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22nd International Epilepsy Surgery Symposium

Malformations of cortical development:
The biology, the identification, the epilepsy
and the pragmatic approaches to treatment

October, 26-29 - 2013 – Campinas, SP, Brasil

ABSTRACTS / RESUMOS

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Órgão Oficial Trimestral da Liga Brasileira de Epilepsia

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Summary

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Scientific Program

Oct. 26 Saturday
PRE-CONGRESS COURSES – SIMULTANEOUS
Epilepsy Comprehensive course

COURSE 1
Review and Scientific Update on Clinical Epileptology
October 26, 2013
Venue: Hotel Vitória – Campinas SP

Saturday - 8:00-19:00h		
08:00am - 08:50am	**Registration**	
Session 1: Carlos Guerreiro (Campinas, Brazil) - Coordinator		
08:50am – 09:00am	Welcome and Opening remarks	Carlos Guerreiro (Campinas, Brazil)
09:00am – 09:25am	Epidemiology and economic impact of epilepsy	Li Li Min (Campinas, Brazil)
09:25am – 09:50am	Epidemiology and economic impact of epilepsy – European aspects	Roberto Spreafico (Milan, Italy)
09:50am – 10:15am	Mechanisms and causes of focal and generalized seizures	João P. Leite (Ribeirão Preto, Brazil)
10:15am – 10:40am	Diagnosis and differential diagnosis of epilepsies	Luciano de Paola (Curitiba, Brazil)
10:40am – 11:00am	Coffee break	
Session 2: Marcia E. Morita (Campinas, Brazil) - Coordinator		
11:00am – 11:25am	Classification of epilepsies & epileptic syndromes	Elza M. T. Yacubian (São Paulo, Brazil)
11:25am – 11:50am	Electrophysiological diagnosis of epilepsies	Paulo Ragazzo (Goiânia, Brazil)
11:50am – 12:15pm	Seizure semiology	Juan Bulacio (Cleveland Clinic)
12:15pm – 12:40pm	Neuroimaging of epilepsies - Overview	Antonio C. dos Santos (Ribeirão Preto, Brazil)
12:40pm – 01:40pm	Lunch	
Session 3: Ana Carolina Coan (Campinas, Brazil) - Coordinator		
01:40pm – 02:05pm	Sudden unexpected death in epilepsy	José E. Cavazos (Texas, USA)
02:05pm– 02:30pm	The best evidences to treat generalized epilepsies	Luiz Eduardo Betting (Botucatu, Brazil)
02:30pm – 02:55pm	The best evidences to treat focal epilepsies	Carlos Guerreiro (Campinas, Brazil)
02:55pm – 03:20pm	Effects of AEDs on cognitive fMRI	Clarissa Yasuda (Edmonton, Canada)
03:20pm – 03:45pm	Treatment of epilepsy in special conditions: women, elderly, clinical comorbidities	Carlos Silvado (Curitiba, Brazil)
03:45pm – 04:10pm	How to manage status epilepticus	Ana Carolina Coan (Campinas, Brazil)

04:10pm – 05:00pm	Coffee break	
Session 4: Luiz Henrique Castro (São Paulo, Brazil) - Coordinator		
05:00pm – 05:25pm	Ketogenic diet	Vera C. Terra (Curitiba, Brazil)
05:25pm - 05:50pm	Vagal Nerve Stimulation for refractory epilepsy	Mario Alonso Vanegas (Mexico)
05:50pm - 06:15pm	Brain Stimulation in epilepsy – Current state and perspectives	Arthur Cukiert (São Paulo, Brazil)
06:15pm - 06:40pm	Epilepsy Surgery: Overview of Successes and Failures	William Bingaman (Cleveland, USA)
06:40pm - 07:00pm	Discussion	
07:00pm	Adjourn	

COURSE 2
Paralell Session 1
October 26 Saturday
Venue: FCM - UNICAMP Campinas SP – Brazil

2.1 - Hands-On Course - live: 10 places - see below
2.2 - Surgical Workshop for Neurosurgeons (in parallel) - (does not include the Hands on part): 60 places - see costs in the table below
Location: Anfiteatro 1 Legolândia at UNICAMP

8:00am – 05:00pm	**Hands-on neurosurgical workshop** Coordinators: Helder Tedeschi (Campinas, Brazil) and Wen Hung Tzu (São Paulo, Brazil)

Proposal:
The hands-on dissection workshop demonstrates some of the most commonly used epilepsy surgery techniques that include approaches to temporal lobe resection and hemispherectomy/ disconnection methods.
Renowned faculty in the field of epilepsy surgery will discuss their choices for surgical techniques, and the participants will be able to perform various surgical approaches in cadaveric specimens.
Registration to the hands-on part of the workshop is limited to ten participants.
The workshop will be broadcasted live to an auditorium close to the laboratory where participants not registered to the hands-on will also have a chance to interact with the instructors during the demonstrations.

Faculty:
Helder Tedeschi (Campinas, Brazil)
Wen Hung Tzu (São Paulo, Brazil)
William Bingaman (Cleveland, USA)
Jorge Gonzalez-Martinez (Cleveland, USA)
Giorgio LoRusso (Milan, Italy)
Carlos Carlotti (Ribeirão Preto, Brazil)
Helio Rubens Machado (Ribeirão Preto, Brazil)
Eliseu Paglioli (Porto Alegre, Brazil)
Manuel Campos (Santiago, Chile)
Bertrand Devaux (Paris, France)
Enrico Ghizoni (Campinas, Brazil)
Andrei Fernandes Joaquim (Campinas, Brazil)

08:00 - 08:15	**Welcome and Introduction**	**Helder Tedeschi (Campinas, Brazil)**
Part 1: Moderator - Jorge Gonzalez-Martinez (Cleveland, USA)		
08:15am - 09:00am	Microsurgical anatomy of the temporal lobe and the sylvian fissure applied to temporal lobe epilepsy surgery	Wen Hung Tzu (São Paulo, Brazil)
09:00am - 09:20am	Trans-temporal approach to the mesial temporal lobe	Eliseu Paglioli (Porto Alegre, Brazil)
09:20am - 09:40am	Trans-sylvian approach to the mesial temporal lobe	Helder Tedeschi (Campinas, Brazil)
09:40am - 10:00am	Neocortical-Amygdalohippocampectomy. Surgical Techniques	Giorgio Lo Russo (Milan, Italy)
10:00am - 10:20am	Discussion/Coffee-break	
Part 2: Moderator: Eliseu Paglioli (Porto Alegre, Brazil)		
10:20am - 12:00pm	Interactive dissection by the participants (there will be a video transmission for all participants that are not participating in the hands on workshop)	
12:00pm - 01:00pm	Lunch	

Part 3: Moderator - Manuel Campos (Santiago, Chile)		
01:00pm - 01:30pm	Microsurgical anatomy of the insula and the cerebral ventricles	Wen Hung Tzu (São Paulo, Brazil)
01:30pm - 01:50pm	Disconnection surgery. Surgical Principles and the Cleveland Clinic Experience	William Bingaman (Cleveland, USA)
01:50pm - 02:10pm	Disconnection surgery. Surgical Principles and the Riberão Preto Experience	Hélio Rubens Machado (Ribeirão Preto, Brazil)
02:10pm - 02:30pm	Functional Hemispherotomy. Surgical technique	Wen Hung Tzu (São Paulo, Brazil)
02:30pm - 02:50pm	Discussion/Coffee-break	
Part 4: Moderator: Carlos Carlotti (Ribeirão Preto, Brazil)		
02:50pm - 04:50pm	Interactive dissection by the participants (there will be a video transmission for all participants that are not participating in the hands on workshop)	
04:50pm - 05:10pm	Surgical management of cortical dysplasias in eloquent areas	Bertrand Devaux (Paris, France)
05:10pm - 05:30pm	Introduction to deep electrodes monitoring techniques. The Cleveland Clinic Experience	Jorge Gonzalez-Martinez (Cleveland, USA)
05:30pm - 05:50pm	Discussion	
05:50pm	ADJOURN	

October 27-29 Scientific Program
22nd International Epilepsy Surgery Symposium
Venue: Hotel Vitória – Campinas - SP

Malformations of cortical development: The biology, the identification, the epilepsy and the pragmatic approaches to treatment

October 27, 2013

8:15am - 8:30am	**Welcome and introduction**	**Fernando Cendes (Campinas, Brazil)**
SESSON 1 - Introductory session **How we got here and where we are** This session will bridge the current understanding of MCD with the main 'milestones' through which knowledge was accumulated. Lessons can be learned from this trajectory that may inform future developments. **Moderator (will comment and coordinate discussion at the end): Roberto Spreafico (Milan, Italy)**		
08:30am - 09:00am	From neuronal migration disorders to malformations of cortical development and focal cortical dysplasia – the conceptual and nomenclature battles	Andre Palmini (Porto Alegre, Brazil)
09:00am - 09:30am	Integrating individual types of MCD with mechanisms of brain development: Part I	Jim Barkovich (San Francisco, USA)
09:30am - 10:00am	The molecular biology of Intrinsic epileptogenicity of MCD and its clinical/ management implications	Imad Najm (Cleveland, USA)
10:00am -10:20am	Discussion	
10:20am - 10:45am	Coffee break (near the poster area)	
The focal cortical dysplasias		
SESSION 2 - Type I FCD: Mechanisms of disease and identification by imaging **Moderator: Jim Barkovich (San Francisco, USA)**		
10:45am -11:10am	What can lead to cortical dyslamination and why this may be epileptogenic?	Ingmar Blümcke (Erlangen, Germany)
11:10am - 11:35am	Identifying FCD type I from MRI: What we have now and what we will have in the near future	Stephen Jones (Cleveland, USA)
11:35am - 12:00pm	Imaging-histological correlations in type I FCD	Roberto Spreafico (Milan, Italy)
12:00pm - 12:25pm	Imaging in FCD type I: How MEG can enhance the role of MRI and PET in localizing the lesion?	Richard Burgess (Cleveland Clinic)
12:25pm - 01:00pm	Discussion	
01:00pm -01:30pm	Poster session I	
01:30pm - 02:30pm	Lunch	

SESSION 3 - Type I FCD: Clinical presentations, decision-making and treatment **Moderator (will comment and coordinate discussion at the end): Hans Holthausen (Vogtareuth, Germany)**		
02:30pm - 02:55pm	The clinical presentation of type I FCD and epilepsy: the different syndromes	Hans Holthausen (Vogtareuth, Germany)
02:55pm - 03:20pm	Medical management of patients with patients with FCD type I: What to AEDs to try in this severe disorder?	Marilisa Guerreiro (Campinas, Brazil)
03:20pm - 03:45pm	Presurgical evaluation in FCD type I: When you know and when you suspect that is the villain	Francine Chassoux (Paris, France)
03:45pm - 04:10pm	FCD type I: The Milano approach to FCD type I: Surgical outcome	Giorgio LoRusso (Milan, Italy)
04:10pm - 04:40pm	Discussion	
04:40pm - 05:20pm	Poster Session II and Coffee break	
Case discussions		
05:20pm - 07:00pm	**Parallel section 1:** Children (two cases) **Room: Vitória Hall** **Moderators:** Maria Luiza Manreza (São Paulo, Brazil) and Hans Holthausen (Vogtareuth, Germany) **Presenters:** Hans Holthausen (Vogtareuth, Germany), Fabio Rogério (Campinas, Brazil) and Maria Augusta Montenegro (Campinas, Brazil)	
05:20pm - 07:00pm	**Parallel section 2:** Adults (two cases) **Room: Abrolhos** **Moderators:** Juan Bulacio (Cleveland, USA), Giorgio LoRusso (Milan, Italy), Jorge Gonzalez-Martinez (Cleveland, USA) **Presenters:** Andreas Alexopoulos (Cleveland, USA) and Juan Rodríguez Uranga (Sevilla, Spain)	
October 28, 2013		
SESSION 4 - Type II FCD: Why they happen and how they present **Moderator (will comment and coordinate discussion at the end): Elza Marcia Yacubian (São Paulo, Brazil)**		
08:00am - 08:25am	New insights into the molecular mechanisms leading to FCD type II	Iscia Lopes-Cendes (Campinas, Brazil)
08:25am - 08:50am	Integrating individual types of MCD with mechanisms of brain development - Part II	A. James Barkovich (San Francisco, USA)
08:50am - 09:15am	The epileptology of type II FCD: Clinical and neurophysiological endophenotypes	Américo Sakamoto (Ribeirão Preto, Brazil)
09:15am - 09:40am	Identifying FCD type II from MRI – What thick cortex, increased signal, transmantle sign and blurring mean? Why these may not be seen?	Fernando Cendes (Campinas, Brazil)
09:40am - 10:05am	Multimodal imaging in FCD type II: When PET, SPECT and MEG are needed and how they help in clinical practice?	Andreas Alexopoulos (Cleveland, USA)
10:05am - 10:30am	Discussion	
10:30am - 11:00am	Poster Session III and Coffee Break	
SESSION 5 - Type II FCD - Getting things right: How to improve surgical outcome in FCD type II **Moderation (will comment and coordinate discussion at the end): André Palmini (Porto Alegre, Brazil)**		
11:00am - 11:25am	Critical aspects to be considered in the approach to FCD type II	Imad Najm (Cleveland, USA)
11:25am - 11:50am	The Saint-Anne approach and results: Emphasis on functional and non-functional cortex in FCD type II	Bertrand Devaux (Paris, France)
11:50am - 12:15pm	The Cleveland Clinic approach and results: Emphasis on selecting the best approaches in visible and 'invisible' FCD type II	Jorge Gonzalez-Martinez (Cleveland, USA)
12:15pm - 12:40pm	The Porto Alegre approach and results: Emphasis on intraoperative decision-making in FCD type II	Eliseu Paglioli (Porto Alegre, Brazil)
12:40pm - 01:00pm	Discussion	
01:00pm - 02:30pm	Lunch and Key note Conference The history, the present and future of invasive EEG evaluation in FCD	Patrick Chauvel (Marseilles, France)
SESSION 6 - Type III FCD **Moderation (will comment and coordinate discussion at the end): Ingmar Blümcke**		

02:30pm - 02:55pm	The rationale behind type III FCD	Ingmar Blümcke (Erlangen, Germany)
02:55pm - 03:20pm	How valid has the concept of FCD type IIIA been?- Has evaluation or surgical planning changed?	Laura Tassi (Milan, Italy)
03:20pm - 03:45pm	The modern approach to DNTs and gangliogliomas: Tackling FCD type IIIB	Tonicarlo Velasco (Ribeirão Preto, Brazil)
03:45pm - 04:10pm	What does it mean having dyslamination surrounding gliotic cortex (FDC IIId)? How to approach patients with congenital vascular destructive lesions?	Eliseu Paglioli (Porto Alegre, Brazil)
04:10pm - 04:40pm	Discussion	
04:40pm - 05:20pm	Poster Session IV and Coffee break	
05:20pm - 07:00pm	**Case discussions** **Moderators:** Manuel Campos (Santiago, Chile), Bertrand Devaux (Paris, France) and Patrick Chauvel (Marseilles, France) **Presenters:** François Dubeau (Montreal, Canada) and Ana Paula Pinheiro Martins (Cleveland, USA)	
October 29, 2013		
SESSION 7 - Polymicrogyria and nodular heterotopia **Moderator (will comment and coordinate discussion at the end): Marilisa Guerreiro (Campinas, Brazil)**		
8:00am - 8:25am	Mechanisms of neuronal migration and cortical organization: The molecular genesis of polymicrogyria and nodular heterotopia	Fabio Rossi Torres (Campinas, Brazil)
8:25am - 8:50am	Syndromes of polymicrogyria	Renzo Guerrini (Florence, Italy)
8:50am - 9:15am	Presurgical evaluation and surgical treatment of unilateral polymicrogyria	Francine Chassoux (Paris, France)
9:15am - 9:40am	Refractory partial epilepsies associated with heterotopic nodules – Clinical/imaging presentations, presurgical evaluation, and surgical management	François Dubeau (Montreal, Canada)
9:40am - 10:10am	Discussion	
10:10am - 10:45am	Coffee Break	
SESSION 8 - Grossly malformed brains **Moderator (will comment and coordinate discussion at the end): Kette Valente (São Paulo, Brazil)**		
10:50am - 11:30am	Genetic mechanisms underlying abnormal neuronal migration in diffusely thick cortex	Iscia Lopes-Cendes (Campinas, Brazil)
11:30am - 12:00pm	The epileptogenicity of displaced neurons and their connections: Lessons for evaluation and surgical treatment	Stefano Francione (Milan, Italy)
12:00pm - 12:25pm	Discussion	
Symposium with Lunch Optimism on the horizon: new knowledge and novel approaches to patients with tuberous sclerosis **Moderation and comments:** Imad Najm		
01:00pm- 01:30pm	Tuberous sclerosis: The science, the epilepsy and new perspectives for medical and surgical treatment	Elza M. T. Yacubian (São Paulo, Brazil)
01:30pm - 02:00pm	Evaluation of epileptogenic networks in children with tuberous sclerosis complex using EEG-fMRI	Eliane Kobayashi (Montreal, Canada)
02:00pm - 02:30pm	Surgical treatment of refractory epilepsy due to TS	Hélio Rubens Machado (Ribeirão Preto, Brazil)
02:30pm - 03:00pm	Moderator comments and Discussion	
03:00pm	Adjourn and departure	

Abstracts / Resumos

Journal of Epilepsy and Clinical Neurophysiology

J Epilepsy Clin Neurophysiol 2013; 19 (Suppl 1): 11-27

22nd International Epilepsy Surgery Symposium

TITLE

CP01 – MODIFIED WADA TEST FOR TEMPORAL LOBE EPILEPSY USING AN ETOMIDATE PROTOCOL WITH A LOADING DOS

Authors

Samanta Fabrício Blattes da Rocha[1]; Fábio Augusto Nascimento e Silva[2]; Abdré Giacomelli Leal[3]; Cristiane Andréia Simão[4]; Murilo Meneses[3]; Pedro André Kowacs[5]

Institutions

1. Neuropsychology Unit, Instituto de Neurologia de Curitiba, Curitiba, Brazil;
2. Faculty of Medicine, Universidade Federal do Paraná, Curitiba, Brazil;
3. Neurosurgery Unit, Instituto de Neurologia de Curitiba, Curitiba, Brazil;
4. Electroencephalography Unit, Instituto de Neurologia de Curitiba, Curitiba, Brazil;
5. Neurology Unit, Instituto de Neurologia de Curitiba, Curitiba, Brazil.

Introduction: The Wada test is routinely used to evaluate the hemispheric dominance of language and memory prior to temporal lobe surgery in patients with medically refractory epilepsy. **Objectives:** To evaluate memory function and language by using the etomidate-modified Wada test in epilepsy patients that are candidates for epilepsy surgery. **Methods:** The neuropsychological data of 34 patients between the ages of 13 and 50 years, who underwent memory and language testing by intracarotid injection of etomidate, were analyzed. The initial loading dose was given as a bolus of either 2 mg or 1.8 mg for each hemisphere. Supplemental boluses of either 0.25 mg or 0.35 mg etomidate were injected if needed. A brief cognitive protocol was administered. Six patients were monitored with an EEG during the test; the other 28 were monitored by only their motor skills. **Results:** Patients regained motor function within an average time of 493.8 seconds. The initial loading dose of 1.8 mg resulted in less sedation. The most commonly reported side effects were tremors and a cold feeling. Three patients were not able to complete the test due to issues with psychomotor agitation, apnea, and excessive sedation. The test succeeded in the remaining 31 patients. **Conclusion:** The modified Wada test using an etomidate protocol, with a loading dose followed by boosters or not, showed to be effective. Thus, we were able to assess the patients' memory and language during the procedure. Therefore, this drug is a suitable option for performing the Wada test, possibly with lower costs.

TITLE

CP02 – MICRORNA EXPRESSION PROFILE IN MESIAL TEMPORAL SCLEROSIS PROVIDES INSIGHT INTO UNDERLYING MECHANISMS

Authors

Danyella B. Dogini[1]; Cristiane S. Rocha[1]; Clarissa L. Yasuda[2]; Helder Tedeschi[2]; Claudia V.Maurer-Morelli[1]; Fernando Cendes[2] and Iscia Lopes-Cendes[1]

Institutions

Departments of Medical Genetics1 and Neurology2; and CINAPCE* Program
Faculty of Medical Sciences, UNICAMP, Campinas, SP, BRAZIL.

*Interinstitutional Cooperation for Brain Research

Introduction: MicroRNAs are a new class of small RNA molecules (21-24 nucleotide-long) that negatively regulate gene expression either by translational repression or target mRNA degradation. MiRNAs are involved in many important biological processes including cell differentiation, embryonic development and central nervous system formation. **Objetives:** The main purpose of this study was to investigate microRNA (miRNA) gene regulation in mesial temporal sclerosis (MTS) and its predicted target genes. **Methods:** Total RNA was isolated from hippocampal tissue of 4 patients who underwent selective resection of the mesial temporal structures for the treatment of clinically refractory seizures. In addition we used control samples from autopsy (n=4) for comparison. RNA samples were used in real-time PCR reactions with TaqMan™ microRNA assays (Life Technologies) to quantify 157 different miRNAs. **Results:** Bioinformatic analyzes identified three miRNAs, which were differently expressed in patients as compared to controls: let-7d and miR-29b were over expressed in patients; whereas, miR-30d was down-regulated in patients. A possible target gene for let-7d is Nme6 which we also found to be down- regulated in patients. In addition, Mcl-1, the putative target gene of miR-29b was also down-regulated in patients. Mcl-1 is a potent multidomain anti-apoptotic protein of the Bcl-2 family and its tight regulation of protein levels is necessary, because insufficient Mcl-1 can result in inappropriate cell death. Nme6 belongs to NME (nm23 /nucleoside diphosphate kinase) gene family in humans and act as inhibitor of p53-induced apoptosis. **Conclusions:** We have identified three different miRNA species differently expressed in MTS and its target genes: let-7d - NME6, miR-30d - SON and miR29b - Mcl-1. Biologic functions related to the possible miRNA gene-targets are mainly neurogenesis, and apoptosis. Our results point to interesting potential molecular targets which should be explored further in additional studies of MTS. **Support:** FAPESP, Sao Paulo, BRAZIL.

TITLE

CP03 – SEARCHING FOR THE MESIAL TEMPORAL LOBE EPILEPSY GENE: VALIDATING CANDIDATE VARIANTS IDENTIFIED BY NEXT-GENERATION SEQUENCING

Authors

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Institutions

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Introduction: Mesial temporal lobe epilepsy (MTLE) is the most common form of human epilepsy. Familial forms of MTLE have been reported by our group. A candidate locus on chromosome 18p11.31 was identified, through genome-wide linkage study in a large family with autosomal dominant transmission. In order to search for the causative mutation, genes localized in the 18p11.31 locus were amplified by long range PCR and sequenced by next-generation sequencing (NGS) in an ABI Solid SystemTM. Bioinformatics analysis revealed 32 deleterious candidate variants localized in 11 genes. **Objectives:** To validate deleterious candidate variants identified by NGS in a family segregating MTLE linked to ch 18p11.31. **Methods:** We studied a total of 28 family members, 14 patients. Genomic DNA was isolated from lymphocytes of fresh blood by standard methods. Genomic regions containing the variants were amplified by polymerase chain reaction (PCR). Amplicons were submitted to capillary electrophoresis in a sequencer ABI 3500XL genetic analyser (Applied Biosystems). Chromatograms were analyzed by Chromas software. Results To date, All affected individuals of the family, including those previously sequenced by NGS, were genotyped for 17 variations located at the following genes L3MBTL4 (exon 15), EPB41L3 (exons 13 e 23), LAMA (exons 29, 32, 41, 43, 62), LRRC30 (exon 1) and ARHGAP28 (exon 12). From the candidate SNPs found by NGS, 13 were not validated by Sanger sequencing. **Conclusion:** A significant number of nucleotide changes identified by NGS on ch 18p11.31 candidate locus were not validated by Sanger sequencing. Other variants are still being analyzed at the moment. Therefore, more studies are necessary to define the major gene predisposing to MLTE with hippocampal atrophy in the family studied. **Financial support:** SAE/Unicamp

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TITLE

CP04 – IMPACT OF THROMBOLYSIS IN POST-STROKE SEIZURES AND POST-STROKE EPILEPSY

Authors

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Institutions

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Introduction: Stroke is a cause of seizures and secondary epilepsy in adults and post-stroke seizures are observed in 2% to 20% of patients. Among risk factors for post-stroke seizures or epilepsy are cortical involvement, bleeding, severity and extension of the ischemic injury. Thrombolytic therapy has been changing the outcome of ischemic stroke and might change the incidence or characteristics of seizures or epilepsy associated with stroke as well. Some evidences suggest that thrombolysis for acute stroke might increase post-stroke seizures, but the impact of thrombolysis in post-stroke seizures or epilepsy remains largely unknown. **Objectives:** To investigate the incidence and risk factors for seizures and epilepsy after ischemic stroke in patients submitted or not to thrombolytic therapy. **Methods:** Case-control study of 153 patients submitted to thrombolysis for treatment of acute stroke and 102 matched controls with acute stroke not submitted to thrombolysis. **Results**: In our study, we observed post-stroke epilepsy in 14.4% of patients submitted to thrombolytic therapy and in 14.7% of control patients. No associations were observed regarding smoking, alcohol abuse, hypertension, ASPECTS score, presence of early detectable signs of stroke in CT-scan, diabetes mellitus, hyperlipidemia, obesity, age, blood pressure levels, and glucose levels at admission. However, we observed an association between seizures and involvement of cerebral cortex during stroke (O.R.=11.4; 95% C.I.=1.53-85.8; p=0.002). Also, we observed that the risk for seizures increases according with NIH scores at admission (O.R.=1.1; p=0.02; 95% C.I.=1.03-1.16, per point) and in those patients with Rankin 2-5 scores after three months, when compared with patients classified as Rankin 0-1 (O.R.=5.2; 95% C.I. = 2.4-11.5; p<0.0001). **Conclusions:** Post-stroke epilepsy were observed in 14.4% of our patients submitted to thrombolytic therapy and in 14.7% of controls. Cortical involvement and severity of stroke, as evaluated by NHI scores at admission, and Rankin scores three months later, were risk factors for post-stroke epilepsy after stroke in patients submitted or not to thrombolytic therapy. We conclude that thrombolytic therapy for acute stroke does not add further burden to post-stroke seizures or epilepsy.

TITLE

CP05 – POSTOPERATIVE SEIZURE FREQUENCY IN MTLE PATIENTS CAN INTERFERE IN MEMORY PERFORMANCE

Authors

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Institutions

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Introduction: Surgical resection of mesial structures yields 60-70% chances of complete seizure control for refractory unilateral MTLE. However, the cognitive effects of postoperative seizures for those with surgical failure are still poorly understood. **Objectives:** We proposed to evaluated pre and postoperative cognitive performance regarding lateralization, seizure control and volume of the surgical lacunae (VSL). **Methods:** We evaluated 47 patients with unilateral MTLE (17 males, 30 females; 44.7±8.7 years of age), 24 operated on left and 23 on the right side, 21 classified as Engel-IA (seizure-free group) and 26 as Engel IB-III (failure-group). They underwent pre/postoperative neuropsychological assessment (NPA), including IQ and memory (general, visual, verbal and delayed recall). We calculated the ratio between post/pre MRI volumetric measurements to perform group comparisons. We manually delineated the VSL using a 3D-T1-weighted MRI acquisition and the software DISPLAY (www.bic.mni.mcgill.ca/software). For group comparisons we used T Test and Man Whitney U test, with significance at $p<0.05$. **Results:** Some degree of cognitive decline was observed in most of individuals, regardless seizure control. Seizure-free group presented better outcome of IQ ($p=0.047$), general ($p=0.041$) and visual memory ($p=0.027$), but verbal ($p=0.673$) and delayed recall ($p=0.441$) tests were not different. Surgical lacuna was larger in seizure-free group, although not statistically significant ($p=0.649$). Left side MTLE patients presented worse outcome of IQ ($p=0.034$). **Conclusions:** These findings indicate that seizure control influences postoperative cognitive outcome. In addition, we also demonstrated that left MTLE patients present worst IQ decline than right MTLE. **Financial Support:** FAPESP

TITLE

CP06 – CENTRAL AUDITORY PROCESSING DISORDERS IN CHILDREN WITH TEMPORAL LOBE EPILEPSY

Authors

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Institutions

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Introduction: Central auditory processing disorder is a deficit in the processing of auditory information, despite normal hearing thresholds. It can be assessed by behavioral tests and auditory-evoked potentials (AEP) that together verify the integrity and functioning of the auditory system. Children with epilepsy may present epileptic activity around auditory and language areas, such as centrotemporoparietal and sylvian regions. This study evaluated central auditory processing abilities in school-age children with temporal lobe epilepsy and verified if the epileptic activity can impair auditory processing. **Methods:** We evaluated twenty five school-age children, age range 8:6 to 14:8 years. Nine children (seven were male) composed the epilepsy group and 16 normal children (eight were male) composed the control group. After neurological assessment, children underwent a peripheral audiological evaluation,behavioral auditory tests(dichotic digits test, gaps in noise test and duration pattern test) and an event related potential (P300). **Results:** We observed a statistically significant difference between children in the epilepsy group and control groupwith the worst performance for the epilepsy group in dichotic digits test, right ear ($p=0.01$), duration pattern test, right ear, humming ($p=0.02$), duration pattern test, left ear, naming ($p=0.02$) and gaps in noise, right ear ($p=0.05$), left ear ($p<0.01$) and P300, latency, right ear ($p=0.02$). **Conclusions:** Children with temporal lobe epilepsy can have abnormalities in central auditory processing information. Epileptic discharges around language and auditory areas may jeopardize the functioning of these areas leading to central auditory processing disorders. **Financial support:** MirelaBoscariol received financial support from FAPESP (#2010/07438-3).

TITLE

CP07 – INVESTIGATING THE ROLE OF MICRORNA-124 AS AN INHIBITOR OF MICROGLIAL ACTIVATION IN THE PILOCARPINE EPILEPSY MODEL

Authors

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Background: MicroRNAs regulate gene expression and are important in many key biological functions such as development,oncogenesis and inflammation. MicroRNA-124 or miR-124, is known to be expressed exclusively in the central nervous system and has been implicated in the maintenance of microglial cells in a non-activated, or quiescent, state. It is well known that activation of microglia is characteristic of neurological pathologies and that at chronic levels it can lead to tissue damage. Therefore, it is clinically relevant to understand which factors contribute to the regulation of this phenomenon. **Objective:** The aim of the present study was to analyze the expression of miR-124 inthe acute phase of the pilocarpineepilepsy model. Thus, investigating whether abnormalities of microglial activation, usually observed in this model, could be mediated by microRNA deregulation. **Methods:** We

obtained total RNA from hippocampus of animals at 1, 3, 6, and 24 hours, as well as 5 days after induction of status epilepticus (SE) by pilocarpine, and from control animals. We quantified expression of miR-124 by quantitative real-time PCR. Only tissue obtained from rats which presented SE were used in our experiments. In addition, to better understand the possible role of miR-124 in the physiopathology of epilepsy, we used TargetScan 6.2, to analyze which genes already known to be down-regulated in epilepsy could be target by miR-124. **Results:** We found thatexpression of miR-124 was significantly decreased after SE, about 60%, in comparison with control samples. MiR-124 expression was decreased already at 1h after SE and remained low until 5 days after SE. Using TargetScan 6.2 we found many genes related to epilepsy such as glutamate receptor, potassium channel andgenes involved in neurogenic differentiation, which can be regulated by miR124. **Conclusion:** Our results indicate that regulation by microRNA, especially miR-124, can play a role in microglia activation after SE induced by pilocarpine. Thus, opening the possibility of using microRNA-based therapies in epilepsy. **Funding:** FAPESP and CNPq

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TITLE

CP08 – OPTIMIZATION OF SIMULTANEOUS RNA AND PROTEIN EXTRACTION FROM RAT HIPPOCAMPUS OBTAINED THROUGH LASER CAPTURE MICRODISSECTION

Authors

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Introduction: The use of animal models to investigate the mechanisms underlying human temporal lobe epilepsy leads to great advances in the better understanding of this disease. However the development of models that can present epileptogenesis similar to that observed in humans is still a challenge. In this context, transcriptome and proteomics studies are promising tools for the identification of key biological processes leading to epilepsy. The power of such 'omics' approaches is dependent on the preparation of homogeneous cell populations, especially in heterogeneous tissues such as the nervous system. Laser-capture microdissection (LCM) presents the ability to select a specific cell population that would give the most informative data. **Objectives:** Therefore, the aim of the present study is to optimize brain collection, histological processing and simultaneous RNA and protein extraction. **Methods:** Wistar rats were kept under illumination-controlled conditions with cycles of 12h light/darkness. They had total access to water and food during all the observation period. Rats were euthanized in a CO2 chamber, and the brain was quickly removed and frozen in liquid nitrogen, by direct immersion, or frozen by immersion in n-hexane at -60º. Frozen sections were produced in a cryostat (Leica) and mounted in PEN covered glass slides (Zeiss). Slides were Nissl stained, and the dentate gyrus (DG), or the whole hippocampus was laser microdissected using Zeiss PALM LCM. RNA was extracted from microdissected DG samples using RNAeasy microkit (Qiagen). RNA quality was assessed employing Bioanalyzer Agilent RNA 6000 Pico. Total proteins were obtained from the collected hippocampus using TRizol reagent according to manufacturer instructions. Proteins were ressuspended in 8M urea and quantified by the Bradford's methods. **Results:** Direct immersion of tissue in liquid nitrogen resulted in fragmentation of samples. Brains processed with n-hexane resulted in reduced freezing artifacts. For the production of frozen tissue slices, best results were obtained with 40µm of thickness. RNA extraction employing RNA easy microkit (Qiagen) produced high quality isolated RNA. We obtained simultaneous isolation of RNA and protein employing the TRizol method, resulting in an average concentration of 1.1µg RNA and 10.6µg protein. **Conclusion:** Tissue processing employing n-hexane and sectioning with 40µm of thickness were the best conditions for LCM. The use of the TRizol method resulted in the simultaneous extraction of RNA and total proteins from the same sample. This study was supported by FAPESP (2011/50680-2).All animal procedures were approved by the UNICAMP Ethics Committee on Animal Experimentation (prot # 2903-1).

TITLE

CP09 – MOLECULAR STUDY OF SLC2A1 GENE IN DIFFERENT FORMS OF IDIOPATHIC GENERALIZED EPILEPSIES OF CHILDHOOD AND ADOLESCENCE

Authors

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Institutions

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Introduction: Several loci for different forms ofIdiopathic generalized epilepsies (IGE) have been found, but the number of identified genes is relatively small, because the correlation between genotype and phenotype is not complete. Furthermore, the prognostic value of the different mutations found in candidate genes, and correlation with clinical subtypes remain controversial.Recently, mutations in the SLC2A1 gene were found in patients with Doose syndrome and subsequently described in other IGE as well. This gene encodes the glucose transporter (GLUT1), responsible for transporting glucose blood-brain, Deficiency of GLUT1 causes inadequate levels of cerebral glucose, and classical phenotype of GLUT1 deficiency is characterized by a serious metabolic encephalopathy with movement disorder, epilepsy and mental retardation, starting about at one year of age. **Objective:** The objective of this study is to characterize the molecular bases of different forms of generalized epilepsies of childhood and adolescence, through the screening of mutations in the

candidate gene SLC2A1. **Method:** We screened for mutations in SLC2A1 gene in 52 patients with JME, 33 with other types of IGEs and 15 with Doose Syndrome. **Results:** Silent nucleotide changes were found in 8 patients of our cohort, 7 described in the literature (27 G> A, 45 C> T, 399 C> T, 588 G> A, 965 C> T, 1011 C> T, 1065 A > G) and one new change (1149 C> T) found in one patient with Doose syndrome. We also found one intronic insertion between exons 9, 10 (IVS9 CTCACCATTT 25), already described as a normal polymorphism in the population. **Conclusion:** Since deleterious mutations were not found in SLC2A1, this gene does not seem to be related to IGEs or Doose Syndrome in our cohort. Study supported by FAPESP and CNPq.

TITLE

CP10 – DENTATE GYRUS TRANSCRIPTOME ANALYZES BY HIGH-THROUGHPUT NEXT GENERATION SEQUENCING IN A CHRONIC EPILEPSY ANIMAL MODEL WITHOUT STATUS EPILEPTICUS

Authors

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Institutions

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Introduction: Animal models which use convulsant drugs, such as pilocarpine, are one of the most used tools to study the mechanisms involved in mesial temporal lobe epilepsy (MTLE). However these models are based in the induction of an initial episode of status epilepticus (SE), usually leading to extensive extra-hippocampal lesions, which are events not commonly observed in patients with MTLE. Animals which receive pilocarpine but do not develop SE can display long term spontaneous recurrent seizures and more discrete SNC lesions. Nevertheless, the mechanisms responsible for the occurrence of spontaneous seizures in this SE-free animals are unknown. Transcriptome analyzes using high-throughput next generation sequencing (HTNS) offers the possibility of profiling global gene expression with great performance. **Objectives:** Gene expression profile by HTNS of the dentate gyrus (DG) of SE-free rats presenting long term spontaneous seizures after the administration of pilocarpine. **Methods:** Eight-weeks old male Wistar rats received methylscopolamine (1mg/kg, i.p.), followed 30 minutes later by pilocarpine (320 mg/kg, i.p.). Control animals received the same dose of methylscopolamine followed by saline administration. Only animals that did not developed SE were used in this study. Rats were video-monitored 24 hours for 6 months after pilocarpine administration and at the end of this period, they were euthanized in a CO2 chamber. The brain was quickly removed and frozen in liquid nitrogen. Frozen sections were produced in a cryostat (Leica) and mounted in PEN covered glass slides (Zeiss) and laser microdissected using Zeiss PALM LCM. RNA was extracted using RNAeasy microkit (Qiagen). The purified RNA was processed with TruSeq RNA Sample Preparation kit (Illumina) for the production of cDNA libraries. HTNS experiments were performed in a HISeq 2000 (Ilumina). Sequence alignment was performed using TopHat and gene expression quantification with HTseq. **Results:** We found a total of 122 genes differentially expressed in pilocarpine treated animals as compared to controls: 35 were up-regulated and 87 were down-regulated. **Conclusions:** Although the DG apparently does not present morphological changes in the present SE-free experimental model, the observed transcriptional changes indicate that more subtle molecular and physiological mechanisms are indeed present. FAPESP grant 2011/50680-2. UNICAMP Ethics Committee on Animal Experimentation prot 2903-1.

TITLE

CP11 – DIAGNOSIS AND PROGNOSIS OF A CASE OF RASMUSSEN ENCEPHALITIS WITH ADULT ONSET

Authors

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Institutions

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Objectives: To describe a case of a patient with history and exams suggestive of Rasmussen's Encephalitis (RE), with good outcome after right hemispherectomy. **Methods:** Case report and literature review. **Case:** Female patient, 28 years-old, with epilepsy onset at 21-years-old. She initially underwent treatment with anti-epileptics drugs. Subsequently, due to drug-resistant seizures, she was submitted to a right amigdalohipocampectomy and, after one year, to a right temporal lobectomy, without improvement (in another hospital). She developed worsening of seizure frequency (daily complex partial seziures) with secondary generalization, progressive left hemiparesis and cognitive deterioration. Five years after onset, she was referred to our clinic and the diagnosis of RE was suggested. Inflammatory markers and serologies were negative. Analyses of CSF, including autoantibodies, were normal. Brain MRI revealed right hemispheric atrophy with worsening over time. EEGs showed right hemispheric slowing and right fronto-temporal epileptiform activity. Initially she was treated with human immunoglobulin and plasmapheresis (2g/kg), but no response was observed. In February 2013, she underwent a functional right hemispherectomy and she has been free of seizures since then. She also had an important cognitive improvement. Histopathology showed recent and old ischemic changes without clear signs of encephalitis. **Conclusions:** The RE is a rare and severe immune-mediated brain disorder that leads to unilateral cerebral hemiatrophy, progressive neurological dysfunction and refractory seizures. Only 10% of cases begin in adolescence and adulthood. The diagnosis is based on clinical, EEG and morphological studies (MRI and in some cases histopathology). Currently, epilepsy surgery is the only "cure" for disease progression. Histopathology allows identification of the nature of the encephalitic disease but in some cases it may be nonspecific.

TITLE

CP12 – CONCOMITANT EEG FINDINGS OF CHILDHOOD ABSENCE EPILEPSY AND ROLANDIC EPILEPSY IN THE SAME PATIENT

Authors

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Institutions

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Objective: To describe a patient with absence seizures and with an electroencephamogram (EEG) showing both generalized epileptic discharges and centro-temporal epileptiform discharges, suggesting the coexistence of two entities. **Methods:** Case report and literature review. **Case:** A 4-year-old girl developed, 8 months prior to presentation in our clinic, recurrent transient impairment of consciousness each lasting about few seconds. Developmental milestones were unremarkable and she had no history of previous seizures. Detailed neurological examination and brain MRI was normal. She had been seen at another clinic and was taking valproic acid with no further seizures. Her EEG on awakeness showed two paroxysms of generalized 3 Hz spike-and-wave complexes, one during hyperventilation, both lasting 9 seconds. During sleep, there were frequent spikes and sharp-waves over centro-temporal regions, bilateral and independent, compatible with rolandic discharges. The patient had no report of focal seizures and she was free of seizures since the introduction of valproic acid. **Conclusion:** There are few reports in the literature describing the coexistence of childhood absence epilepsy (CAE) and rolandic epilepsy (RE) in the same patient. We report a case of a child who presented with absence seizures, and with and EEG showing abnormalities typical of absence and rolandic epilepsy. Despite the fact that she hasn´t developed partial seizures yet, the follow up is very important because she might start focal seizures in the future. Although the coexistence of these two different syndromes is not common, it suggests the hypothesis that CAE and RE are two distinct epileptic conditions and genetic links cannot be excluded.

TITLE

ES01 – DEEP BRAINS STIMULATION FOR THE MANAGEMENT OF SEIZURES IN MECP2 DUPLICATION SYNDROME

Authors

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Institutions

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Introduction: MECP2 duplication (MECP2-dup) leads to cognitive delay, minimal or absent speech and dysmorphic features. **Objectives:** Here we describe clinical features of an adult with severe seizures of multiple types, and their management challenges, including response to deep brain stimulation (DBS). **Methods:** Developmental delay was recognized at 9 months. At 14 years of age he began experiencing complex partial, atonic, tonic, secondarily generalized tonic-clonic, and eating reflex seizures. Several antiepileptic drugs failed to control his seizures. At the age of 23 years his monthly seizure frequency was of 125. The patient received DBS to the anterior thalamic nuclei. At 35 years of age microarray analysis showed a clinically significant 0.641 Mb duplication in chromosome region Xq28, which involves 25 RefSeq genes including eight genes ABCD1, L1CAM, AVPR2, NAA10, MECP2, OPN1LW, OPN1MW, and FLNA. Results: Treatment with DBS caused 65% decrease in seizure frequency. Despite a significant seizure improvement, his cognitive and motor skills continue to deteriorate. Frequent respiratory infections are the most severe and life-threatening events. **Conclusion:** MECP2-dup is a condition rarely seen/diagnosed in adults. Almost 40% of all boys with MECP2-dup that were reported until 2009 died before completing 25 years of age. This case shows that cognitive and motor dysfunction continue to deteriorate as patients age. It also shows that seizures may be extremely difficult to treat and DBS may improve seizure control. As opposed to some other genetically determined severe epilepsies such as Dravet syndrome, seizure frequency and severity do not improve in adulthood.

TITLE

ES02 – TEN YEARS AFTER: A RETROSPECTIVE STUDY OF 166 PATIENTS SUBMITTED TO SURGICAL TREATMENT OF EPILEPSY IN A PRIVATE TERTIARY CARE CENTER FROM APRIL 2003 TO APRIL 2013

Authors

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Institutions

Núcleo Avançado de Tratamento das Epilepsias do Hospital Felício Rocho, BH, MG.

Objectives: The main purpose of this study was to describe a series of 166 consecutive patients submitted to epilepsy surgery in a single tertiary-care hospital from April 2013 to April 2013, reviewing their demographic and seizure characteristics, pathologic substrates and seizure outcome. A secondary goal was to evaluate the long term evolution of surgical results after eight to ten years of the first 30 patients of the series. At last, we aimed at analyzing the kind of surgeries performed according to the year, in order to determine whether there was or not a progression towards more complex pathologies or techniques with growing experience of the group. **Methods:** A review of the charts of all patients consecutively evaluated and operated on in a tertiary-care hospital was performed. Epilepsy outcome was correlated to pre-surgical findings, including neuroimaging data, video-EEG findings and seizure characteristics. Patients were subdivided into categories according to pathologic substrates of their epilepsies, and surgery results were compared between groups. **Results:** From all patients submitted to presurgical investigation between April 2003 and April 2013, only 166 were eventually submitted to surgical treatment of epilepsy. From these 166 individuals, 117 (70.5%) had mesial temporal lobe epilepsy (MTLE), and were submitted either to anterior temporal lobectomy (13 patients) or to selective amygdalohyppocampectomy (104 patients); 14 (8,4%) had tumors (7 gangliogliomas, 2 DNET and 1 oligodendroglioma + astrocytoma); 11 (6,6%) had cortical dysplasias – of which 3 type III; 4 patients had Lennox-Gastaut Syndrome (LGS), and were submitted to corpus callosotomy; 3 patients were diagnosed with Rasmussen encephalitis, and underwent hemispherectomy; 7 patients underwent lobectomy or quadrantic resections for the treatment of gliotic lesions or leukomalacia. Finally, there were 9 patients for whom resective surgery was not an option, who received vagal nerve stimulator (VNS) implantation. The best postsurgical results were found in the MTLE group, as expected. On the other hand, all patients submitted to corpus callosotomy had Engel classes III or IV outcomes.

TITLE

ES03 – MORBIDITY AND MORTALITY IN EPILEPSY SURGERY USING GRIDS (ECOG) OR DEPTH ELECTRODES (SEEG) OR BOTH (ECOG + SEEG)

Authors

Authors: Benech D; Besocke AG; Comas B.; Aberastury M.; Maineri C., Cristiano E., Ciraolo C., Garcia MC, Agosta G., Silva W.

Institutions

Introduction: Epilepsy surgery is a therapeutic option in drug resistant focal epilepsy. Some patients require invasive neurophysiology (NFI) to tailor the epileptogenic zone (EZ) and /or avoid undesirable neurological deficits and improve prognosis. **Objectives:** To analyze the complications of patients requiring NFI with the different methods used in our program: EcoG, SEEG or ECoG+SEEG. **Methods:** Retrospective observational study that included 52 patients with focal drug-resistant epilepsy evaluated with NFI, between 2005 and 2011. Morbidity was assessed in relation to medical complications and neurological deficit (ND). ND were classified into temporary and permanent. The permanent ND, was further associated to the implant or resection procedure, and the latter classified in expected or unexpected, in relationship to the location of the EZ. Results: Twenty four patients were male, with a mean age of 21.1y/o (1-45). All were chronically implanted: 10 (15%) with SEEG, 19 (36%) with ECoG and 24 (49 %) with SEEG+ECoG. In 5 patients resective surgery was not performed. Nineteen patients had temporary ND: ECoG: 9; SEEG: 2, ECoG+SEEG : 8. Ten patients (21%) had permanent ND: ECoG: 4, SEEG: 1, ECoG+SEEG: 5. Three of them had non expected ND regarding the location of EZ: 2 underwent SEEG + ECoG , and 1 with ECoG. Seventeen patients, suffered medical complications, which were more frequent with the use of ECoG or ECoG+SEEG. A patient with bilateral combined implant died. **Conclusion:** Both medical complications and permanent ND were more frequent in patients implanted with ECoG or ECoG+SSEG. The mortality in our series was 1.9%.

TITLE

ES04 – ASSOCIATION BETWEEN INTERICTAL EPILEPTI FORM DISCHARGES AND SURGICAL OUT COME OF PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

Authors

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Institutions

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Introduction: Refractory epilepsy is defined as "failure of adequate trials of two tolerated and appropriately chosen and used AED regimen (whether as monotherapy or in combination) to achieve sustained seizure freedom". Presence of a known structural cause of epilepsy, particularly hippocampal sclerosis (HS), is a consistent clinical predictor of drug resistance. Previous studies have already shown the prognostic value of preoperative data to predict seizure recurrence. However there is limited data on the importance of postoperative EEG regarding surgery outcome. **Objective:** To investigate the association between interictal epileptiform discharges in postoperative EEGs and surgical outcome of patients with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS). **Methods:** Patients with refractory TLE with HS were submitted to surgery after a comprehensive noninvasive evaluation. Patients with at least two postoperative EEG stored in digital format were selected. We included104 patients, total of 304 postoperative EEGs, and reviewed these seeking for presence of interictal epileptiform discharges (IED). Later on, we quantified spikes by visual analysis. We used mean IED frequency to divide patients in two groups: patients with no or less than 10 discharges/15min (few spikes), and those having more than 10 discharges/min (frequent spikes). We also compared patients

with normal EEGs and those who had postoperative spikes. In order to study the association between IED and seizure recurrence we used survival analysis curves considering seizure recurrence as final endpoint and compared by Mantel method. **Results:** The curves of patients with presence and absence of IED were not significantly different. But when we stratified groups by IED frequency (few versus frequent spikes), there was a significant difference ($p<0.05$). **Conclusions:** These results highlight the association of frequent IED with seizure recurrence, rather than only the presence of infrequent spikes. Prospective studies are necessary as to support our data. EEG should be regarded as a useful tool during follow up of patients with TLE with HS in order to guide medication withdrawal. This study has been supported by FAPESP.

TITLE

ES05 – FDG-PET AND 3T MRI CO-REGISTRATION IN CHILDREN WITH TYPE I AND TYPE II FOCAL CORTICAL DYSPLASIA BENEFITS AND PITFALLS

Authors

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Institutions

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Introduction: FDG-PET and MRI co-registration (PET-MRI) is extremely useful for identification and definition improvement of focal cortical dysplasia (FCD). **Objetives:** To analize PET-MRI findings in children with FCD and epilepsy, focusing attention in two aspects: 1) benefits of PET-MRI for neuroimaging typication of FCD, 2) results variability and pitfalls associated with the electroclinical status at the time of evaluation. **Methods:** Eighty children with FCD and epilepsy (aged 0,1-18 years) were studied with PET-MRI, using high resolution 3T MRI. EEG/video-EEG was monitored during brain FDG uptaking. Results were analysed according to MRI findings, electroclinical features, pathology (in 50 surgically-treated patients), and neuropsychology. PET-MRI was repeated in some cases with negative, non-congruent, or multiple metabolic PET-MRI changes, and during postsurgical follow-up. **Results:** Among histologically-classified cases (50 patients),76% of type II FCD cases (22 in 29) revealed a clear-cut focal hypometabolic area superimposed on MRI abnormalities, in congruence with an electro-clinical focus. This finding was crucial to identify botton-of-sulcus dysplasias. In most type I FCD cases (19 in 21) PET-MRI revealed hypometabolic areas less delimited and less correlated to MRI abnormalities than in type II cases. Among all eighty children, focal hypermetabolic areas were found in 10 patients suffering from focal status epilepticus (SE) or with minor continous seizures at the time of evaluation. These hypermetabolic areas turned into hypometabolic ones after the cease of the SE in 5 re-explored cases. Secondary hypometabolic areas (SHA) beyond MRI visible lesion were found in 51 patients (64%). SHA showed multifocal or bilateral distribution in 10 children suffering from age-dependent epileptic encephalopathies. In 15 patients SHA turned into normometabolic cortex when transition to a less severe focal epilepsy or seizure freedom status was achieved by epilepsy surgery or pharmacological treatment. These changes were linked to a neuropsychological improvement in 80% of them. In other patients, SHA reflected FCD non-detected by MRI, as probed by invasive EEG and/or pathology. **Conclusion:** PET-MRI may contribute to presurgical typification of FCD in children. PET-MRI findings may reflect not only the existence of dysplastic tissue, but also epilepsy-mediated dysfunction in non-lesional conected cortical areas. Distinction between both scenarios is not always easy to get, particularly in children with FCD type I and in patients with age-dependent epileptic encephalopathies.

TITLE

NA01 – TRYPTOPHAN HYDROXYLASE 2 GENE (TPH2) POLYMORPHISMS MIGHT BE RISK FACTORS FOR ALCOHOL AND DRUG ABUSE IN TEMPORAL LOBE EPILEPSY

Authors

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Institutions

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Introduction: Neuropsychiatric comorbidities are frequent in temporal lobe epilepsy (TLE) and serotoninergic pathways might play a role in its development. Thus, it is biologically plausible that alterations in serotonin-related genes may be involved in higher susceptibility for psychiatric comorbidities in individuals with temporal lobe epilepsy. The enzyme tryptophan hydroxylase 2, also known as TPH2, is an isozyme primarily expressed in serotonergic brain neurons. TPH2 is highly expressed in the raphe nucleus of the midbrain, where it is a rate-limiting enzyme in serotonin synthesis. TPH2 rs4570625 and rs17110747 polymorphisms have been associated with psychiatric disorders and psychiatric comorbidities susceptibility in neurological diseases. **Objetive:** To investigate the association of tryptopham hydroxylase 2 polymorphisms in psychiatric comorbidities of TLE. **Methods:** Case-control study of 163 adult patients with temporal lobe epilepsy. The influence of rs4570625 and rs17110747 TPH2 polymorphisms were investigated for psychiatric comorbidities in these patients. All individuals were evaluated with Structured Clinical Interview for DSM-IV (SCID). Polymorphisms were studied using real-time PCR. **Results:** In our study, no association between rs4570625 or rs17110747 TPH2 polymorphisms was associated with mood, anxiety or psychotic disorders in TLE. However the rs17110747 TPH2 polymorphism was associated with alcohol and drug abuse. Alcohol and drug abuse was observed in 4.2% of our patients, being 78% of them males. Risk factors for alcohol abuse in epilepsy were the presence of adenine allele homozygosis in rs17110747 (O.R. = 8.5; 95% CI = 1.4 to 52.6;

p<0.05) and male sex (O.R. = 7.3; 95% CI = 1.5 to 36.3; p<0.01). **Conclusion:** In our study, alcohol and drug abuse was observed in 4.2% of patients with temporal lobe epilepsy and it was significantly more frequent in male patients. We observed that variability in the TPH2 gene might be associated with alcohol and drug abuse, once the presence of adenine allele homozygosis in rs17110747 was a risk factor for this comorbidity. In our view, this is an interesting finding suggesting possible molecular mechanism predisposing psychiatric comorbidities in epilepsy. This study was supported by CNPq and FAPERGS.

TITLE

NA02 – DECISION MAKING IN ROLANDIC EPILEPSY

Authors

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Institutions

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Purpose: The aim of this study was to evaluate the decision-making style in children with rolandic epilepsy (RE) and compare their performance with healthy children taking into account clinical variables of epilepsy. **Method:** We evaluated 42 children, 17 with RE (RE Group) and 25 healthy controls (Control Group). All children were assessed with the Iowa Gabling Task (IGT), the most used instrument to evaluate the decision-making style, and the Wechsler Intelligence Scale for Children (WISC-III) to investigate the intellectual level (estimated IQ). The clinical variables of epilepsy were: age of seizure onset and remission, type of seizure (partial versus generalized), use of AED (none, monotherapy or polytherapy), and seizure lateralization (right, left, and bilateral). **Results:** No significant differences were found between the two groups. However, when analysing the RE group, we observed that the later the onset of epilepsy, the best style of decision making presented (p=0.04). The same was true when comparing the intellectual level of the RE group: the higher the IQ, the better the decision-making style (p=0.02). **Conclusion:** We conclude that although RE is known as a benign entity, difficulty in decision-making ability may be observed. More studies are necessary to corroborate our findings.

TITLE

NA03 – QUALITY OF LIFE AND DAILY PHYSICAL EXERCISE HABITS OF PATIENTS WITH REFRACTORY TEMPORAL LOBE EPILEPSY

Authors

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Institutions

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Introduction: The diagnosis of epilepsy leads to changes in how the patients picture themselves in their social and economic circles and future plans. Therefore, this diagnosis compromises not only their physical health as well as quality of life (QOLIE).The treatment of epilepsy goes beyond the control of the seizures; it has been shown that alternative treatments can improve the well being and emotions of these patients. There are scientific evidences that the physical activity (PA) contributes to QOLIE of groups with different pathologies. However, there are controversies related to the benefits of PA to people with epilepsy. **Objectives:** This work evaluates the lifestyle and PA of patients with refractory Temporal Lobe Epilepsy (TLE) and its relationship to their QOLIE. **Methodology:** We used the International Physical Activity Questionnaires (IPAQ) and Quality of Life in Epilepsy Inventory-31 (QOLIE-31) in 57 patients with TLRE in order to divide them in two groups (A – Active and B-Inactive). We used the Mann-Whitney U test to compare differences between continuous variables between the groups; the Fisher Exact Test to compare the frequencies observed; and Pearson's correlation Test was used to analyze the correlation between continuous variables. **Results:** Better QOLIE was observed in patients with active life; furthermore patients who were employed also present better QOLIE than the unemployed ones. From the 57 patients evaluated, **Palavras chaves:** Epilepsia, qualidade de vida e atividade física Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). Only 11 practiced leisure physical activities, and they presented better life quality compared to those who did not practice leisure physical activities. **Conclusion:** This work demonstrated that people with refractory TLE who are employed and have active life experience better QOLIE. It also showed that a small number of patients practice leisure physical exercise. Programmed physical exercise can be used as an adjunct treatment for people with refractory TLE. This approach not only leads to physiological benefits as well as the improvement of QOLIE of these patients.

TITLE

NI01 – MALFORMATIONS OF CORTICAL DEVELOPMENT AND EPILEPSY

Authors

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Institutions

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Malformations of cortical development (MCDs) are an important cause of medically refractory epilepsy. Many recent discoveries have altered our concepts of MCD. In particular the discovery that mutations of Tubulin genes can cause many types of MCDs, as well as axonal pathway-finding disorders, have revealed that "tubulinopathies" are an important cause of MCDs and epilepsy (1-6). Important new discoveries have also impacted our understanding of the importance of the attachment of radial glia to the pial basement membrane as a cause of Cobblestone Malformations (7-11) and the location of heterotopia as a manifestation of specific syndromes (12-14). This talk will cover these new concepts and well as establishing the place of these new disorders in the framework of the MCD classification tables.

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TITLE

NI02 – BEHAVIORAL ANALYSIS OF ZEBRAFISH LARVAE DURING HYPERTHERMIA INDUCED-SEIZURES

Authors

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Institutions

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Introduction: Animal models have been contributing to a better understanding of mechanisms underlying seizures. Recently, abnormal electrographic activities were described in zebrafish larvae during seizures induced by hyperthermia (Hunt et al., 2013). Despite its significance, this study was conducted using agar-immobilized larvae and no behavior analysis was performed with free-swimming animals. **Objectives:** (i) to establish a protocol for seizures induced by hyperthermia on free-swimming zebrafish larvae, (ii) to describe the behavioral pattern of the larvae during the seizures. Methods: free-swimming zebrafish larvae at five days post-fertilization (dpf) were separated in: 1. Hyperthermia group (HG) and 2. Control group (CG). Different protocols to induce seizure by hyperthermia were applied to HG. The CG was submitted to the same handling conditions but in normal water temperature (25oC). The zebrafish behavior was recorded by a video camera (JVC HD Everio GZ-EX210) and described by a qualified observer. **Results:** the best protocol

to achieve seizures in free-swimming zebrafish larvae at 5dpf was conducted using dry-bath equipment. Animals were individually placed into a Becker containing 30mL of water at 35oC for 10 minutes (n=5 each group). About 90 seconds after being placed into the Becker, the animals showed an increased swimming activity, clonus-like behavior and loss of posture. Seizures ceased when the animals were replaced into a tank with water at 25oC. Animals from CG did not present any seizure-like behavior. **Conclusion:** Our study brings a protocol for hyperthermia-induced seizures using free-swimming zebrafish larvae and describes the behavior associated with this hyperthermia assay. Additional studies are underway in order to enlarge the sample number, and to observe the long-term effects of the "febrile seizures" on the developing brain. **Support:** FAPESP #2013/08235-7

TITLE

NI03 – STUDY OF STRUCTURAL CHANGES ON MRI SCANS OF PATIENTS WITH EPILEPSY AND REFLEX SEIZURES

Authors

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Introduction: Reflex seizures (RS) are those triggered by a specific afferent stimulus or some specific activity. RSs result from factors that facilitate the recruitment and synchronization of a large group of neurons by the discharge of the afferent stimulation. The appropriate recognition of RS can add knowledge to the pathophysiological mechanisms of epilepsies. **Objectives:** To evaluate the presence and distribution of structural abnormalities in patients with focal epilepsies and RSs. **Method:** This is a cross-sectional study that included 83 adult individuals with focal epilepsy followed in the Epilepsy Clinic of the clinical hospital of UNICAMP. All patients were evaluated with standardized questionnaire about the presence of RS and its triggering factors. The analysis of structural changes in gray (GM) and white matter (WM) on magnetic resonance imaging (MRI) of patients with and without RS was performed using the technique of Voxels Based Morphometry (VBM) that allows automated analysis of the whole brain structure, without the prior definition of an area of interest. Images from patients were compared with a control group of 79 healthy individuals. The patients were divided according to clinical and electroencephalographic criteria into: 1) temporal lobe epilepsy (TLE) or 2) extra-temporal epilepsy (ETE). TLE patients with structural lesions other than hippocampal sclerosis were excluded from the VBM analysis. The statistical analysis of clinical data was performed with Systat9 ® software. **Results:** Forty-three patients reported RS and 40 denied RS. Patients with TLE with or without RS had GM atrophy in the ipsilateral hippocampus and thalamus. Patients with TLE and RS had more diffuse neocortical GM atrophy, including ipsilateral precentral gyrus and cuneus and mesial frontal region. Patients with ETE with or without RS had GM atrophy in the ipsilateral thalamus and precentral gyrus. Patients with ETE and RS also had GM atrophy in the bilateral cuneus. Diffuse WM atrophy was observed in TLE and ETE and no significant difference was observed between patients with or without RS. Conclusion: There are differences in the pattern of GM atrophy between patients with focal epilepsies with or without RS. Diffuse GM atrophy in patients with RS may contribute to the susceptibility to afferent stimuli to trigger seizures in these patients. This study was funded by the São Paulo Research Foundation - FAPESP

TITLE

NI04 – ABNORMAL NEUROGLIAL DIFFERENTIATION IS A KEY EVENT IN FOCAL CORTICAL DYSPLASIA (FCD) TYPE II

Authors

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Introduction: FCD is characterized by a spectrum of abnormalities in the development of the laminar structure of the human cerebral cortex. Microscopically, FCD is usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells. Since dysplastic tissue is highly epileptogenic, patients with FCD frequently need surgery to control their seizures. To date, the mechanism underlying the development of FCDs is poorly understood. **Objectives:** Our main objective was to determine whether abnormal microRNA regulation could be present in FCD. More specifically, we wanted to evaluate microRNA expression pattern in FCD and to identify potential microRNA target genes whose expression would be deregulated in FCD. **Methods:** We used total RNA isolated from brain tissue obtained after epilepsy surgery performed in 17 patients with type II FCD and 20 controls from autopsy. MiRNA expression profile was assessed by AffymetrixGeneChip platform miRNA array. Quantitative PCR (qPCR) and in situ hybridization (ISH) has been used to validate results miRNAsexperiments and to access expressionand localization of target genes. **Results:** MicroRNA expression studies using microarray revealed 39 microRNAs which were downregulated and only one microRNA overexpressed. Decreased expression of three miRNAs was confirmed by qPCR: hsa-miR-31, hsa-miR34a and hsa-let-7f. In addition, we found that NEUROG2, a possible target gene regulated by hsa-miR-31 is over expressed in FCD. **Conclusions:** The three microRNAs confirmed to be downregulated act as tumor suppressors and may lead to the abnormal histopathological features seen in FCD type II. Furthermore, overexpression

of NEUROG2,would lead to failure in the transition between neurogenesis and gliogenesis and could explain the existence of immature or poorly differentiated cell types, such as balloon cells, which are typical of FCD type II. **Financial support:** FAPESP, CAPES and CNPq.

TITLE

NI05 – IDENTIFICATION OF BIOMARKERS FOR PHARMACORESISTANCE OF EPILEPSY IN FOCAL CORTICAL DYSPLASIAS

Authors

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Introduction: Focal Cortical Dysplasia (FCD) is often associated with intractable epilepsy in up to 90% of patients. Therefore, surgical resection of abnormal tissue is frequently performed in order to achieve better seizure control. Nevertheless, surgery indication may be delayed due to a long investigation and still expensive process. Circulating microRNAs (miRNAs) have emerged as a powerful new class of biomarkers due to their high stability in plasma, strong association with specific disease states, noninvasive and easy quantification. **Objectives:** To identify if specific miRNAs species may be useful as biomarkers of pharmacoresistance in patients with FCD. **Methods:** To date, blood samples were collected from 17 patients (nine patients with FCD and intractable epilepsy; four patients with mesial temporal lobe epilepsy (MTLE) who responded well to treatment with antiepileptic drugs as well as four patients with pharmacoresistant MTLE) and 17 healthy control subjects. RNA was isolated from plasma of all samples by the miRNeasy Serum/Plasma Kit (Qiagen) according to the manufacturer's protocol. MiRNA quantification has been performed by quantitative PCR (qPCR). **Results/Conclusions:** We successfully established a protocol to isolate and quantify miRNAs from human plasma, aiming to minimize sample-to-sample variability and ensure quality of downstream analysis. Reverse transcription using TaqMan miRNA kit (Applied Biosystems) were used with modifications in the manufacturer's protocol. Six miRNAs (RNU 24, RNU 48, hsa-miR-16, hsa-miR-191, hsa-miR-451and hsa-miR-486) were chosen to be analyzed as endogenous controls and two of them were validated: hsa-miR-191 and hsa-miR-451 in our cohort. **Financial support:** FAPESP and CNPq.

TITLE

NI06 – THE RELATIONSHIP BETWEEN EXTRA-HIPPOCAMPAL GRAY MATTER ATROPHY AND TYPES OF AURAS AND IN MESIAL TEMPORAL LOBE EPILEPSY

Authors

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Institutions

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Introduction: Mesial Temporal Lobe Epilepsy (MTLE) is characterized by complex partial seizures frequently preceded by autonomic, epigastric and psychic auras. The types of auras can vary significantly among patients; however, they tend to be stereotyped in a given patient. Objectives: The purpose of this study was to investigate whether changes in gray matter volume (GMV) differ according to different subtypes of aura. **Methods:** We included 175 patients with mesial temporal lobe epilepsy (MTLE). The patients' auras were described and classified in 3 groups: Viscero-sensorial, Experiential and Autonomic. Voxel-based morphometry (VBM) was applied to magnetic resonance imaging (MRI) brain images. Statistical parametrical maps were used to compare structural changes between the different subtypes of aura and controls. **Results:** The analysis revealed specific areas of GMV reduction when compared to the different subtypes of auras between them and when compared to controls. Conclusion: Different subtypes of aura in MTLE are related to different areas of GMV reduction. These different morphologic changes support the hypothesis that patients with MTLE present a heterogeneous and widespread network of damage. **Financial support:** CNPq/PIBIC (Programa Institucional de Bolsas de Iniciação Científica) 2012/2013

TITLE

NI07 – EXPRESSIONAND LOCALIZATIONOF THE PTPRM GENE IN THE CENTRAL NERVOUS SYSTEM DURING DEVELOPMENTIN ANIMAL MODELS ANDIN PATIENTS WITH MESIAL TEMPORAL LOBEEPILEPSY (MTLE)

Authors

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Objetives: The present study aims to evaluatethe normal pattern ofexpression of the PTPRMgene duringmouse development, as well as to quantify and localizeitsgene productin samplesof human hippocampus,in order to investigate its possible role in MTLE. **Background:** The epilepsy syndromes displaying complex inheritance are still elusive when it comes to the identification of susceptibility genes even in the era of large genome wide association studies. Therefore, the use of candidate gene approach to study a more limited, but well characterized clinical sample still a valuable strategy. Our preliminary results indicate that protein tyrosine phosphatase, receptor type, M gene (PTPRM) may be up-regulated in brain tissue from patients with refractory MTLE. In addition, genetic association was identified in a case-control study of MTLE and SNPs within PTPRM. PTPRM gene product regulates a variety of cellular processes including cell growth, differentiation and mitotic cycle. **Design/Methods:** We investigated the expression of PTPRM in the brain tissues of patients with mesial temporal lobe epilepsy (MTLE) and inmouseusing real-time quantitative RT-PCR. Hippocampi were obtained from four patients with MTLE who underwent surgery for seizure control. Normal hippocampi were obtained from autopsies. Total RNA was isolated from animal whole brain at different time points (E15, E17, E18, P1, P7, P14, 4, 6, 8 and 24 weeks) or from human hippocampi. ComplementaryDNA(cDNA)wassynthesized using SuperScript® II Reverse Transcriptase (RT) (Life Technologies). We use the genes SDHA, BACTN,ENO/NSE as endogenous controls. All procedures were carried out in accordance with our Ethics Research Committees. **Results:** We did not observe a significant difference in the expression of PTPRM in human hippocampi of patients with MTLE when compared to controls after appropriate use of multiple endogenous controls. In addition, the analysis of PTPRM gene expression during mouse development indicates that this is probably a constitutive gene. **Conclusions:** This is the first study to investigate PTPRM expression in epilepsy. Although we did not observed significant differences in expression in samples from patients with MTLE, we believe that additional studies using laser capture microdissectionin human specimenis necessary to further investigate the matter. In addition, we will evaluate PTPRM expression in tissue obtained from rat induced epilepsy model.

TITLE

NI08 – LONGITUDINAL AND CROSS-SECTIONAL ANALYSIS OF HIPPOCAMPAL T2-SIGNAL IN FAMILIAL MESIAL TEMPORAL LOBE EPILEPSY

Authors

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Introduction: The relationship between seizure frequency and presence of hippocampus T2 signal abnormalities on MRI visual analysis in familial mesial temporal lobe epilepsy (FMTLE) has already been described. However, analyses using quantitative methods to evaluate progression of T2-signal have not yet been performed. **Objectives:** To correlate seizure control with hippocampal T2-signal in FMTLE patients and to analyze progression of T2-signal over time. **Methods:** We have analyzed 26 patients with FMTLE, 9 asymptomatic relatives (first or second degree relatives belonging to families with FMTLE) and 40 healthy controls. Patients were divided into 2 groups according to seizure frequency: infrequent seizures (less than three complex partial seizures (CPS)/year and no more than two secondary generalization/year; n=23); and frequent seizures: more than three CPS/year; n=3). Aftervoxel software was used to measure values of T2-signal on coronal two dimensional fast spin echo (2D-FSE) images (3T). MRI visual analysis was performed and patients with right hippocampal sclerosis were flipped to the left side, so that we could compare T2-signal values from the atrophic hippocampus and contralateral side. T2 values were compared between seizure frequency groups using analysis of variance (ANOVA) with Tukey´s post-hoc test for paired comparisons. A group of 22 FMTLE patients repeated MRI after 1 year or more in order to compare values of T2 signal over time. For this longitudinal analysis we used paired t-test. **Results:** There were significant differences between the relaxometry values of atrophic hippocampus comparing infrequent seizure group versus controls ($p<0.0001$) and frequent seizures versus controls ($p=0.014$), but not between the 2 groups of patients ($p=0.624$). When we analyzed contralateral hippocampus there was a significant difference between infrequent versus frequent seizure groups ($p=0.049$) and between frequent seizure and controls ($p=0.005$), but not between infrequent seizure group and controls ($p=0.287$). Longitudinal analysis showed increase in T2-signal on the atrophic hippocampus over time ($p<0.0001$). There was no change in T2 signal on the contralateral hippocampus. **Conclusion:** We identified T2-signal abnormalities mainly in the refractory group. This group also presented significant abnormalities on contralateral hippocampus. In addition, our results suggest a progression of hippocampal T2-signal occurring mainly on atrophic hippocampus. This project was financially supported by CNPq (PIBIC).

TITLE

NI09 – EXTRA-HIPPOCAMPAL GRAY MATTER ATROPHY IN PATIENTS WITH ANTIEPILEPTIC DRUGRESPONSIVE TEMPORAL LOBE EPILEPSY

Authors

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Institutions

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Introduction: Temporal lobe epilepsy (TLE) is related to areas of diffuse gray matter atrophy and its causes are not well understood; recurrent seizures are considered as one of the possible mechanisms. **Objectives:**The objective of this study was to investigate the reduction of gray matterin patients with TLE in remission of seizures with drug treatment. **Methods:** Thirty-one patients with TLE, seizure-free for at least two years with antiepileptic drug (AED) treatment, were studied. Eighteen of them had signs of hippocampal sclerosis on 3T magnetic resonance imaging (MRI) and 13 had normal MRI. T1-weighted images were analyzed with voxel-based morphometry technique, which allows the automatic comparison of whole brain volumes of different groups. The gray matter volumes of patients were compared to a group of 74 healthy controls (two samples t-test, p value<0.001, minimum of 30 voxels grouped). The images of those with right-sided epileptogenic zone were flipped in the right-left orientation, and the same was done with a comparable proportion of controls. **Results:** The images of TLE patients showed diffuse atrophy of gray matter. Maximum atrophy was found at hippocampus ipsilateral to the epileptogenic zone, but also at amygdala and ipsilateral precentral cortex and bilateral thalamus. **Conclusions:** Patients with TLE and seizure remission under AED treatment have gray matter atrophy in extra-hippocampal regions. These results suggest that causes other than seizures should be involved in the occurrence of diffuse brain damage observed in TLE.

TITLE

NI10 – INVESTIGATION OF LARGE-SCALE GENE EXPRESSION IN GENETIC MODELS OF EPILEPSY

Authors

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Background: Wistar audiogenic rat (WAR) is a genetic epilepsy model susceptible to audiogenic seizures, after high-intensity sound stimulation. Another genetic model we have recently identified is the generalized epilepsy with absence seizures (GEAS) rat. **Objetive:** The aim of the present study was to characterize and compare the genetic profile of these two strains using gene expression analysis.**Methods:** We obtained total RNA from five susceptible WAR (hippocampus and corpora quadrigemina), and two resistant WAR, as well as from hippocampus of three GEAS rats and three control Wistar. Gene expression analysis was performed using the GeneChip® Rat Genome 230 2.0 Array (Affymetrix™), and analyzed in R environment using the Affy and RankProd packages from Bioconductor. Overrepresented gene ontology categories and gene interactions and correlation networks were identified with MetaCore software. The main genes with differential expression and a possible biological role in epileptogenesis were validated by qRT-PCR. **Results:** Enriched gene ontology categories identified in WAR were involved in oxidative phosphorylation, neurophysiological process GABA-A receptor life cycle, as well LRRK2 in neurons in Parkinson`s disease. The genes validated by qRT-PCR were Grin1, Nedd8, Il18 and Slc1a3. In GEAS rats the top enriched gene ontology categories included: oxidative phosphorylation, LRRK2 in neurons in Parkinson`s disease and cytoskeleton remodeling neurofilaments. The genes validated by qRT-PCR were Grin1, Gabbr1 and Slc6a1. **Conclusion:** Our results clearly show the heterogeneous and intricate nature of the molecular mechanisms involved in epileptogenesis as well as the importance of studies looking at different regulatory pathways at once, in order to better appreciate this complexity. **Supported:** FAPESP-FAPEMIG.

TITLE

NI11 – IS MEMORY IMPAIRMENT RELATED TO SEIZURE FREQUENCY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY?

Authors

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Institutions

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Introduction: Patients with mesial temporal lobe epilepsy (MTLE) are frequently refractory to clinical treatment. However, there is a subgroup of MTLE patients with good response to antiepileptic drugs (DAEs), referred to as "benign MTLE". It is well established that MTLE patients have memory deficits due to hippocampal damage, however, little is known about the impact of seizure frequency on memory performance in these patients. **Objective:** To compare memory performance between MTLE patients refractory to DAEs and MTLE patients with good seizure control. **Methods:** We measured MRI hippocampal volumes (HV) and performed neuropsychological assessment in 22 patients refractory to DAEs (at least one complex partial seizure [CPS] per month) and 20 patients with good seizure control (three or less CPS per year and no secondary generalized seizures), all with MRI signs of hippocampal sclerosis (HS) on visual analysis. We also included 29 controls for comparison of volumetric data. Hippocampus manual segmentation was performed by a single observer using the Display software (http://www.bic.mni.mcgill.

ca/ServicesSoftware/MINC) without prior knowledge of disease history and participant's identification. The neuropsychological assessment included: the Edinburgh Handedness Inventory; subtests of the Wechsler Memory Scale-Revised; Rey Auditory Verbal Learning Test and subtests of the Wechsler Adult Intelligence Scale-III. **Results:** We observed a significant bilateral reduction of HV in MTLE patients groups when compared to controls ($p<0.00001$). The degree of hippocampal atrophy (HA) between MTLE patients groups was not different; however there was a negative correlation between seizure frequency and HV ($r= -0.3$ for the side ipsilateral to the HS; $r= -0.55$ for the contralateral to the HS). There was also a positive correlation between age of onset and degree of HA ($r=0.37$). There was no difference in memory performance between patients refractory to DAEs and patients with good seizure control. **Conclusions:** Our results suggest that despite of different seizure frequencies patients with MRI signs of HS had the same memory performance in neuropsychological testing. This finding suggests that memory impairment in MTLE patients is more influenced by hippocampal damage than by seizure frequency. **Financial Support:** FAPESP.

TITLE

NP01 – REVERSIBLE DEMENTIA INDUCED BY PROLONGED USE OF VALPROIC ACID: A CASE REPORT

Authors

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Introduction: Although it is well known that Valproate is a remarkably safe and effective antiepileptic drug in a wide range of epileptic conditions, explaining its long-term clinical usage for treatment of epilepsy, it has also come to acknowledge that VPA maybe the cause of reversible cognitive decline, parkinsonism and pseudo-atrophy on the neuroimaging. **Case report:** We presented the case of a 67 years-old male patient, presenting focal symptomatic epilepsy, using carbamazepine 1200 mg and Valproic Acid 1500 mg for 2 years, which was taken by family to the ER department due to a history of progressive amnesia and decline in the daily live activities. In the neurological examination, the patient presented a mental status examination of 17/30 (points lost on orientation, attention, evocation, verbal command), with marked apathy and delay in answering questions or commands. Patient also presented rest tremor, gait disturbance and hypomimia, but there was no history of urinary incontinence. Head CT presented a discrete cerebral atrophy, and laboratory screening for reversible dementia (VDRL, TSH, T4-L, B12 vitam, folicacid, viral sorologies, anmonia) were normal. VPA blood levels were whitin therapeutic range. CSF studies were also normal. VPA was changed to lamotrigine, with gradual normalization of cognitive functions and gait. After 4 months the mental status examination was 26/30, patient regained total Independence on daily life activities, and did not present any signs of parkinsonism. **Conclusion:** Valproic acid is a broad spectrum antiepileptic drug, with relatively few side effects, but the possibility of cognitive side effects should always be remembered.

TITLE

NP02 – DAY TIMES LEEPINESSAMONGPATIENTSWITH EPILEPSY: DO BENZODIAZEPINES PLAY A ROLE?

Authors

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Introduction: Several studies suggest that poor sleep quality and drowsiness during the daytime can have a negative impact on the quality of life of people, which is especially true in patients with epilepsy, frequently attributed to antiepileptic drugs and seizures. Benzodiazepines are used as antiepileptic drugs, but also have sedative and hypnotic effects. **Objective:** The aim of this study was to evaluate excessive daytime sleepiness (EDS) in patients with epilepsy and the impact of adding benzodiazepines on their daytime sleepiness. **Methods:** 75 unselected patients (66% were male, median age were 46.7 years) on monotherapy or polytherapy for focal epilepsy had their sleep assessed by the Epworth Sleepiness Scale (ESS). Patients were then divided in three groups (monotherapy, poliytherapy and polytherapy with benzodiazepinic drugs). Patients with depression, anxiety or another psychiatric diagnosis, patients with mental retardation, or using other psychotropic drugs other than antiepileptic drugs were excluded. **Results:** The median age 44 (58.66%) patients presented an ESS score >10. Out of the monotherapy group, the median score on ESS was 8.8, 9.4 in the polytherapy group and 10.2 for the group with benzodiazepines (no statistically significant difference). **Conclusion:** The prevalence of excessive daytime sleepiness was high in comparison to other studies conducted in patients with epilepsy in other countries, but similar to other Brazilian studies. The use of benzodiazepines increased the median ESS score, but not enough to play a pivotal role on excessive daytime sleepiness on patients with epilepsy.

TITLE

NP03 – POLYMORPHISMS IN DRUG METABOLISM AND DRUG TRANSPORTER GENES ASSOCIATED WITH PHARMACORESISTANCE IN MESIAL TEMPORAL LOBE EPILEPSY

Authors

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Introduction: Many patients with mesial temporal lobe epilepsy (MTLE) do not respond to adequate drug therapy. Previous studies suggest that genetic variability in genes encoding drug-transporter and drug-metabolism proteins could lead to pharmacoresistance. **Objectives:** To investigate whether single nucleotide polymorphisms (SNPs) on drug-transporter and drug-metabolism genes could be associated with pharmacoresistance in a cohort of patients with MTLE. **Methods:** We evaluated DNA sample of 242 MTLE patients, including 78 responders to drug therapy and 164 considered to be pharmacoresistants. A total of 121 SNPs in two different drug-transporter (ABCB1, ABCC2) and nine drug-metabolism genes (CYP1A1, CYP1A2, CYP1B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4, CYP3A5) was genotyped using the Applied Biosystem SNPlexTM system. Genetic association was calculated using logistic and stepwise regression analysis by R software, with Bonferroni correction for multiple comparisons. Furthermore, in order to evaluate population stratification, we estimated Fst using 119 additional SNPs. **Results:** We found significant association for rs3740066 in ABCC2; rs2551188 in CYP1B1; rs4086116, rs2153628 and rs1934963 in CYP2C9; and rs2070677 in CYP2E1 gene. In addition, we observed that specific combination of genotypes and alleles was able to predict up to 15% of the total variance in pharmacoresistance; whereas, hippocampal sclerosis on MRI had a 9% contribution. In addition, we did not find population stratification in our sample (Fst=0.0055). **Conclusion:** We found evidence that these multiple genetic factors combined could be involved in pharmacoresistance in patients with MTLE, and this information can be useful in the future for clinical stratification of patients. **Finantial support:** FAPESP (Fundação de Amparo a Pesquisa do Estado de São Paulo, Brazil); CNPq (Conselho Nacional de Pesquisa, Brazil).

TITLE

NP03 – PROTEOMIC PROFILING OF THE HIPPOCAMPUS OF RATS SUBJECTED TO THE PILOCARPINE MODEL OF EPILEPSY

Authors

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Background and Purpose: The temporal lobe epilepsy (TLE) is the most common type of partial complex seizure in adulthood. High doses of pilocarpine to rats induce status epilepticus (SE) and reproduce the main characteristics of TLE. This model appears to be highly isomorphic with the human disease. We employed a two-dimensional gel electrophoresis (2-DE) to study differential expression of proteins in the hippocampus of rats exhibiting SRS induced by pilocarpine. We also assessed the proteomic profile of rats apparently naturally resistant to SE induction. **Methods and Results:** Male Wistar rats (weight ~ 250g). Groups: PILO SE: animals treated with pilocarpine (360mg/kg, N=6) presenting SE and PILO SE free (same dose of pilocarpine). Control: SALINE (N=6). Both groups were analyzed 90 days after SE onset or pilocarpine administration. Hippocampi were dissected and homogenized in a lysis buffer. Homogenates were used to perform 2-DE. Protein spots were analyzed by PDQuest software revealing forty proteins differentially expressed in the hippocampus of epileptic rat compared to control ($p<0.05$, Student's test). LC MS/MS results were analyzed with MASCOT. Thirty-one of the identified proteins were up-regulated in epileptic rat, among them dihydropyrimidinase, V-type proton ATPase and alpha-synuclein. Seven proteins were down-regulated, i.e. fructose-bisphosphate aldolase, phospholipase A2, ATP-binding cassette, malate dehydrogenase and guanine nucleotide-binding protein subunits beta-1 and beta-3. Two proteins were expressed only in the control: L-lactate dehydrogenase, and phosphatidylethanolamine-binding protein. In the free SE group were identified twenty-five differentially expressed proteins compared with epileptic and control animals, between them dihydropyrimidinase was up-regulated and V-type proton ATPase was down-regulated. Statin and creatine kinase B were expressed only in the SE free group. **Conclusion:** Some of the proteins differentially expressed in the hippocampus of rats with SRS were also observed altered in the hippocampus of patients with TLE. Animals SE free exhibit alterations in protein expression. Financial support: Fapesp, INCT-MCT, CNPq and CAPES. We acknowledge the Laboratório Nacional de Luz Sincrontron- LNLS, Brazil for their support with the mass spectrometry analysis.
