissue cerebral were obtained from 3 groups: control (C, n=3), TLE (n=6) and TLE with HFS (HFS, n=6). HFS consisted of continuous stimulation with biphasic pulses (duration: 0.45 sec; frequency: 130 Hz; amplitude: 0.2-0.4 mA). Ammon's horn (AH) in hippocampus and parahippocampal cortex (PC) GABAA and BZD receptors system were evaluated using autoradiographic technique. GABA and Glu content were determined by high performance liquid chromatographic analysis. Neuronal population count was performed using Nissl staining technique. Results: Concerning hippocampus TLE showed a decrease for GABAA and BZD receptor binding, tissue content of amino acids and neuronal count were similar to previous reports. HFS exhibited increased for GABAA receptor levels in AH (1086%) compared with TLE, BZD receptor binding was increased in AH compared with C (339%) and TLE (207%). GABAA receptor binding in PC (85%) exhibited decreased values compared with C, whereas BZD receptor binding did not show changes in this region. The regions AH (46%) and PC (44%) exhibited increased neuronal population count compared to TLE. There was a direct correlation between increased levels of the GABA and Glu in PC with decreased percentage of interictal spikes from the HFS. Conclusions: These results suggest that the antiepileptic effects of HFS involve increase GABAA and BZD receptors in AH, enhanced GABA and Glu amino acid levels and less neuronal loss in PC.

25P2

Inhibitory effect of 5-HT1A receptors on experimental limbic seizures in rats

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The purpose of this investigation was to evaluate the participation of 5-HT_{1A} receptors on pentylentetrazol (PTZ, 60 mg/Kg i.p.), kainic acid (KA, 10 mg/Kg i.p.) and amygdala kindling (daily 1s train of 1ms pulses at 60 Hz and 400 mA)- induced seizures in male Wistar rats, employing two agonists (8-OH-DPAT 0.01, 0.1, 1 mg/Kg and indorenate 1, 3, 10 mg/Kg) and an antagonist (WAY100635 1 mg/Kg) of these receptors. Neither of these 5-HT_{1A} ligands modified the latency to the PTZ- induced clonic-tonic seizures. However, 8-OH-DPAT enhanced twice the number of clonus induced by PTZ, effect associated with decreased mortality. On the other hand, 8-OH-DPAT and indorenate augmented the latency to the first wet dog shake (WDS) (44-58% and 67%, respectively) induced by KA, effect that was blocked with the antagonist. Additionally, 8-OH-DPAT diminished the frequency of WDS (44-59%) and generalized seizures (GS) (78-84%) during the KA- induced status epilepticus (SE). Similarly, Indorenate decreased in 69-75% the number of GS. Interestingly, WAY100635 decreased non significantly the number of WDS and GS. In addition, 8-OH-DPAT and indorenate diminished the percentage of animals with SE (63-83%). In contrast, the evaluated drugs did not alter the kindled seizure expression. Nevertheless, indorenate decreased the seizure susceptibility during the postictal depression (34%), effect reverted by WAY100635. These results suggest that 5-HT_{1A} receptors induce inhibitory effects on the KA- induced SE and during the postictal depression associated with the amygdala kindled seizures.

Supported by CONACyT (scholarship 153240).

25P3

Increase P-glycoprotein expression in several limbic brain regions in the phenytoin resistant amygdala-kindled rats

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Studies have shown that multidrug transporter P-glycoprotein (PGP-1) is overexpressed in endothelial cells (EC) from brain blood vessels of patients with refractory temporal lobe epilepsy (TLE), suggesting the role of PGP-1 in pharmacoresistance to antiepileptic drugs (AEDs). In this study we used the amygdala-kindled rats, a refractory model to AEDs, to evaluate the PGP-1 expression in limbic brain regions thought to be involved in TLE. Male Wistar rats (250-350 g) were kindled by basolateral amygdala stimulation. After kindling acquisition, four independent acute phenytoin (75 mg/kg i.p.) trials were done. Response to phenytoin was determined using a threshold after-discharge; the response was sensitive (KSEN), variable (KVAR) or resistant kindled rats (KRES). PGP-1-expression was analysed 24 h after the last kindled seizure by immunohistochemistry. Cerebral cortex, hippocampus and amygdala were examined by confocal and fluorescence microscopy. In kindled rats PGP-1 staining was observed in EC, astrocytes in hippocampus and cortex, and neurons in amygdala. In KSEN rats PGP-1 staining was observed in EC and astrocytes, whereas in KVAR rats it was found in EC, glia and neurons both in all testing areas. The KRES rats showed an increased PGP-1 expression in EC and astrocytes in cortex and hippocampus; neurons and glia in amygdala. The data indicate that PGP-1 over-expression in KVAR and KRES rats mainly in capillary endothelial and glial cells of the blood brain barrier is likely to reduce the penetration of AEDs into brain parenchyma, which could explain the variability of the response and the phenytoin resistant in this epilepsy model.

25P4

Febrile seizures modify the benzodiazepine receptor binding in the developing rat brain

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It has been described that immature brain is more susceptible to seizures than the mature one and that febrile seizures early in life may lead to epilepsy. The present study was carried out to evaluate the benzodiazepine (BDZ) receptor binding in specific brain areas of immature rats at different times. So, pups of 10

days old were placed on the floor of a 3 l glass container and an air stream was directed ~50 cm above them. Hyperthermia was maintained for 30 min, aiming for a core temperature of 41°C. Thereafter, rats were placed on a cool surface, monitored for 15 min, and then returned to their home cages for rehydration by the mothers. The control group was normothermic temperature. Animals were sacrificed by decapitation 30 min, 24 h and 20 days after seizures and their brains were used for autoradiography assay with the purpose to determine BDZ receptor binding in different brain areas. Animals sacrificed at 24 h increased BDZ receptor levels in cingulate cortex (79.55%), frontal cortex (70.51%), parietal cortex (70.53%), striatum (23.94%), basolateral amygdaloid nuclei (51.29%), central amygdaloid nuclei (32.16%), medial amygdaloid nuclei (49.88%), entorhinal cortex (35.09%) and substantia nigra, compact part (33.41%). In contrast, the groups sacrificed at 30 min and 20 days after febrile seizures did not present significant changes as compared to the control ones. The results indicate that the febrile seizures do not induce permanent BDZ changes in the immature rat brain. Moreover, it is possible that the enhanced BDZ receptor levels 24 h after febrile seizures may play a protective effect in the immature brain.

25P5

In vivo study of transgene expresión of pgfa2-GAD67 into rat hippocampus

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Decreased GABAergic inhibition has been suggested to induce hyperexcitability. The present study evaluates the potential for preventing seizure generalization by increasing local GABAergic inhibitory activity by applying of a new technique: to express the GABA-synthesizing enzyme GAD67 in the host's own astrocytes. Using a transgene in which the activity of GAD67 is under the control of a glial fibrillary acidic protein (GFAP) promoter, it confers astrocyte-specific expression. The rats were transfected with 1, 2 and 4 µg of gfa2-GAD67 (GAD) or pgfa2-Lac-Z (LZ) into hippocampus. Sham control rats (CSh) were not transfected. Three days following microinjection of the transgene, the rats received a single administration of pentylenetetrazol (PTZ, 70 mg/kg i.p.). The latency and duration of the seizures were evaluated. The hippocampal tissue samples were obtained 24 hours after of administration of PTZ and

expression of transgene was detected by RT-PCR. In the GAD group the latency to the first clonic seizure was decrease in 76% compared to CSh. Nevertheless, an increase of duration of postictal period was observed in the GAD groups. The duration of mioclonic seizures was significantly decreased in the GAD group (2 µg) (4.8 ± 0.6 sec) compared to CSh (16.14 ± 5.2 sec). The duration of tonic seizures was decreased in the GAD group (1µg) compared to CSh (28.67 ± 16.29 sec and 52.67 ± 18.8 sec, no significant). Increased expression of GAD67 was found in animals transfected with pGfa2-GAD67 transgene. The present results suggest that transfection with pGfa2-GAD67 have inhibitory effects on the PTZ-induced seizures.

25P6

Immunological disorders in epileptic patients are associated to the epileptogenic focus localization

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Clinical and experimental data support the role of immune mechanisms in the pathogenesis of epilepsy. The purpose of this work is to study the immunologic aspects in 30 epileptic patients with complex partial crisis resistant to antiepileptic drugs. The patients were evaluated by EEG-Video and they were grouped attending to epileptogenic focus localization in: temporal (n=16), lateralized (n=6) and extratemporal (n=4). We also studied a group with psychogenic epilepsy (n=4); this group was diagnosed after EEG-Video evaluation. The following immunologic evaluations have been carried out: levels of serum immunoglobulins (IgG, IgM e IgA) by radial immunodiffusion test and lymphocyte subpopulations using immuno-cytochemical methods. We measured the percent of lymphocytes T and B (CD3 and CD20), lymphocyte T helper/inductor (CD4), suppressor/cytotoxic (CD8), interleukine-2 receptor (CD25) and human leukocyte antigen (HLA-DR). The results show a significant increase of CD8+ lymphocytes ($p < 0.05$) and in the activation markers (CD25+ and HLA-DR+ cells). The evaluation of immunologic parameters applied to different group of epileptogenic focus localization showed that the increase of CD8+ lymphocytes is limited to temporal and lateralized patients ($P < 0.01$). The patients with extratemporal localization of focus and the psychogenic cases showed normal values for the evaluated immunologic

lymphocytes markers. We did not find a deficit in the humoral immunologic aspects. Taking into account that patients diagnosed as psychogenic received an antiepileptic drug treatment identical to that of the other group, the observed immunologic changes might be related with the pathogenia of certain epilepsy variants associated with the focus localization and not with the medication.

25P7

Biochemical and morphological parameters in temporal lobectomised patients

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Temporal lobe epilepsy (TLE) is one of the most frequent types of human focal epilepsy. The main goal of the present work was to examine some biochemical markers in cerebrospinal fluid (CSF) and tissue from 8 lobectomized patients (TLE) and to determine the contribution of apoptotic mechanism to epileptic process in these patients. Patients and methods: levels of amino acids were measured by HPLC method in tissue and CSF. We studied the evolutive levels of amino acids in CSF; the samples were taken before and after (1 and 6 months) surgical treatment. The CSF control group (n=10) was obtained from surgical patients who did not present neurological diseases and the tissue control group (n=4) was obtained from death not-neurological patients. The immunohistochemical evaluation was carried up using the following cellular markers: enolase, Neun, GABA and GAD 67/65. The apoptosis study was carried out for the occurrence of terminal deoxynucleotidyl transferase-mediated UTP nick end labeling (TUNEL) and Annexin-V markers. The final evaluation of cerebral tissue was done by confocal microscopy. The results showed increased levels of glutamate in cerebral tissue. There are significant decreased of glutamate levels between pre-treatment and before (6 months) treatment. Numerous TUNEL-positive cells were observed whereas Annexin V-positive cells were not significant. We found a decrease of enolase, Neun, GABA and GAD 67/65 positive cells. The results evidence there is death but not only by apoptotic phenomena but also by necrosis. The surgery process can restore the amino acids levels.

25P8

Effect of carbamazepine on convulsive activity and brain damage induced by administration of kainic Acid

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Several animal models of epilepsy have been used in order to evaluate drugs with anticonvulsant efficacy. Since administration of Kainic Acid (KA) causes physiological and anatomical disturbances similar to those in temporal lobe epilepsy of humans, the kainate treated rat has been considered as an experimental model of temporal lobe epilepsy. Carbamazepine, an antiepileptic drug, has been utilized in clinical for controlling certain types of epileptic attacks. The objective of this work was to analyze the action of carbamazepine on convulsive crisis and brain damage induced by KA administration. Experiments were carried out on chronically implanted wistar white rats. One group of five rats was treated with KA (10 mg/kg) alone, while other similar group was pretreated with carbamazepine (25 mg/kg) 30 minutes before administration of KA. Ten hour polygraphic recordings were continuously obtained under the two mentioned conditions. Under general anesthesia, brain were removed from the skull for histological analysis ten days after administration of drugs. Animals receiving administration of KA alone presented convulsive activity and brain damage. Carbamazepine pretreatment induced a slight decrement of convulsive activity but brain damage was still present.

25P9

Epilepsy surgery. A preliminary Study

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Epilepsy surgery dates back to more than two millennia and the first intervention was cranial trepanation. This pathology occurs in 0.1% of the population. Its initial medical treatment only achieves control of crisis in a 50% to 80%; the remaining 20% is consid-

ered medically untreatable and surgically remediable. Method and Material: 8 patients with refractory temporal lobe epilepsy, of 23 candidates for surgical treatment were operated in the second semester of last year. The surgical technique used was the adjusted temporal lobectomy. Transoperative Electrocorticographic recordings before and after resection were performed. A follow-up of the cases took place at one, three and six months for a posterior evaluation in a year time. Results: 88 % of operated patients are free of crisis and only one has suffered an occasional crisis. The complications were as follows: three patients with hemosiderotic meningitis, one with a transitory dysfunction of the type III cranial pair; one a diminishing of the verbal memory whereas another patient presented an inadequate syndrome of the antidiuretic hormone. Conclusions: Resective surgery of temporal lobe is the technique that we had selected for the treatment of refractory temporal epilepsy and the patient had a satisfactory evolution.

25P10

Antiepileptic effect of an extract of *Ambrosia paniculata* (Willd.) O. E. Schultz (mug-wort) in several models of experimental epilepsy

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The acute effect of *Ambrosia paniculata* in several animal models of epilepsy was studied. Intraperitoneal injections (0.01 mL x g of body weight) of a decoction of the dry leaves significantly enhanced the latency of the first convulsion and the survival time in mice injected with picrotoxin (7mg/kg) or isoniazid (210 mg/kg). Epileptic spikes were induced by topical application of penicillin -a glass electrode filled with penicillin-agar-saline mixture- and recorded in sensorimotor and occipital cortices. The plant decoction reduced significantly the spike amplitude in both sites. The same decoction was not effective against the electroshock-induced convulsions in mice. Since convulsions induced by isoniazid, picrotoxin and penicillin -differing from electroshock-implicate a disruption of the GABAergic neurotransmission, these results suggest that *Ambrosia paniculata*, like several conventional antiepileptic drugs, has a selective effect on this neurotransmitter system, that explain the traditional use of the plant in epilepsy.

25P11

Therapeutic effect of ozone in the brain ischemia: mechanism of action seems to involve hydrogen peroxide

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Brain can be considered as a main target organ for active oxygen species. It is the highest oxygen-demanding organ, has a high content of unsaturated fatty acids, a poor antioxidant defense and a high ferrum ion content. During brain ischemia, free radical reactions increase. There are some evidences suggesting that SOD activity reduces edema, mortality and infarct volumes. Other findings found links between hydrogen peroxide and selective gene expression, differentiation and neuronal plasticity. On the other hand, therapy with ozone is based in the generation of ozonids, including hydrogen peroxide. Then, ozonids could be carried by body fluids to the target tissue and exert therapeutic effects. It has been suggested that maximal effects be obtained after a period of preconditioning. In that sense, we treated Mongolian gerbils with intrarectal ozone (1 mg/Kg) for three weeks before ligation of the right carotid artery. Treatment prevents impairment of spontaneous exploratory activity, observed 7 days after ligation in oxygen-treated gerbils. In these animals a significant damage in CA1 pyramidal neurons of the right hippocampus was found, compared with the contralateral hemisphere. In another experiment, the spontaneous exploratory activity before and 7 days after 5 min bilateral carotid occlusion was tested. Ozone was administered in the six subsequent days of reperfusion. The results show that ozone treatment also prevents impairments of the spontaneous exploratory activity. These findings suggest that ozonids - particularly hydrogen peroxide - are protecting memory and learning-related synapses through improving survival of brain cells.

25P12

Three-synaptic hippocampal response during repeated electrical stimulation of entorhinal cortex in the Mongolian gerbil. Effect of clonidine

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The Mongolian gerbil (*Meriones unguiculatus*) has been considered as a model of temporal lobe epilepsy, which involves the hippocampal formation. In the present work the effect of clonidine and fenitoin on the electrophysiological response of dentate gyrus to electrical stimulation of entorhinal cortex was studied in anaesthetized gerbils (20 % urethane, 0,01 mL x g of body weight). Intracerebral electrodes - following the stereotaxic atlas of Loskota- were used. The amplitude of the population spike was obtained after averaging 20 stimuli (500 μ A, 1 Hz and 100 μ s). Clonidine (100 μ g/kg ip.) and fenitoin (10 mg/kg ip.) reduced significantly the spike amplitude 1 h after injection. In a group of animals the entorhinal cortex was stimulated with a 7 Hz frequency: a second and third population spikes appeared about 20 seconds after the starting the stimulation. These two spikes immediately disappear after coming back to the initial 1 Hz frequency and reappear again with 7 Hz stimulation; this process can be repeated several times with similar results. These spikes also disappear if the 7 Hz stimulation persists for the next 30 to 60 seconds. Fifteen minutes after clonidine injection (100 μ g/kg ip.) the primary spike was not modified, but the second spike was retarded to about 20 seconds, with an increased latency and decreased amplitude; the third spike -with very low voltage- completely disappeared. These results show a particular hippocampal hyper excitability of the seizure-sensitive gerbils and new data about the mode of action of coniine in epilepsy.

Memory and language

25B1

Functional neuroimaging of amnesic disorders

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Memory disorders constitute the most frequent accompaniments of brain damage as well as of psychiatric disorders such as posttraumatic stress disorder or schizophrenia. In fact the neural mechanisms leading to problems in encoding, consolidation, storage, and retrieval of memory may be similar in patients with psychiatric and neurological disorders. Studying a number of patients with either organic brain damage or with memory disorders due to psychic stress or trauma conditions were studied in order to elucidate brain circuits and brain mechanisms leading to mem-

ory problems. Extensive neuropsychological testing static and dynamic neuroimaging was used; in addition, data on the social and personal background were collected. Results indicate that there are a number of so-called bottleneck structures, embedded in certain neural circuits, which are crucially involved in either the formation or retrieval of information. Dysfunction of these bottleneck structures can occur as a consequence of focal brain damage or as a result of changes in the release of stress hormones (glucocorticoids). As a consequence, especially recent results from functional neuroimaging suggest strong similarities between neuronal and psychiatric patients with respect to the neural networks needed for appropriate memory processing and thereby provides important implications for the therapy of memory disorders.

25B2

Brain activity related the emotional valence of familiar faces

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Familiar faces possibly activate two different routes, related to semantic information and affective valence respectively. Evidence for these two routes (obtained from normal subjects and a prosopagnosic patient) is presented here. Two oddball paradigms using frequent unfamiliar faces as standard stimuli were used to obtain P300 in normals. The two paradigms used different infrequent targets: newly learned faces (devoid of emotional associations) in one case, and faces of close relatives in the other. Despite similar target-detection in both tasks, they elicited different P300. The P300 evoked by newly-learned faces was later in time and showed a centro-parietal distribution, whereas that obtained for faces of relatives exhibited two sub-components, an early one located at left frontopolar sites, and the same centroparietal P300 as above. These sub-components could be activated by affective and semantic knowledge respectively. This idea was supported by studies of covert face recognition in the prosopagnosic patient FE, for whom the P300 elicited by faces of (unrecognized) close relatives resembled the early frontal sub-component found in normal subjects for faces of close relatives but not for new-learning faces. An fMRI study with FE and controls showed larger brain activation for familiar than for unfamiliar faces in ventromedial

cortex. This suggests that the emotional valence of faces activates ventromedial cortex and generates the frontal P3, which possibly mediates covert recognition in FE.

25B3

Massed practice in neurorehabilitation: Intensive short-term intervention in patients with chronic aphasia leads to improved language functions and correspondent changes in brain physiology

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The aim of the present study was to collect evidence for the effectiveness of 3 different types of intensive language therapy for patients with chronic aphasia after vascular stroke (> 12 months after stroke). Evaluation criteria included neurolinguistic testing (Aachen Aphasia Test Battery) as well as questionnaires on the quality and the amount of everyday communication. Functional brain imaging was performed using magnetoencephalography (MEG), co-registered with structural magnetic resonance scans (MRI). 35 patients of three intervention groups [1. Constrained-Induced Aphasia Therapy (Pulvermüller et. al. 2001), 2. a modified version of CIAT, adding a written language module and additional training, with relatives, 3. Model-based aphasia therapy] were investigated and received 30 hours of language therapy over a period of 2 weeks. Neuropsychological testing and MEG assessment were performed before and after therapy as well as 6 months after therapy. All intervention groups improved on average. Single case analysis revealed significant improvements in about 90% of the patients. The amount of day-to-day communication was enhanced, furthermore relatives rated communicative abilities as improved. There was no difference between intervention groups concerning improvements in language performance which emphasises the importance of massed practice irrespective of treatment specific factors. Perilesional dysfunctional slow wave activity decreased in about 60% of patients that improved in the AAT, which might be an indicator of re-recruitment of these areas. An increase of perilesional activity in 9 patients with improved language functions might be explained by further segregation of dysfunctional components from the speech network with correspondent slow wave synchronisation.

25B4

Aphasia: Characterization and Treatment

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The patients who developed encephalic static lesions are liable to suffer neurolinguistic alterations like aphasia. This language impairment is determinant for the individual's quality of life, from this, the importance of the rehabilitation. Due to the complexity of this disorder and the manifestation of its clinical status, it is necessary to perform a solid and efficient approach. The objective of our investigation was to characterize a sample and to emphasize a strategy for intervention. For this reason 30 aphasic subjects were studied as sample, which were therapeutically approached and characterized using Sviatkova's modified method. This method was used as assessment scale before and after the therapeutic approach. 70% were men, 60% of them, intellectuals who had lost their work link, 67% were bearers of mixed aphasia predominantly motor impairment; and 100% willingly accepted the applied therapy. A 40% of them overcame the impressive deficit. In a 100% of patients with total lack of expressive language, functional verbal emissions appeared.

A regression analysis showed no relationship between the improvement of language skills and variables like age, professional and education level. Only the type of aphasia was relevant to the treatment, obtaining mixed aphasia patients significant scores in the final evaluation (p: 0.02).

A significant correlation (-0.37) between time from onset and the impressive and expressive final evaluation support the importance of starting the aphasia therapy early. Time from onset could be a prognostic factor for the clinical recovery.

25B5

Efficacy of the Neurological Restoration Program in the treatment of aphasic patients

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Recovery of language is one of the most complex aspects within neuropsychological practice. A reason why for a long period of time, multiple rehabilitation techniques have been emphasized. The objective of this work was to evaluate the evolution of verbal communication, performed on a sample of 14 patients with aphasic syndrome as a result of ischaemic vas-

cular lesions of the left side. These patients were submitted to the Neurological Restoration Program at CIREN's department of Logopedics. Patients were classified as to the type of diagnosed aphasia. The sample was conformed of 3 anomic, 1 global and 10 motor ones. The analysis of renderings was performed through the adaptation into Spanish of the Boston's Neuropsychological test for the evaluation of aphasias which was applied before and after treatment. Wilcoxon test was used for the comparison of treatment effectiveness between two evaluative situations in this group of patients. Results show that language abilities of chronic aphasic patients can be thus improved in a short period of time by using rehabilitation methods that have significant differences as to their comprehension capacity. The level of severity in aphasias was evaluated through Boston's severity scale which evidenced qualitative changes in patients within the same level, but not sufficient enough to pass to another range. There were no significant differences in the patient's communicative capacity in his/her daily lives.

25B6

Interferon alpha2B recombinant improved the cognitive dysfunction in patients with relapsing remitting multiple sclerosis

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Introduction: Some experimental, Phase II clinical trials and the preliminary reports of the Cuban Phase III clinical trial indicate that alphaIFN (IFN) may be useful in relapsing-remitting (RR) multiple sclerosis (MS). The reports in Cuba showed that 70% of the MS patients have cognitive dysfunction. Objective: To assess the efficacy of IFN alpha 2b recombinant in the cognitive dysfunction of RRMS. Patients and methods. 57 RRMS clinical definite (Poser et al) patients from the randomized, double blind, placebo controlled study of 225 patients with RRMS and brain MRI confirmed. Patients were randomly assigned to receive intramuscularly IFN alpha2b (HeberonR®) 10 million IU (high dose), 3 million IU (low dose) or placebo twice week for 2 years. Outcome results were blinding evaluated considering changes in the following tests: Luria, WAIS, Benton and PASAT3. Adverse events and side effects were not evaluated to maintain physician blinding. Results: The initial comparison of the groups did not show

any differences among the placebo (n= 20), low dose (n= 18) and high dose (n= 19) considering age (p= 0.234), gender, ethnic group (p= 0.012), years ill (p= 0.787), EDSS (p=0.203) and rate of relapses (p= 0.432). The Luria's Test showed an improved in the low dose group from 2.50±1.34 to 1.39±1.85 (p= 0.029) and in the high dose group from 3.22±1.89 to 2.17±1.50 (p= 0.006) vs. placebo 2.85±1.66 to 2.90±1.97 (p=0.723). The results of the Benton's test demonstrated that the low dose group had an improved from 5.50±1.10 to 6.22±1.31 (p= 0.047), in the high dose group from 4.87±1.85 to 5.78±1.35 (p= 0.005) where as in the placebo group worse from 5.15±1.76 to 5.05±2.11 (p= 0.893). The WAIS test showed the same results, the low dose group increased from 5.17±1.34 to 6.06±1.21 (p= 0.022), the high dose group from 4.56±1.38 to 5.39±1.29 (p= 0.007) and the placebo group worse from 5.25±1.25 to 5.05±1.57 (p=0.354). Finally, the PASAT3 test increased in the IFNs groups: from 45.72±10.61 to 49.94±11.68 (p= 0.015) in the low dose group, from 42.67±11.04 to 48.72±8.84 (p= 0.03) in the high dose group, but in the placebo group worse from 44.55±10.86 to 41.95±13.74 (p= 0.655). Conclusion. IFN alpha improved the cognitive dysfunction in RRMS patients. The higher dose is more beneficial.

Neuroimaging studies of reading and speech processing in dyslexia

25B7

Neuropsychological assessment of neurological patients using cognitive event-related potentials

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Assessment of neuropsychological function in brain injured, non communicative populations represents a major health care problem. Difficulties with assessment often lead to reduced/refused rehabilitative interventions because apparent incapacity is assumed to reflect genuine incapacity. It was within this context that the Innovative Methods of Assessment Program (IMAP) was developed. IMAP uses cognitive event-related potentials (ERP) in lieu of verbal/motor output as the patient's response to neuropsychological tests. In IMAP, neuropsychological tests are adapted for computer presentation and simultaneous ERP recording. Its application has been to provide neuro-

psychological assessment in non communicative patients who are impossible to assess traditionally and to monitor progress during rehabilitation. In effect, the ERP measures obtained in these standardized tests have proven to be a valid and reliable substitute for verbal/motor behaviour. Even in patients able to be assessed traditionally, IMAP has proven to be a valuable ancillary measure. Traumatic brain injury (TBI) and stroke data will be presented to demonstrate the applications and utility of IMAP. These methods have also been used to differentiate good from poor readers and in revealing the mechanisms by which a phonologically-based reading remediation program improves the reading skills of problem readers. A particularly interesting feature of these ERP changes to remediation is that they precede behavioural signs of reading improvement. The ability of cognitive ERP to monitor non communicative patients and neuroplastic changes to behavioural interventions demonstrates the value of this neuroimaging modality and its rightful place in the armamentarium of the cognitive or clinical neuroscientist.

25B8

Differences in between readers with developmental dyslexia and normal readers as revealed by MEG

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A series of studies used magnetoencephalography (MEG) to explore brain activation in adult competent readers with a history of reading problems and readers who had not experienced such problems. A study of single-word reading revealed an early abnormality in the dyslexic readers with impaired activation in the left inferior temporo-parietal area at 150 ms after stimulus presentation. Dyslexic readers also lacked activation in the middle and superior parts of the left temporal lobe between 200 and 400 ms, showing instead activation in left frontal inferior areas (Broca's area). A second study focussed on sentence reading revealed similar responses to anomalous sentence-ending words in both dyslexic and normal readers, these N400m activations being 100 ms delayed in the dyslexic group. When sentences were presented aurally, the same pattern was seen, now with a 50 ms delay in the dyslexic group. Later experiments explored the early posterior abnormality in brain activation seen in single word processing in

dyslexic readers. The area in question was found to specifically respond to letter strings. When other visual stimuli were used that gave rise to activation in partly overlapping areas, responses were found to be similar for dyslexic and normal readers, suggesting that the abnormal lack of response was functionally and not physiologically determined.

25B9

Dynamic visual processes in normal reading: implications for developmental dyslexia?

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Data from two studies relating visual task performance to contextual reading are presented. The first study investigated the relationship between contextual reading and, a) relative spatial encoding for symbol arrays, and b) central versus peripheral sensitivity to the frequency doubling illusion. In the first study, thirty school children were measured on their ability to solve a foveally-presented spatial encoding task, as well as their sensitivity to the frequency doubling illusion across the retina. Their performance in the frequency doubling and spatial encoding tasks was uncorrelated, suggesting that these tasks tap independent visual processes. Peripheral (but not central) sensitivity to frequency doubling, and spatial encoding, predicted statistically significant, independent proportions of variance in contextual reading (Neale Analysis of Reading). These effects persisted even when variance due to age, IQ, phonological skill and short-term memory was statistically accounted for. The data suggest that successful reading requires not only information about letter identity, but also at least two additional sources of information, probably related to spatial processing of words. The first is a central mechanism that may define the relative spatial location of letters within words, and the second is a peripheral mechanism that we speculate may be related to the attentional processes involved in coarse-scale localisation within a body of text. Consistent with this speculation, we found in the second study, that reading accuracy for dyslexic readers was most impaired relative to chronological- and age-matched controls when contextual material was presented in whole paragraphs, rather than line-at-a-time or word-at-a-time reading conditions.

25B10**Electrophysiological investigation of implicit and explicit phonological processing in dyslexia**

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In a series of experiments we attempted to characterize phonological impairments of dyslexic adults as indexed by auditory Event-Related Potentials (ERPs). First, we addressed the question of implicit phoneme awareness by looking at ERP correlates of phoneme expectancy during a lexical decision task involving alliterated stimuli. The P300 elicited by non-alliterated deviants in controls was not found in dyslexic adults, suggesting deficient phonological awareness in the latter. Furthermore, P300 peak amplitudes correlated significantly with individual reading scores obtained in a pre-test. Second, we used a phoneme deletion task to characterise phonological awareness when attention is devoted to phonological manipulation. The P300 observed in dyslexic adults was not significantly different from that seen in adult controls. We concluded that well-compensated dyslexic adults display normal phonological awareness when their attention is focussed on phonological manipulations. Third, we used a 2x2 paradigm developed by Connolly and Philips (1994) to compare implicit phonological processing and semantic integration stages. We presented 12 dyslexic adults and 12 matched controls with sentences ending with words of different Cloze probability regarding their meaning and their first phoneme. Preliminary results indicate that the N400 ERP modulation induced by semantic mismatch is virtually identical in dyslexic adults and controls whereas the N200 modulation induced by phonological mismatch (Phonological Mismatch Negativity) is delayed in dyslexic adults. Overall, these results suggest that well-compensated dyslexic individuals are impaired both at the level of implicit and explicit phonological processing, although the time-course of semantic processing appears to be normal.

25B11**Measuring phonological awareness and remediation in dyslexic children with ERP**

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We have discovered an ERP component called the PMN (phonological mismatch negativity) that is associated with phonological processing of spoken words. Our early studies elicited both a PMN and a N400 often making it difficult to see the PMN clearly. Two paradigms have been developed that elicit the PMN in the absence of the N400; one task involves cross modal priming while the other has adapted a clinical test (the Rosner test) involving phoneme deletion. The new paradigms not only isolate the PMN but address issues related to the nature of this response – in particular, whether the response is pre- or postlexical. Data demonstrating the PMN's prelexical nature will be presented. Also, the phoneme deletion task has been used to examine the PMN in poor readers. In this experimental protocol, participants were asked to select the correct aural representation of "Clap /klæp/ – without the /k/ sound." Good readers showed clear PMNs to incorrect choices (e.g., /kæp/, /æp/) while problem readers either failed to show PMNs or showed small and significantly delayed PMNs to the incorrect choices – a result that supports clinical findings that phonological awareness is deficient in problem readers. Recent experiments have tracked problem readers through a reading remediation program and found changes in phonological processing mechanisms as reflected by the PMN and behavioural measures. The PMN appeared during the remediation process in previous non-responders while problem readers who showed small and delayed PMNs also responded positively to remediation with increased PMN amplitude and a normalization of its latency.

Posters**25P13****Generalized dystonia is sensitive to bilateral pallidotomy: preliminary report on Neuropsychological concerns**

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Dystonia is a severe motor disease, which imposes a substantial burden on individuals and society as a whole. The majority of previous movement disorders research has been found on clinical and psychological evolution after conventional or surgical therapies in

Parkinson's disease. Considering recent evidences of usefulness of pallidotomy for treatment of dystonia, we have proposed a Neuropsychological battery (NPB) to be include in the protocol which will evaluate the efficacy and safety of this surgical approach to dystonia treatment taking into account results from the first 5 patients with generalized dystonia submitted to bilateral pallidotomy. We performed a Neuropsychological Battery (Short Neuropsychological Test in Spanish. NEUROPSI, Auditory Verbal Learning Test, and Intelligence test of Progressive Matrix for Adults. Raven) and the Hamilton Scale for Depression, before and 6, 12 months after bilateral pallidotomy. The reduced sample permits us only to report a descriptive characterization of effects, if any, of the surgical procedure on different domains of cognition and emotion. Attention and memory functions showed a positive outcome at 6 and 12 month's post-surgery (60% of patients). Additionally, depressive symptoms exhibit a marked decrement, (4/5 patients). We suggest that the observed changes were related to the improvement of patient's quality of life as well as the improvement of particular disease symptoms. It will be important include those tests that permit us subtle distinctions within different levels of health perceptions, physical / mental health, physical /mental role in social daily activities in patients.

25P14

Neuropsychological evaluation of epileptic operated patients

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The description of the patient's cognitive status is among the objectives of the neuropsychological evaluations to the epileptic population resistant to pharmacological treatment, to determine the patient's profile allowing to evaluate the risk or benefits of surgical intervention; and thus to evaluate the success in post surgical neuropsychological evolution. The objective of the present paper is to show the neuropsychological evolution related with general cognition and memory process, in a sample of 8 patients diagnosed with temporal epilepsy, which had been operated, in a post-operative period ranging from six months to a year. Results. We observed a tendency to an increase in rendering in general cognition, so much at six months as a year after surgery. In mnemonic tasks, in those cases that present a diminishing in

rendering, this cognition is presented in oral modality when it is ipsilateral to the lesion. In the visual modality the tendency is to increase rendering independently of the side of surgery. Conclusions. In a general way, the findings coincide with reports in the literature. The evolutive explorations in these patients allow us to appreciate the effects of surgery as to the quality of life and therefore, to determine the evolutive profile of epileptic patients and in this way to offer information in relation to epileptic patients candidates to surgical treatment.

25P15

Verbal Fluency in Parkinson's Disease (PD)

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Disturbances in cognitive functions in PD has been reported and defined as a frontal 'like' syndrome, including working memory dysfunction, visuospatial disorientation and a disexecutive syndrome. One of the main component of the last one is the alteration of verbal fluency. This impairment appears as a very good marker of frontal dysfunction and is easy to explore. Frontal dysfunction could promote or amplified motor behavior disturbances. We have conducted a study to define both verbal and semantic fluency in early and advanced stages of PD and to define the correlations of the degree of impairment of the verbal fluency with sociodemographics, motor performance and cognitive state. Study design includes an extense neuropsychological battery and the UPDRS score. Hundred eighteen patients were enrolled and studied between Jan 2001 to Sept 2003 and all of them complete the evaluation. Patients were stratified according age, school level, stage and severity of the disease. Phonological verbal fluency was more affected than semantic in all groups and both categories were significant altered when compared with health controls. There is a high correlation ($p < 0.005$) between age, evolution time, educational level and severity and verbal fluency. We observe a high correlation with MMSE and the Frontal Assessment Battery scores. It is very significant that verbal fluency is affected in the very early stages of the disease. Our preliminary results have some implications in the explanation of the motor behavioral and speech disturbances and in the design of rehab programs in PD.

25P16

Speech training and verbal fluency in patients with neurodegenerative diseases

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The phonologic and semantic verbal fluency tests are used to evaluate the semantic storage capacity, the information retrieval capacity and the indemnity of the executing functions. Such skills deteriorate with age according to studies carried out by others. Objective: To evaluate the impact of the therapy to improve the verbal fluency in patient with neurodegenerative diseases. Sample: 29 patients, (age between 50 and 60 years) 5 of them with cognitive impairments, 4 of them with Supranuclear palsy (PSP) and 20 with Parkinson disease. We applied the Mattis Scale (DRS), semantic and phonologic verbal fluency subtests from the FAB (frontal assessment battery) as the starting and ending control test. We applied a logopedic strategy to stimulate the verbal fluency in a cycle of 28 days of therapy. In order to analyze the verbal fluency behavior according to the different neurological diseases, we used T-Test for dependent samples and Wilcoxon Matched Pair Test. Results: In the general analysis, there is more deterioration for the phonological fluency than the semantics. The patients with Parkinson's disease presented a better evolution than the other patients, in the semantic (p:0.000089) and the phonological fluency (p:0.000356). Patients with cognitive impairments showed an improvement (p:0.043) only in the semantic fluency test after the treatment. PSP patients didn't reach statistical significance comparing their performance before and after treatment. We conclude that it's possible to improve verbal fluency in short periods of time, which favors the communication capabilities and quality of life of patients with neurodegenerative diseases.

25P17

Visuo-spatial memory and its relationship with age

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We tried to determine the relation of visuo-spatial memory to age by means of a computerized task. Fifteen pairs of figures are distributed randomly on the screen and are initially all face down. The subject can flip up only two figures at a time and must try to identify and remember where each pair is located. When a pair is flipped consecutively it disappears, the test ending when no figures are left. Dependent

measures were TIME needed to complete the test as well as the NUMBER OF FLIPS used. Independent variables were AGE, search STYLE (random or systematic) and the level of training (on a scale of 1 to 5). The sample studied comprised 33 normal subjects with an educational level higher than 12th grade, with an age range from 18 to 81. The NUMBER OF FLIPS was modeled by a generalized linear model with a Poisson link function which showed that AGE was not a significant covariate, while the amount of TRAINING, search STYLE and their interactions were. Log transformed response TIME was modeled by a linear model in which AGE, TRAINING and STYLE were all significant. For both outcome measures the systematic search STYLE, was most efficient. Thus elderly people take more time because they processed information more slowly but they can be just as efficient at this task as younger subjects using an appropriate search strategy. Consequentially this aspect of visuo-spatial memory might be trained, independently of the age of the subject.

Technologies for Restorative Neurology and Neurosurgery

25C1

Multi-modality approaches to brain imaging

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A variety of approaches to brain imaging have been developed. Some are generally anatomic such as computed tomography (CT) and magnetic resonance imaging (MRI). Others provide images of physiology and function, such as single photon emission computed tomography (SPECT), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Typically, these functional modalities do not provide the same anatomical detail as CT and MRI. Thus, approaches that combine the functional capability of SPECT, PET and fMRI with the anatomical information of CT and MRI are of great utility in brain imaging. Both hardware and software approaches have been derived to provide such multi-modality presentations. Hybrid PET-CT and SPECT-CT scanners are commercially available in the USA that provide good correlation between modalities. For clinics without such technology, software approaches are more appropriate. These involve three steps: converting both image sets to a

common computer platform, registering one of the images sets to the other and displaying the results. The registration can be performed either manually or automatically. In turn, there are three approaches used for automatic image registration: fiducial or point-based, surface-based or voxel-based methods. Once the image sets have been registered to each other, an appropriate interface must be used for the display and analysis of these multi-modality image sets. In this presentation, we will review both hardware and software approaches to image fusion as well as the optimal ways to display and analyze these data sets.

25C2

EEG/MEG Tomography and beyond: Multimodality Image Fusion

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During the past decade our group has contributed to the establishment of an EEG/MEG tomography. The inherent non-uniqueness of the electrophysiological Inverse Problem has been overcome by the use of anatomical information obtained by the structural MRI, as well as by imposing variable smoothness constraints (VARETA). The resulting neuroimaging modality has a spatial resolution in the order of several mm. and an unlimited temporal resolution. It does suffer, however, from a depth bias that emphasizes sources nearer the sensors. This bias can be overcome to a certain degree by the use of Statistical Parametric Mapping techniques for electrophysiological tomography, also developed at the Cuban Neuroscience Center. In particular a frequency domain application of these methods has led to the development of Tomographic qEEG (qEEG). Several examples show the potential clinical usefulness of this method in the evaluation of stroke patients and in looking for early signs of Alzheimer's disease. It is documented in both examples that significant increases of specificity and sensitivity of Tomographic over Topographic analysis can be obtained. Further improvements in EEG/MEG tomography will come from two directions: inclusion of anatomical connectivity information obtained from Diffusion Tensor MRI and of functional information obtained by fMRI. The direct and inverse problems for these new sources of information are discussed. Image Fusion is achievable by Bayesian statistical methods that are outlined. A particularly favorable situation occurs when joint EEG/fMRI recordings are available. In this case a dynamic image fusion method is possible.

The applications of this method are shown for an analysis of the alpha rhythm. It is discussed that multimodality image fusion will provide a new generation of Neuroimages with higher temporal and spatial resolution than any current technique.

25C3

Control of EMG signals for computer-based communication systems

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Computer-based communication systems greatly improve the quality of life of persons with severe motor impairments, like locked-in or quadriplegic patients. In EMG-based interfaces, the user controls the computer by means of myoelectric signals. This non-invasive technique is applicable in any patient with some preserved motor function, e.g., eye movements. However, the efficiency (throughput) of the communication system directly depends on the controllability of the EMG signals. We studied the controllability of EMG signals in face and hand muscles with 40 young healthy volunteers. A visual feedback indicated the amplitude of the EMG signal in real time. The subject had to reach a target (i.e., an interval of amplitude) in either of two modalities: impulsion or sustained, i.e., the subject had to stabilize the signal within the target interval of amplitudes for a duration of 1 s. Two levels of precision were used by dividing the range of amplitudes in 4 intervals (low precision) or 8 intervals (high precision). No significant difference of speed or accuracy was found between facial and distal muscles. However, accuracy was significantly lower for intermediate amplitudes relative to the smallest or highest amplitudes. Finally, a clear tradeoff between speed and accuracy was observed across response modalities: the sustained modality was associated with slow but highly accurate responses whereas the impulsion modality allowed faster but less precise responses. The average speed and error rate allow calculating a theoretical upper bound for text entry with EMG interfaces of 2.5 bit/s, i.e., above 15 words/minute.

25C4**Automatic system for three-dimensional anatomic-physiological correlation during stereotactic and functional neurosurgery**

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This paper describes the automatic 3D-graphic possibilities that are offered by a PC-based software to facilitate the anatomic-physiological targeting during stereotactic and functional neurosurgery, using deep brain recording. This software has been developed to substitute complex electronic equipment with a PC for deep brain electrical activity recording, display and processing. It also allows greater possibilities for on-line graphic analysis, automatic management of the recorded information and flexibility to implement different forms of signal analysis. This software has been made using a combination of two programming languages. A low level one (Assembler) was used for the on-line working modules. For the rest of the system a high level language (Pascal) and its compiler were used. The system uses an analog-digital converter card and allows to record, show, process and store up to two simultaneous signals with 12 bits accuracy. The software can also automatically show a 2D- and/or 3D-representation of the electrode track with the superimposed electrophysiological findings, and the corresponding sagittal, coronal and axial view of a brain anatomic atlas, after its automatic scaling for each patient. It allows graphic analysis of the recorded information and its correlation with the anatomy, even during the surgical procedure. This software has already been successfully used in Spain, Chile and Cuba in more than 400 neurosurgeries, allowing to increase the targeting accuracy and safety.

25C5**A method for accurate determination of the first target in functional neurosurgery**

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Accuracy in target determination is one of the fundamental requirements of any surgical planning sys-

tems. We developed a system for intraoperative planning of frame-based stereotactic neurosurgery that integrates, in one complete module, all of the basic facilities that are present in other advanced programs. All of the techniques used for our system were optimized in order to increase the performance and precision of the system, especially facilities involved in functional neurosurgery. Based on the vector approach used for calculation of stereotactic coordinates we developed an algorithm for correction of first target in functional neurosurgery. A vector method can be used to determine a frame-independent coordinated system from the coordinates of anterior commissure (AC), the posterior commissure (PC) and another point located on the interhemispherical line, considering the intercommissural middle point as origin. For any point in the images we have AC/PC-based coordinates independently of its frame-based coordinates. Likewise this correction can be used for calculations of target's trajectory. Due to its generality this corrective procedure can be used with any stereotactic frame included in our planning system and overcomes geometrical errors that are introduced when the intercommissural line and interhemisphere plane are not parallel and orthogonal to transaxial images respectively.

Nuclear Neuroscience Symposium**25C6****Mild cognitive impairment and brain SPECT**

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There is an imperative need to develop sensitive biomarkers as adjuncts to current clinical and neuropsychological tests to improve detection of early brain changes suggestive of Alzheimer's disease (AD), particularly as new agents to delay the onset of dementia become available. The subtle onset of AD suggests that most of the patients pass through a prodromal phase of mild cognitive impairment (MCI) before dementia is diagnosed. Previous neuroimaging studies have revealed that structural and functional changes are already present in this stage of the disease. Based on basal SPECT data, longitudinal studies have shown acceptable percent of correctly identified MCI subjects who progressed to AD. An ongoing research project of our group is presented in this conference. This project is intended to address if the acetazolamide test by SPECT can improve prelini-

cal prediction of AD. The hypothesis is based on: 1) previous data strongly support that sporadic AD is first provoked by premorbid vascular-related events; and 2) other reports show preserved vascular reserve, but not normal, in patients with probable AD. The first results of the project are presented.

25C7

Toward clinical application of neuroactivation probes with SPECT

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The review presents neuroimaging studies which explored the functional anatomy of a variety of cognitive processes represented by the prefrontal cortex (PFC). Overall, these studies demonstrated that standard prefrontal neuroactivation tasks recruit a widely distributed network within the brain of which the PFC consistently forms a part. As such, these results are in keeping with the notion that executive functions within the PFC rely not only on anterior (mainly prefrontal) brain areas, but also depend on posterior (mainly parietal) brain regions. Moreover, intervention of similar brain regions in a large number of different executive tasks suggests that higher-level cognitive functions may best be understood in terms of an interactive network of specialized anterior as well as posterior brain regions.

25C8

Radionuclides in nuclear neurology

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This conference is a review of the sources of the most commonly used radionuclides in Nuclear Neurology, the state and evolution of the market in this field and the possibilities of the local supply of these products. It is also considered the installation and operation of a cyclotron as the most promising and feasible source of radionuclides in this area. A comparison of the existing imaging technologies is given in the framework of the available radionuclides, including a brief summary of the most commonly used radiopharmaceuticals for diagnostic and therapeutics in this particular field. The presentation shows the view of the Cuban national producer of radiopharmaceuticals and its necessary interaction with the final user.

25C9

Analysis of brain SPECT studies

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Nowadays, with the most powerful computers and software packages available, the analysis of brain images is not the most difficult part of a brain SPECT study. The most difficult questions are encountered before the actual analysis, namely while choosing the study design, the tracer, the acquisition protocol, the collimators, the reconstruction algorithms, the physical processes to correct for, the existence of confounding factors, the inclusion criteria, etc. Many problems during the analysis of brain images may be avoided by carefully designed study. Therefore, we first give an overview of the most important issues to be solved before the data acquisition. Once the data have been acquired and the images are reconstructed, one can start analysing the images. In order to focus our attention, only two important and well known software packages are discussed, being "Statistical Parametric Mapping" (SPM, Wellcome Department of Imaging Neuroscience, UCL, London, UK) and "Brain Registration and Analysis of SPECT Studies" (BRASS, Nuclear Diagnostics Ltd, Northfleet, UK). The former is designed to address most research questions concerning brain studies, while the latter has been optimised for use in a routine clinical setting. Both the idea behind each package and their use will be covered.

Posters

25P18

Topographic evaluation of bilateral subthalamotomy using an MRI-based analysis

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The result of stereotactic ablative surgery is critically dependent of the exactitude of the lesion localization. The aim of this work was to develop a methodology to obtain a precise anatomic localization of stereotactic lesions and perform an accurate audit of the precision of our stereotactic target placement. Methods: Postoperative MRI studies of 15 parkinsonian patients submitted to bilateral subthalamotomy were examined. Each MRI study was transformed into Talairach space using an automatic algorithm to de-

termine non-linear transformation between the individual volumes and a model brain. Individual and average X, Y and Z coordinates of center of gravity (COG) of the lesions were determined for each hemisphere, and used as input into the software Talairach Daemon (TD), which shows the anatomical region labels corresponding to the calculated x-y-z coordinates. Results: According to TD, average coordinates in Talairach space correspond with subthalamic nucleus. Differences in lesion location between hemispheres did not achieve statistical significance. Conclusions: This study has proved that surgical methodology applied at CIREN is accurate enough for determining optimal lesion localization. This type of analysis may also be used to examine the results of other types of stereotactic procedures in the subcortical nuclei. As well, careful anatomic analysis can be useful in demonstrating the characteristics of lesion resulting in known complications of this surgery.

25P19

Subthalamic nucleus targeting and spatial variability

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The goal of this study was to assess the effectiveness of anatomic localization (EAL) of the subthalamic nucleus (STN) and to analyze the contralateral symmetry (SCN). The authors conducted a retrospective analysis of 11 consecutive patients submitted to bilateral subthalamotomy with ablative lesioning. To assess EAL - the percentage so much of first trajectory (p1) as to the total of trajectories (pt) that hit the target - the rest of subthalamic nucleus average distance (d) was calculated. The anatomic localization error (e) is determined as a difference between first trajectory coordinates with those of medial determined nucleus point, through electrophysiological data as to the statistical significance of this error. SCN is analyzed by contrasting equality hypothesis at the nucleus maximum height along both sides of a trajectory, average electrophysiological position center and spatial distribution of all intranuclear recordings found in each hemisphere in all patients. The pi, pt and d obtained values were 86.36%, 86.13% and 1.41±1.01 mm respectively. The e value was greater in anteroposterior direction of 1.11±0.83mm without statistical significance. The average number of re-

corded trajectories for the first procedure was 6.45 and 6 for the second. The asymmetry of contralateral nucleus was not significant. An indirect method with CT brain images and a new electrophysiological mapping method with a multiunit recording for first and second nucleus is safe enough and it yields a high effectiveness in anatomic and functional nucleus localization. The nuclei of a same patient are symmetrical. There is little space variability among patients non-related to the differences in the intercommisural distance.

25P20

Dynamics of digital EEG pattern in operated patients with Moyamoya disease

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Purpose of study. Our goals were investigate a different parameters in 12 patients with Moyamoya disease. The treatment of Moyamoya disease (nonatherosclerotic obstructive vascular disease) remains difficult problem in neurology and neurosurgery. Material and methods. The clinical picture demonstrated transient ischemic attacks (TIA; 6 cases), transient optical complications (2 cases) and epileptiform paroxysms (4 patients). All patients (male 7, female – 5) were underwent surgical treatment. Mean age 34 years. We performed our method of surgical revascularisation of brain – arterioencephaloanastomosis (unilateral 8 cases and 4 bilateral). All operations were performed after long unsuccessful medical treatment for reduce cerebral ischemia. Diagnostic methods till and after surgery included transcranial Doppler (TCD), magnetic resonance angiography (MRA), and digital EEG examinations with standard functional tests (fotostimulation, hyperventilation). We performed EEG at the time 3-6-12 months after surgical treatment. Results. In preoperative period EEG registered seizure pattern, slow activity, three Hz spike-slow waves and photo-paroxysmal response. After surgery all patients showed in EEG alpha rhythm and alpha variant rhythms; paroxysmal activity absent. Therefore, in follow-up period the results of surgery were beneficial. Conclusion. We support surgical treatment lead to reduce cerebral hypoxia/ischemia and neurological deficit. It can explain better of brain. Dynamic EEG data might indicate that arterioencephaloanastomosis is effective treatment of Moyamoya disease.

25P21**Diffusion Tensor in Magnetic Resonance Imaging and its applications**

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It is presented a review of methods based on Diffusion Tensor Magnetic Resonance Imaging for the estimation of neural fiber mean directions in each voxel of the brain. Two indexes calculated from diffusion tensor are mentioned briefly which help in tissue segmentation and disease detection. Also, it is made a review of the algorithms used in calculating neural fibers and probabilistic paths taking into account anisotropical tensor geometrical shape. Those algorithms are based on the methods mentioned before. Finally, a brief discussion of the potential application of such fiber pathways in the inference of anatomic connectivity measures between different zones in the brain is done.

25P25**Transcranial doppler sonography in brain death diagnosis**

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The Transcranial Doppler (TCD) is a useful technique to confirm cerebral blood flow alterations. Objective: To evaluate the TCD usefulness in the brain death diagnosis. Method: A prospective study was made in 21 neurocritical patients admitted in the Intensive Care Unit of the Centro de Investigaciones Medico Quirúrgicas, in the year 2002. TCD pattern were collected and if clinical brain death was present. Sensibility, specificity, and Kappa index was calculated. Results: Clinical brain death was present in 10 cases. The TCD patterns most frequently in these cases were oscillating blood flow (reverberating flow) in 5 cases, and short systolic spikes in 4 cases. The relationship between this TCD pattern and clinical brain death were 100% in sensibility and specificity. Conclusions: The TCD method is useful and reliable to determine the absent cerebral blood flow.

25P23**Model for calculation of temperature distribution in resistive magnetic resonance scanner**

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The magnetic resonance (MR) scanners are medical equipment for imaging diagnostic of central nervous system illnesses mainly: cerebral infarcts, cortical and cerebral atrophies, skull traumatism, some degenerative illnesses. These equipment works due to the action of magnetic field on the tissues. When a resistive magnet is used for generation of magnetic field the intensity, homogeneity and temporary stability of the magnetic field define the clinical images quality. The thermal behavior of winding and therefore, the characteristics of the magnet and of their cooling system exercises decisive influence on these magnetic field parameters. In this paper a physical-mathematical model for the thermal process description of resistive MR scanners is presented. The model was applied to Cuban equipment, and the analysis of the temperature distribution in winding facilitated a valuation of constructive parameters and design of the cooling system heat exchangers.

The model was developed according to the laws of the thermodynamic and the heat transfer. Their effectiveness was proven for a level of significance of 0.05. The temperature maps of the magnet were obtained. The maximum temperatures to nominal electric current are around the 146°C. These temperatures are not dangerous for the materials of winding. The heat transfer in radial sense is significantly bigger than in axial one. This aspect should consider as design approach for future equipments. The winding is compact and the heat exchangers were assembling appropriately.

25P24**Age-related perfusion changes by brain SPECT in healthy subjects**

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This study characterizes the effects of aging on brain perfusion using HMPAO – SPECT in healthy subjects. The study population consisted of 10 women and 19 men with age range of 20 - 79 y. Their past medical histories, physical examinations, and laboratory screening tests were normal. The sample was divided in three age groups (GI: 20 – 39 y; GII: 40 – 59 y; GIII 60 – 79 y). HMPAO – SPECT scans of the brain were performed with a standardized acquisi-

tion and processing protocol on a single-head camera equipped with high-resolution collimator. A Butterworth filter and a correction for uniform attenuation were applied after back projection reconstruction. Brain perfusion evaluation was performed both visually and by a relative quantification method using the cerebellum as the reference region. To that end, cortical bilateral and regular regions of interest (ROIs) were drawn on adjacent SPECT slices. Group comparison was performed using ANOVA. Brain perfusion decreased significantly with age in frontal and parietal regions (groups GII and GIII less than GI, $p < 0.01$). These results are in agreement with previous reports. As a conclusion, aging significantly affects brain perfusion in healthy subjects. It decreases in parietal and frontal region and it seem to occur after thirties. The brain perfusion appears to remain relatively stable throughout middle age.

25P25

Contribution of brain SPECT to the presurgical evaluation of temporal lobe epilepsy: CIREN experience

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The aim of this study is to show the contribution of interictal and ictal brain SPECT to localize the epileptogenic zone in patients with Temporal Lobe epilepsy (TLE) submitted to surgery at CIREN. As part of presurgical evaluation, interictal and ictal SPECT scans were performed to assess cerebral perfusion in 18 patients with pharmacoresistant TLE. A double-head gamma camera was used (SMV DST Xli, SMV International) connected to a workstation IBM RISC System 6000, provided with a processing system Vision 5.0 (SMV America, Inc). After visual analysis, cerebellar perfusion ratios were calculated on irregular regions of interest (ROI), drawn on lateral and mesial lobe and basal ganglia. Also, asymmetry indexes were calculated between homologous ROIs (including the cerebellum). Visual analysis detected focal hypoperfusion involving the whole temporal lobe in 100% of the patients. The hypoperfusion was extended into the frontal lobe in 50% of them. Quantitative analysis using the ROIs method showed that the changes in lateral temporal perfusion were the most suitable lateralizing indicator of the seizure. It was ipsilateral to the epileptogenic zone defined by surgery in 87.4 % ($p < 0.0001$). Interhemispheric asymmetry indexes of 13 % and 28 % were found in left and right TLE, respectively. Ictal SPECT showed

mesiolateral temporal lobe hyperperfusion ipsilateral to the epileptogenic zone in all patients and also demonstrated contralateral cerebellar activation in 25 % of them. In addition ipsilateral basal ganglia activation was observed in 75 %. Interictal SPECT defined an extensive functional deficit zone in TLE patients. Ictal and interictal SPECT changes are a reliable lateralizing indicator of epileptogenic zone in TLE.

25P26

Epidermal Growth Factor receptor hr-3 monoclonal antibodies radiolabelled with rhenium-188 in the adjuvant treatment of high grade astrocytomas

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Intralesional radioimmunotherapy (RAIT) may improve the management of malignant gliomas whose prognosis is, at present, very poor. Current treatment modalities cannot prevent tumor recurrence. This study was performed to evaluate toxicity, dosimetry, biodistribution and clinical efficacy of the h-R3 monoclonal antibodies labeled with Re-188 after intralesional RAIT in cases of malignant gliomas. Following surgical operations, radiotherapy and chemotherapy, 4 patients with recurrent malignant gliomas, 2 with anaplastic astrocytomas and 2 with glioblastoma underwent RAIT with h-R3 antibodies raised against epidermal growth factor receptor (EGFr) labeled with rhenium-188 in different escalating doses. The dosimetry and biodistribution had been performed using Single Photon Emission Computerized Tomography (SPECT), whole body and quantification studies. In these patients the follow-up study period ranged from 6 to 12 months. No significant life-threatening toxicities were observed. Acute side effects following treatment were seizures and worsening of pre-existing neurological symptoms. Late side effects were radio necrosis in 1 case. Objective response consisted in one patient with tumor stabilizations during 6 months and two with complete remissions. RAIT is safe and an effective procedure, mainly in cases with peripheral and reduced tumor border. Further investigations should focus on optimizing the dose delivery to the surrounding tissue and should be set up to confirm these findings.

25P27**Brain perfusion SPECT in schizophrenic patients with negative symptoms**

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One of the polemic aspects in schizophrenia deals with the Cerebral Blood Flow (CBF) in patients with negative symptoms. The most frequent finding is frontal hypoperfusion. In the present study we intended to evaluate CBF by SPECT in a relatively homogenous sample of schizophrenic patients with negative symptoms and compare them to a control group of healthy subjects, using a semiquantitative methodology for CBF quantification. Ten male healthy volunteers and 15 male patients with a clinical diagnosis of residual schizophrenia (295.60 points according to the DSM-IV criteria) and without inability for communication were studied. Their ages ranged between 32 and 50 years (mean 44.6 years), and the evolution time, between 10 and 24 years (mean 16 years). All patients were being treated with Haloperidol and Fluofenazine. The positive and negative symptom scale (PANSS) was used for the evaluation of these symptoms. In each patient or healthy subject an evaluation of the CBF by ^{99m}Tc-HMPAO SPECT was performed both visually and by a relative quantification method using the cerebellum as the reference region. Cortical bilateral and regular regions of interest (ROIs) were drawn on SPECT slices. An index of asymmetry was also calculated (IA) for every pair of homologous ROIs. The results showed significant differences (less CBF in the group of patients) bilaterally in the frontal and temporal regions ($p < 0.05$). In the group of patients, the asymmetries found were not different from those observed in the normal group. As a conclusion, a symmetrical bilateral decrease in the frontal and temporal lobes seems to characterize schizophrenic patients with negative symptoms.

25P28**Dose assessment and individual monitoring of workers and public during the first phase of the clinical study for the radioimmunotherapy of cerebral tumors in Cuba**

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Taking into account the international experience and the approval of the regulatory authorities, last year it began in the Republic of Cuba the first phase of the clinical research of the humanized monoclonal antibody h-R3 labeled with ¹⁸⁸Re, for radio-immune therapy (RIT) of cerebral tumors. This monoclonal antibody was obtained in the country and it is required to evaluate its toxicity, biodistribution and internal radiation dosimetry. Five groups of three patients of each one with an administered activity from 0.37 GBq to 1.1 GBq are considered. The aim of this work is to assess workers and public doses for this research and to compare projected doses with the first results related to the individual monitoring. The contribution to the total effective dose and equivalent dose in extremities are calculated with the code Micro shield Version 4.0 by each activity level, operation and total quantity of patients, considering the results of the radioactive decay calculation for ¹⁸⁸Re. It is demonstrated that individual doses are acceptable and lower than world average effective annual dose of natural radiation background (2.4 mSv), because for the operations of more risk are considered the use of individual protection means. Nevertheless, it is identified that nurses are the most exposed. The projected maximum equivalent dose to hands is 3 mSv and it belongs to the neurosurgeon. Five workers and public (four individuals) are monitoring with direct reading dosimeters DOSICARD and TLD for extremities. The conservative assumptions in the assessment and the compliance with established safety procedures determine that the registered doses are lower than those were projected.

25P29**Relative indexes of brain perfusion by ^{99m}Tc HMPAO SPECT utilizing a mean value of the visual cortex to the cerebellum ratio derived from normal subjects**

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Previous results show the cerebellum (CER) is the best reference to calculate relative indexes of brain perfusion (IP) by HMPAO SPECT. It cannot be used on patients with CER perfusion deficit. In such cases the visual cortex (VC) or others reference values are recommended. The use of different references makes the comparison of SPECT scans almost impossible. We developed a method for calculating IP using a reference value, which acts as a model of "normal

CER counts". This value was designated as CER* and it was calculated using the mean value of the VC/CER ratio derived from a normal database. We tested statistically the VC/CER ratio on a group of 60 scans from individuals without involvement of VC and CER. To demonstrate that $IPCER^* \gg IPCER$, we calculated the mean value of the absolute differences $\langle |IPCER - IPCER^*| \rangle$ on two groups of scans: 10 normal subjects (GI) and 40 patients without involvement of VC and CER (GII). Using an indirect procedure the method was tested on a third group of scans of 30 patients with CER perfusion deficit (GIII). The VC/CER ratio was constant at a 95% confidence level; $\langle |IPCER - IPCER^*| \rangle$ for GI and GII was less than the replicability of the HMPAO SPECT studies; and it was proved in GIII that CER* is comparable to CER as reference value with the only condition being that perfusion in subject's VC must be unaffected. The method allows generalizing CER as a reference value, inapplicable only in those cases with concurrent hypoperfusion on VC and CER.

25P30

Absolute quantification of cerebral blood flow by SPECT

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Quantification of cerebral blood flow (CBF) is useful in patients with neurological diseases because of the diagnostic and therapeutic implications of such quantification. CBF quantification by SPECT can be achieved in relative or absolute units. Relative quantification is more used due to it is less time consuming and because most of the absolute quantification methods require a more expensive instrumentation or blood sampling of the patient, which makes absolute quantification an invasive procedure. In 1992, a new method was developed by the Japanese investigator H. Matsuda without those previous handicaps. This method substitutes the blood sampling by a graphical procedure, which is applied to a first-pass dynamic study. Mean CBF (mCBF) can be calculated by this way for both brain hemispheres. Regional CBF values (rCBF) can then be calculated using the Lassen correction for the distribution of the radiotracer estimated with a standard SPECT study. We implemented Matsuda's method in ten healthy individuals using ^{99m}Tc - ECD. Values of mCBF were between 44 ml/min/100g and 50 ml/min/100g for all individuals. Values of rCBF in gray matter were around 70

ml/min/100g. Values of rCBF in white matter were around 20 ml/min/100g. These values are similar to those reported by Matsuda. We concluded that Matsuda's method is simple, not invasive and can be implemented with the technology of our country. This method can become a valuable tool to enhance clinical diagnosis and research in other important neurological problems.

25P31

A way to reduce radius of rotation in brain SPECT with a single-head system

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To optimize spatial resolution in SPECT it is essential to minimize the radius of rotation (rrot). In brain studies, different solutions have been employed in order to avoid the shoulder interference when rrot is minimized: rectangular fields of view, modifications to the shielding around circular detectors and fan or cone beam collimators. However, few single-head systems can utilize these developments, particularly old cameras. A non-standard image acquisition method to reduce rrot in brain SPECT with a single-head gamma camera is presented. The method applies a defined transformation to the original acquired images, keeping all the brain inside the field of view without the shoulder interference and meeting the condition: pixel size \leq FWHM/3. With this method it is possible to reduce rrot to 16 cm and to obtain a transaxial spatial resolution of 15.98 mm, 3.5 mm less than standard method used in our laboratory. This procedure was implemented for a gamma camera Siemens Gammasonics ZLC 3700 and has been validated through single-slice brain phantom studies. The method has the advantage of not introducing any complex or costly hardware implementations.

25P32

Quality assurance in brain SPECT

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SPECT is a highly sophisticated technology, which needs a strict quality assurance, if one wishes the data generated by this procedure to be reliable. The objective of this paper was to evaluate different functioning parameters of the gamma camera at our depart-

ment, in order to establish which parameters most affect the quality of brain SPECT images and to find out with which periodicity they are to be evaluated. This study was performed for a year by making periodic evaluations. A double-head gamma camera was used (SMV DST Xli, SMV International) connected to a workstation IBM RISC System 6000, provided with a processing system Vision 5.0 (SMV America, Inc). Sources of ^{99m}Tc were used to perform different tests, as well as a SPECT phantom, props for radioactive source, ruler, syringes, disposable vials, lead containers and other materials to perform the tests were also utilized. The obtained results show an annual mean value of 2.69 % for tomographic uniformity; and an annual mean value of 1.2 mm for the displacement of the center of rotation. As a conclusion, we can assert that such parameters that most affect the quality of SPECT brain images are: the displacement of the center of rotation and tomographic uniformity. Tomographic uniformity and the displacement of the center of rotation should be evaluated weekly and monthly, respectively, in order to assure the optimum quality of brain SPECT images.

25P33

Stroke due to vasculitis associated to Systemic Erythematosus Lupus in children. A case presentation

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Colagenosis is a multisystemic disease with a great evolutive variability. In the case of Systemic Erythematosus Lupus, the neurological commitment is present in almost half of all cases and it provokes vasculitis by convulsions caused by stroke or brain hemorrhage. Diagnosis is established with the aid of Computer Tomography. The objective of our work is the presentation of a clinical case. Material and Method. A case under pediatric age with an autoimmune disease of the vascular-type is presented. The disease provoked a motor sequel of the left-hemiparesia. We applied the evaluation of motor function (at the beginning and end of neurorestorative treatment). Discussion of results and conclusions. Keeping in mind the patients peculiarities, we evidenced that with an adequate structured application and by giving special attention to different developmental areas with the use of the Intensive Multifactorial

Neurorestorative Program at the Children's Clinic of Neurology progress can be obtained. From a quantitative viewpoint the Gross Motor Scale was applied to the patient at the beginning and end of treatment. The results showed that in the initial evaluation, the patient reached a 22,2% and 37,5% in the final one, for an improvement of 15,3%. This made possible to conclude, that it is possible to improve the patient's quality of life.

25P34

New scale for the classification of paraplegic patients after a spinal cord lesion

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Medullar lesions constitute one of the more frequent causes of disability in the world. This is produced by the rupture of nervous pathways. These axons, once broken, are unable to regenerate causing loss of sensitiveness, and permanent and irreversible paralysis below the lesion level. In our work we tried to validate a test we made to demonstrate that it is reliable to quantify and classify the restoration in the physical sphere of paraplegic patients due to a medullar lesion. The test we present here is a variant to the Barthel index where we included only physical items. This investigation was carried out at CIREN's Neurology Clinic for Children and the Clinic of Spinal Lesions. The sample was composed of 33 patients with ages between the 3 and 40 years old, all diagnosed with spinal lesion, either congenital or acquired. They were subjected to a period of rehabilitation of 28 days, and were evaluated with the test mentioned before, during and after treatment. To establish the validity of the test, we used the statistical technique of product moment of Bravais Pearson, and for reliability, we used variance analysis. The results demonstrate the validity and reliability of the test proposed to evaluate the recovery of a paraplegic patient.

25P35

Influence of physical exercises on patients bearers of muscular dystrophy of Duchenne and Baker type

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Until recently, dystrophies have not been considered for rehabilitation treatment due to the course of the disease, the role of fatigue on affected muscles and the absence of therapeutic effects of muscular exercises. Today, it can be asserted that considering dystrophies as a kind of paralysis is wrong. The total absence of the muscular activity will hinder patients from the stimuli that provoke energetic reactions, which are necessary to keep the functional value in the patient. Immobilization is said to be harmful as it disturbs deep circulation. From this, the role of rehabilitation is important to keep functional possibilities to a maximum. Purpose: To demonstrate the influence of an integral rehabilitation treatment to patients bearers of muscular dystrophy of the Duchenne and Baker type. Material and method: We performed a retrospective study to selected sample of patients diagnosed with Duchenne \ Becker muscular dystrophy for children. Each child was submitted to a rehabilitation treatment approximately between four and eight weeks with 6 weekly frequencies. We performed basic motor tests at the psychomotor integral evaluation lab (LEIS) at the beginning and the end of treatment. Patients were evaluated in their gross motor function (GMF) and muscular test or Daniel's test of each body segment in order to determine the level of improvement reached during treatment. Results: A significant improvement was obtained in treated patients.

25P36

Chiropractic treatment for lumbar disc herniations

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A total of 100 patients between 25-35 years of age, with proven disc herniations on MRI, with grade II classifications were treated with chiropractic specific adjustments to the lumbar spine where the segments involved were mainly L4 and L5, with pain at site of palpation, muscle spasm, radicular pain into legs and feet, paresthesias, some loss of strength on leg muscles and 15% presented with neurovascular reflexes with ankle and foot swelling. A series of 15 chiropractic adjustments were performed with 50% of symptoms resolved within the first 5 visits, other patients improved gradually up to 90-98% recovery on the 12th visit. The most common symptom to prevail was the numbness at distal portion of the involved extremity. Only 10 patients needed to have an epidural steroid spinal block and only 3 of them discontinued conservative management to undergo selective endo-

scopic discectomy. This patients were treated with 5 adjustments first week, 3 adjustments per week the following two weeks and once a week the following four weeks, no medications were prescribed only i.m. vit. B12 and icing the involved area of pain 20 mins every hour the first 2 days then 3 times a day for 5 days. No adverse effects were presented with the adjustments and only 2 patients had adverse allergic reaction to the vit. B12. The patients were all evaluated with a full spine view 14x 36 and IIs, flexion-extension views of lumbar spine in order to identify vertebral misalignment and pelvic instability that influences the pressure vectors over the disc and facet joints of the motor unit involved, as well as MRI with gadolinium contrast where all patients had grade II disc herniations with symptoms related to disc compression all this imaging performed preceded by chiro/ortho/neuro examination to determine ivdh classification and the site of vertebral subluxation complex. Three had questionable symptoms and a bone scan (gamagram) performed to rule out sacroiliitis 2 were negative and 1 positive for sacroiliitis, this patient was removed and replaced from the treatment group for ivdh. Conclusions were made upon taking chiropractic treatment as a primary conservative approach to treat ivdh. of the lumbar spine with radicular ssx with excellent results to avoid spinal surgeries.

25P37

Effect of cellular metabolism increase and decrease on lipoperoxidation process after traumatic spinal cord injury

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Traumatic spinal cord injury (TSCI) often results in permanent paralysis. The final lesion results not only from the physical trauma to the tissue, but also from the progressive cellular damage that expands the injury to caudal and rostral levels of the spinal cord. This secondary injury includes ischemia where mitochondrial function fails and ATP concentration drops within minutes, and reperfusion process which promotes autodestructive phenomena like tisuular damage by reactive oxygen species (ROS) and lipoper-

oxidation process (LP). With the aim to evaluate the effect on LP process, metabolism activity was increased and decreased using the cocarboxilase non degradable (CND) enzyme and 5 mitochondrial inhibitors respectively in 48 Long Evans, female, adult rats divided into 8 groups: Group 1, laminectomy without TSCI; Group 2, TSCI plus physiologic solution; Group 3, TSCI plus CND; Groups 4, 5, 6, 7, and 8 plus rotenone, 3-nitropropionic acid, antimycin A, sodium azide, and cyanide respectively. Animals were subjected, under anesthetic conditions, to a moderate TSCI (T-9) using the NYU impactor system. Treatments were injected intraperitoneally 5 minutes after TSCI. The effects of CND and mitochondrial inhibitors on NADH dehydrogenase, succinate dehydrogenase, cytochrome oxidase and LP process were evaluated 24 hr after treatment. CND treatment increased LP processes ($p < 0.05$), while all mitochondrial inhibitors, except cyanide, decreased the LP process, specially rotenone and sodium azide ($p < 0.05$). Our results suggest that the decrease in metabolism activity, early after a TSCI could be an autoprotective response instead a secondary mechanism of damage since it could reduce LP process.

25P38

Treatment with laser on ischemic ulcers for patients with medullar lesions

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A clinical trial was made based on controlled, descriptive and prospective analysis of patients admitted at the military hospital Dr. "Luis Díaz Soto" between February 2002 to February 2003 suffering from medullar lesions and other neurological dysfunctions with ischemic ulcers. It's a ten-patient sampling. Subjects were selected at random and equally grouped into two sections with 5 cases each. The first group of patients was treated with 1% Cetavión in order to wash ulcers, later rinsed with 0.9% serum following the lesion necrotic tissue debridement, careful wiping and an application of infrared Hene laser by means of a Fisser-III-brand equipment made in Cuba at 7 Joule/cm² and 25 watts (MW) of power which optic fiber device is placed perpendicular to the lesion ridge for 60 second/point. The second group was treated with washing and debridements process the same as in the previous case. This time, however, a light coat of skin growth ointment applies. In each case, sterilized dressings were placed on the ulcers until the last day of the treatment in order to evaluate the action of laser rays in the cicatrization

process. The subgroup composed of 15-19 year-of-age patients (60%) prevailed male individuals (80%) who had car accidents (50%) resulting in paraplegia; major sequel found in 8 patients.

25P39

Bladder education with nurse neurological restoration strategies

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The study and follow up of neurogenic bladder in spinal cord injuries are of vital importance for the multidisciplinary team that cares for this patients. We presented a prospective and retrospective study of 601 patients admitted in Spinal Cord Injury Clinic of International Center for Neurological Restoration during the period between January 2000 and September 2003. The main goal was to obtain bladder reeducation. We used the urological scale and the nurse evaluation during reception in 100% of the patients being able to conclude that 95% of the patients came without bladder education and with history of urinary infection in 97%, as principal consequences of bladder neurogenic dysfunction. We obtained, with our intervention, the reduction of complications related with this disease.

25P40

Neurological restoration in paraplegia: The CI-REN experience

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We will perform a review of principal aspects related to multifactorial management in paraplegic patients at the Spinal Cord Injury Clinic of the International Center of Neurological Restoration, Havana, Cuba. The results will be shown too. All patients were studied using haematologic, imagenologic and neurophysiologic tests before the beginning of neurological restoration. The Barthel index, spasm, motor and Asworth scales were applied too. Physical rehabilitation, occupational and speech treatment were performed. A good evolution was found in our casuistic and life quality was significantly increased in 25 evaluated patients.

25P41**The written language, an actual alternative for patients bearers of cervical medullar lesion**

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Spinal cord lesions can produce different motor disorders according to the level of alteration suffered by the spinal cord. When segments between C4-C8 are lesioned, superior limbs are most frequently affected, and as a consequence, skilled hand activities. With the aim of evaluating the influence of the system of therapeutic activities, developed for the correction of the functional disorders of the superior limbs, the Oligraf quantitative scale for writing (created by CI-RENS Clinic of Movement Disorders and Neurodegenerations) was applied. We applied this scale to 20 patients with high spinal cord lesions (C4-C7) divided into three groups according to the level of lesion, before and after therapeutic intervention. The patients were evaluated using the LEIS Standard Scale (CI-REN). Alterations in writing were found in the majority of the sample, where macrographia, agglutination and expansion of writing predominated in patients with C6-C7 lesion. Upward, downward and agglutinated writing was found in patients with C5-C6. Writing on top of the other letter was found in patients with C4-C5 lesions. OLIGRAF quantitative scale influenced in a positive way the identification of alterations in writing in almost the totality of the sample.

25P42**Effect of a physical rehabilitation program on gait and Independence level in paraplegic patient with spinal cord injury**

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Introduction: Spinal cord injury is one of the most common causes of disability in adults. Trauma over the spine can develop a fracture, luxation or ligament damage. Objective: to evaluate the effect of a rehabilitation program on the gait and the independence level in paraplegic patients. Methods: we selected 10 patients with dorso-lumbar spinal cord injury. We evaluate patients with the Barthel index and the preparatory activities for the gait (mattress work and

stand work) before and weeks after an intensive rehabilitation program. Results: nine patients increased the ability in mattress work, according to repetition of the exercise (15 repetitions over baseline in hip's flexion). Barthel index increased in all patients (mean of 20 points). Conclusions: an intensive rehabilitation program seems to be effective for training the gait an increase the independence level of paraplegic patients.

25P43**Post-paralytic sinkinesis in peripheral facial palsies**

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In the facial neuropathies with an axonal lesion very predominant or exclusive axonal, takes place in a systematic way, an aberrant regeneration that produces a clinical phenomenon named facial cross-innervation, so called post-paralytic hemifacial spasm. In these cases, the answers R1 and R2 of the Blink Reflex are obtained in other facial muscles outside of the muscle Orbicularis oculi, as the Frontal, Orbicular oris or Cutaneous of the neck. The physiological explanation commonly accepted is the arrival of the nervous fibers belonging to the muscle Orbicularis oculi to other facial muscles in the regeneration process. In such a sense, we gave ourselves to the task to explore the existence of this phenomenon, also called post-paralytic sinkinesis, in patients with peripheral facial palsies in different moments of the illness's evolution. In this study we present the Blink Reflex obtained in the Orbicularis oris muscle bilaterally of 4 cases with an important facial palsies in which was obtained electrophysiological confirmation of aberrant regeneration of the facial nerve, in some cases even before the clinics signs appear. This study could be used as a therapeutic guide in the treatment of the post-paralytic syndromes of the peripheral facial palsies.

25P44**A comprehensible program for the rehabilitation and restoration of the neurological dysfunction for Multiple Sclerosis patients and their caregivers in Cuba**

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Introduction: The recent disease-modifying drugs have not eliminated the need of rehabilitation strategies in the management of MS. Even if there were that could fully prevent progression of the disease, hundreds of thousands of patients worldwide would still be left with residual neurological damage and the associated impairment and disability. **Objective:** To introduce a comprehensive rehabilitation and restoration program for MS patients and their caregivers in a natural rehabilitation hospital in Cuba. **Design-methods:** The multidisciplinary team of rehabilitation and restoration has developed and integrated, comprehensive and intensive rehabilitation program for MS patients. This multidisciplinary team is composed by: neurologists (with training in MS), physiatrist, psychologists, neuropsychologists, social workers, occupational therapist, natural medicine specialists and nurses. The program is an intense short term rehab in 6 weeks 2 sessions for each patient and will have a single physiotherapist (one to one) and a neuropsychologist. The evaluation of the rehabilitation and restoration include the physical and cognitive disability and the clinical evaluation by means of international disability scales (EDSS, Guy Scale), quality of life scales (MSQLI), psychological and neuropsychological tests (Luria, WAIS, Benton, PASAT-3) to evaluate the efficacy of the program. Finally, we will teach to the MS patient and her/his caregiver to learn, at their own home, the exercises for the physical and cognitive dysfunction when the patient left the rehabilitation MS hospital. **Results:** The results will be presented at the meeting. **Conclusions:** This is one of the most extensively program for physical and cognitive rehabilitation / restoration for MS patients and their caregivers in a Latin-American country.

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Multiple Sclerosis in the Cuban women. An update

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Objective: To evaluate the clinical and social-economical status of the Cuban women with MS. **Introduction:** Multiple sclerosis (MS) is the cause of greater disability in the young woman in Cuba. **Design and Method:** Epidemiological study: We carried

out a case-control study, in 57 women with MS clinical definite (Poser et al) and their relatives. The evaluation was gotten by means of the questionnaire of Boiko et al. **Clinical, disability and social-economical studies:** 271 women with clinical definite MS. The clinical, demographic and social-economical data were taken from the Cuban Computerized Register of MS. **Results:** Epidemiological study: The risks factors were: High educational level (OR= 2.293; 95% CI= 0.9-5.4), 2 or more children (OR= 2.84; 95% CI= 1.22 -6.59), 4 or more pregnancies (OR= 3.60; 95% CI= 0.69-18.7), 3 or more deliveries (OR= 1.939, 95% CI= 0.44-8.4), measles infection (OR= 2.042; 95% CI= 0.76-5.47), migraine (OR= 2.538; 95% CI= 0.81-7.94), stress (OR= 3.768; 95% CI= 1.64-8.62), and insomnia (OR= 2.95; 95% CI= 1.14-7.14). **Clinical, disability and social-economical studies:** MS was observed, in women of 30 to 51 years, relapsing-remitting form with family history of autoimmune and psychiatric disorders and 8% with one or more relatives affected. The disability met, 62.57% of the women with moderate or severe impairment of the ambulation and 20% of them are in wheelchair or on bed. The Cuban women with MS have a high educational level, but 50% are divorced/single, received low or not annual salaries or are vacated. **Conclusions:** It is mandatory to carry out a program in Cuba in order to improve the medical attention, the disability and the social-economical level of the women with MS.

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Neurological restoration in Multiple Sclerosis: the CIREN experience

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Multifactorial therapeutic was used in patients with Multiple Sclerosis at the International Center for Neurological Restoration, Havana, Cuba. Our proposal was the evaluation of this therapy in Multiple Sclerosis patients. We studied 20 patients that were admitted at CIREN during 2000-2002 with different clinical manifestations. They were evaluated within the first week and after 4, 8 and 12 weeks. The Kurtzke, Hauser, Chronic fatigue and Asworth scales were applied. Symptomatic and specific treatment, bio-physical stimulation, physical therapy, occupational and speech treatment were performed. The best results were observed and life quality was increased in all patients. Our conclusions show that Neurological

Restoration is an important aspect in order to improve the life quality in patients with Multiple Sclerosis.

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Results of LEIS evaluation on patients with multiple sclerosis after a neurorestorative treatment

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Multiple sclerosis (ME) is a demyelinating disease affecting the brain and the spinal cord. The fundamental objective of this investigation was to show the improvement reached by 17 patients with multiple sclerosis, after a 28-day rehabilitation cycle, through initial and final evaluations of tests applied to measure strength, breathing capacity and gait. All studies were performed at the Psychomotor Integral Evaluation Lab (LEIS) in CIREN. The tests applied at LEIS have the required reliability and sensitiveness to detect changes undergone by the patients during their rehabilitation. Statistical tests applied (Wilcoxon matched pair test) showed results under the significant levels. Results. After having analyzed and compared the results of both evaluations, we verified that the patients obtained positive results in the evaluated items after a treatment cycle. Conclusions. Of the 17 evaluated patients, 7 increased their strength (41,17%); 16 changed their gait possibility (94,11%) and 14 increased their breathing capacity (82,35%). The positive changes observed in the treated patients confirm the efficacy of the rehabilitation program applied.