Infantile Seizure Society

ILAE-CEA

LICE
Lega Italiana contro l'Epilessia

Bambino Gesù
OSPEDALE PEDIATRICO

ISSET

19TH INTERNATIONAL SYMPOSIUM ON SEVERE INFANTILE EPILEPSIES: OLD AND NEW TREATMENTS

Rome, September, 20th - 22nd 2018

Pre-Congress Meeting

5th Tagliacozzo International Course on Drug Resistant Epilepsies
Rome, September, 19th - 20th 2018

PROGRAM AND ABSTRACTS

PONTIFICIA UNIVERSITÁ URBANIANA

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Marigold Study

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POTENTIAL NEW THERAPY FOR
GENETIC EPILEPSY

Do you know someone with CDKL5 deficiency disorder (CDD)?

A new clinical trial is underway to test the use of ganaxolone in children and young adults with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD).

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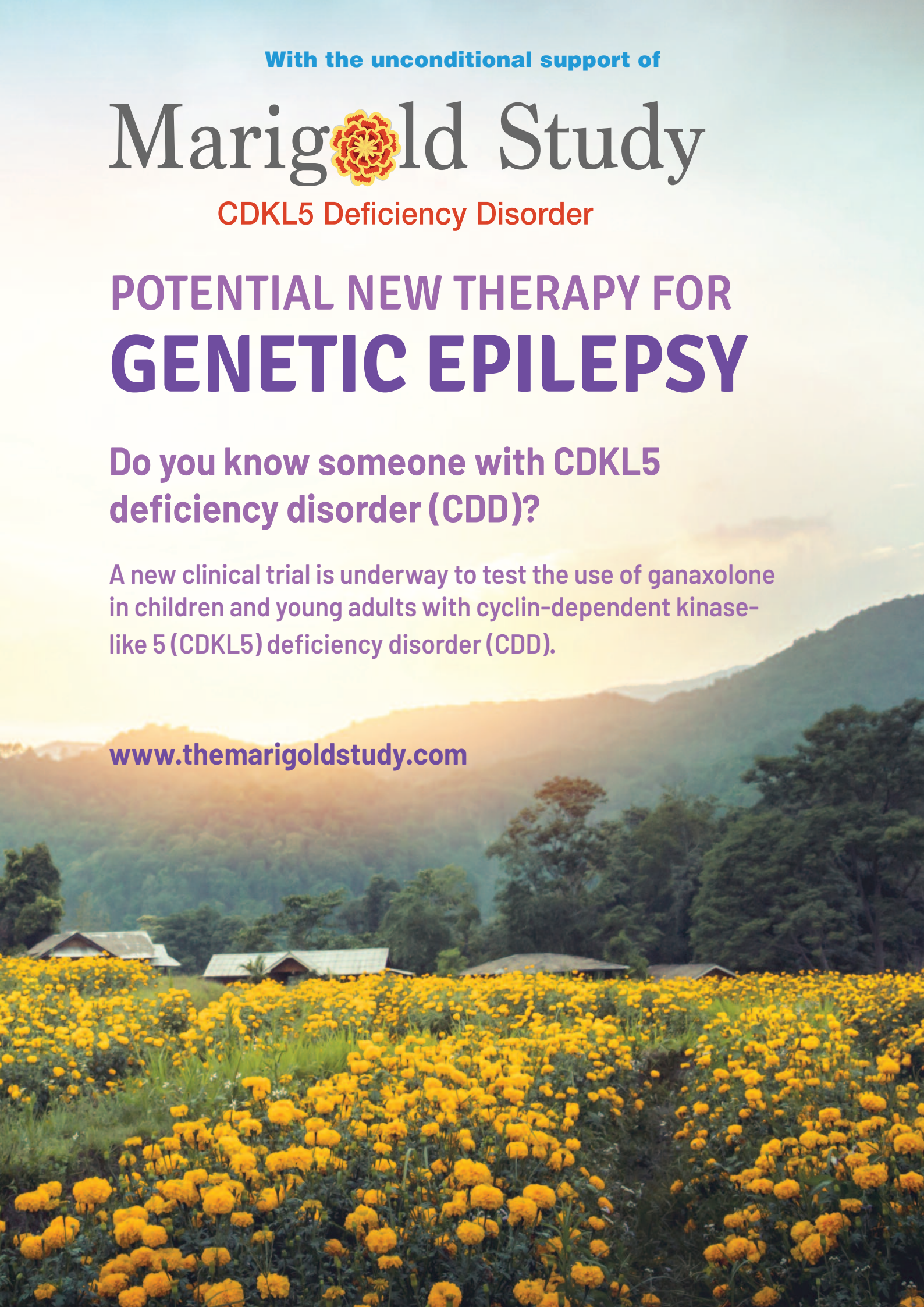
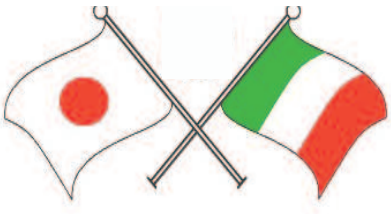


With the unconditial support of

hhc Human Health Care

19th Annual Meeting of Infantile Seizure Society (ISS)
International Symposium on Severe infantile Epilepsies: old and new Treatments (ISSET 2018)



Welcome letter

Dear Friends and Colleagues,

it gives us a special great privilege to host the 19th Infantile Seizure Society meeting which for the first time takes place in Europe, namely in Italy. It is a big honor and privilege to host the 19th ISS Meeting in Rome and we would like to express our sincere thanks to the ISS Advisory Board having trusted in the Bambino Gesù Paediatric Hospital team.

The current edition of ISS meeting is dedicated to the treatment of Severe Infantile Epilepsies, analyzing old and new treatments.

We would like to present our compliments to all academic colleagues and attendees, young researcher and clinicians from Europe and other countries worldwide coming in contact with the ISS, a so prestigious scientific society in the field of epilepsy.

We express our deep satisfaction for sharing this important moment for the development of epilepsy across our countries.

Our sincere thanks to our eminent speakers, who honored us with their presence, making our congress an high level international initiative.

We are greatly honored and pleased to welcome you to Rome, also on behalf of the ISS Advisory Board and on behalf of ISS Chairperson Prof. Makiko Osawa.

We will have an up-to date on the treatment of the most severe epileptic entities with onset during infancy as symptomatic focal epilepsy, and epileptic encephalopathies looking at the new insights coming from the genetics. The indications and the use of old and new antiepileptic drugs will be discussed, together with the surgical procedures and alternative treatments. We will have also platform and poster presentations with extensive discussions between the attendees and the invited speakers.

Result - as you could see from the hand out material - is an attractive scientific program, in which we wanted to include the best scientists in the area, and current leaders in the fields of epilepsy.

We have to thank all the scientific societies who endorsed ISSET, as International League Against Epilepsy Europe (ILAE -Europe) and Italian League Against Epilepsy (LICE). We also thanks companies and non-profit associations that put their trust on us and gave their financial support for the realization of this event.

The congress is hosted in the Vatican City, one of the most important places in the world.

Rome, the eternal city, with its artistic and cultural beauties, welcome all of you for a memorable ISS meeting.

We trust that this will be an unforgettable and rewording experience to all of you.

Chairperson of Infantile Seizure Society

Makiko Osawa (Japan)

President of ISSET 2018

Federico Vigevano (Italy)

Vice-President of ISSET 2018

Nicola Specchio (Italy)

Advisory Board

Alexis Arzimanoglou (France)
Meir Bialer (Israel)
Kai-Ping Chang (Taiwan)
Paolo Curatolo (Italy)
Lieven Lagae (Belgium)
Oriano Mecarelli (Italy)
Solomon Moshe (USA)
Shinichi Niijima (Japan)
Emilio Perucca (Italy)
Eugen Trinka (Austria)
Samuel Wiebe (USA)
Hitoshi Yamamoto (Japan)
Hideo Yamanouchi (Japan)

OVERVIEW OF DAILY PROGRAM

Time	Day 1 Wednesday, September 19th	Day 2 Thursday, September 20th	Day 3 Friday, September 21st	Day 4 Saturday, September 22nd
08:30		08:30-10:45 **Pre-Congress Meeting** 5th Tagliacozzo International Course on Drug Resistant Epilepsies **Room 3**		
09:00			09:00-10:30 **Session 3** Dravet Syndrome	08:45-10:15 **Session 7** Alternative treatments
10:00	09:30 **Registration desk for Pre-Congress Meeting open**	10:45-11:00 Coffee break	10:30-11:00 Coffee break	10:15-10:45 Coffee break
11:00	11:00-12:45 **Pre-Congress Meeting** 5th Tagliacozzo International Course on Drug Resistant Epilepsies **Room 3**	11:00-12:30 **Pre-Congress Meeting and Closing remarks** **Room 3** 11:00 **Registration desk for Congress open**	11:00-12:30 **Session 4** Tuberous Sclerosis	10:45-11:30 **Keynote Lecture 4** H. Yamanouchi
12:00				11:30-13:00 **Session 8** Platform 2
13:00	12:45-13:45 **Lunch**	12:30-13:30 **Lunch** (for Pre-Congress meeting and ISSET participants)	12:30-13:30 **Keynote Lecture 3** M. Bialer	13:00-14:30 **Poster Session and Lunch**
14:00	14:00-17:00 **Pre-Congress Meeting** 5th Tagliacozzo International Course on Drug Resistant Epilepsies **Room 3**	**Aula Magna** 13.30-14:00 Opening Address 14:00-15:00 **Keynote Lecture 1** E. Perucca	13:30-15:00 **Poster Session and Lunch**	
15:00		15:00-16:30 **Session 1** Early onset epilepsies	15:00-16:00 **Session 5** Platform 1	14:30-16:00 **Session 9** SUDEP
16:00		16:30-17:00 Coffee break	16:00-17:30 **Session 6** Epilepsy Surgery	**Closing Remarks**
17:00	17:00-17:30 Coffee break	17:00-18:00 **Session 2** Epilepsy and associated disorders	17:30 End of the session	
18:00	17:30-19:00 **Pre-Congress Meeting** 5th Tagliacozzo International Course on Drug Resistant Epilepsies **Room 3**	18:00-18:45 **Keynote Lecture 2** N. Specchio 18:45-19:15 Break	18:30 Departure from the Congress Venue	
19:00		19.15 **Openning Ceremony** 19.45 **Concert**	19:30-21:30 **Farewell Reception** *To the Residence of the Ambassador of Japan to the Holy See*	
20:00		20.30 **Welcome Reception**		

GENERAL INFORMATION

Congress Venue

Pontificia Università Urbaniana
Via Urbano VIII, 16
Roma - Vatican City

The **Pontifical Urban University**, also called the ***"Urbaniana"*** after its names in both Latin and Italian, is a pontifical university under the authority of the Congregation for the Evangelization of Peoples. The university's mission is to train priests, religious brothers and sisters, and lay people for service as missionaries. Its campus is located on the Janiculum Hill in Rome, on extraterritorial property of the Holy See.

Instructions for Oral Presentation

- A single projection screen with sound is available for presentation
- Conflict of Interest (COI) should be presented ahead of the presentation
- All speakers are requested to register and deliver their presentation to the technician at the Reharsal Room at least two hours before their presentation
- All presentations should be given within the allotted time under the management of chairpersons

Poster Sessions

Will take place in conjunction with lunches on
September 21st from 13:30 to 15:00 will be discussed posters from nbr. 1 to 27
September 22nd from 13:00 to 14:30 will be discussed posters from nbr. 28 to 47
In Room 1
The secretariat will provide 1x2 size - vertical panels and material to hang up the posters

Certificate of attendance

A certificate will be delivered to every Participant at the end of each Meeting.
Please apply to the Secretariat Desk

Secretariat

The Secretariat remains open at the following times:
Wed, September 19th - 08:30 - 19:00
Thu, September 20th - 08:00 - 20:30
Fri, September 21st - 08:15 - 18:30
Sat, September 22nd - 08:15 - 16:00

Name badge

All attendees will be issued with a name badge upon registration.
This badge will be the official pass to enter the "Urbaniana" - Congress Venue, sessions, coffee breaks, luncheons, Welcome and Farewell Receptions.
Attendees are kindly required to wear it at all times.
Admission to the Pre-Meeting and Symposium will not be allowed without badge identification.

In case of loss please contact the Secretariat Desk for a replacement

Welcome Reception (for registrants only)

Thursday 20th at 20:30 - at Urbaniana

Farewell Reception

Friday 21st at 19:30 - hosted by the Ambassador of Japan to the Holy See at his Residence

Coffee breaks and Lunches (for registrants only)

Complimentary coffees and lunches are included in the registration fees and will be provided at Urbaniana

Accompanying program (only for registered persons)

September 21st - at 13:00 - Meeting point - Congress Secretariat - "Urbaniana"
Departure by private bus and English speaking guide for the visit of St. Peter Basilica and Vatican Museums

Mobile phones

On behalf of the Organizer Committee we highly recommend to switch off your mobile phone before enterring the Session Rooms

Climate

September is a great time to visit Rome if you want to enjoy the city and sunshine without feeling overwhelmed or uncomfortable because of the heat. Rome weather in September is very mild with cooler temperatures than previous months and plenty of sunshine.
The climate cools down in September and temperatures are more comfortable with highs of 27°C. At night, you can expect temperatures to lower to around 16°C. You'll have ten hours of sunlight per day, which is rarely interrupted by cloud coverage. The average rainfall is around 68mm spread over nine days of the month

Currency

Like most of the rest of the European Union, Italy uses the Euro as its currency. You'll see the Euro represented by both the symbol - € - and the initials: EUR.

Time Zone

Rome follows Central European Time (CET) which is one hours ahead of Greenwich Mean Time (GMT) and six hours ahead of Eastern Standard Time (EST). At the time of the conference, summer daylight saving will be in operation which is two hours ahead of GMT.

Organizing Secretariat

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www.ptsroma.it/isset2018

REGISTRATION FEES (expressed in Euro) All rates are subject to VAT 22%

	From July 1st
ISS MEMBER	
Congress	€ 400,00
Tagliacozzo & Congress	€ 500,00
Young Participant*	€ 300,00
Young Participant* Tagliacozzo & Congress	€ 400,00
NON ISS MEMBER	
Congress	€ 500,00
Tagliacozzo & Congress	€ 600,00
Young Participant*	€ 400,00
Young Participant* Tagliacozzo & Congress	€ 500,00
Tagliacozzo Pre-Congress only	€ 150,00
Accompanying persons	€ 200,00

*Under 35 years of age. The Participant must not have completed 35 years on the day of the beginning of the congress.

REGISTRATION FEES INCLUDE:

- Scientific Sessions
- Congress kit
- Certificate of attendance
- Coffee and lunches as in the program
- Reception on September 20 (not included for Participant joining “Tagliacozzo pre-congress” only)
- Farewell Dinner on September 21st

ACCOMPANYING PERSON REGISTRATION FEE INCLUDES:

- Reception on September 20th
- Farewell Dinner on September 21st
- Visit of the Vatican Museums and St. Peter Basilica on September 21st at 1 pm

Wednesday, September 19th

Pre-Congress Meeting

5th Tagliacozzo International Course on Drug Resistant Epilepsies

Chairs: ***Nicola Specchio - Federico Vigevano*** **(Italy)**

09:30 Registration Desk open

Room 3

11:00 - 12:30 Classification of epilepsies: new insights from the recent report of the ILAE Commission
Ingrid Scheffer (Australia)

How to classify epileptic seizures: development of a new algorithm
Federico Vigevano (Italy)

12:30 - 12:45 Discussion

12:45 - 13:45 Lunch

Chair: ***Paolo Tinuper*** **(Italy)**

14:00 - 15:30 Seizures with either focal or generalized onset in adult
Paolo Tinuper (Italy)

Focal and generalised seizures in children
Floor Jansen (The Netherlands)

Chair: ***Nana Tatishvili*** **(Georgia)**

15:30 - 17:00 The concept of "Impairment of consciousness" in adults
Francesca Bisulli (Italy)

How to define the impairment of consciousness in children
Lucia Fusco (Italy)

17:00 - 17:30 Coffee break

Chair: ***Nicola Specchio*** **(Italy)**

17:30 - 18:15 Refining the concept: epileptic encephalopathies versus epilepsies with developmental encephalopathy - the role of the etiology
Dana Craiu (Romania)

Thursday, September 20th

Pre-Congress Meeting

5th Tagliacozzo International Course on Drug Resistant Epilepsies

Room 3

Chair: ***Hideo Yamanouchi*** **(Japan)**

08:30 - 09:15 Emerging Concepts on the Classification of Status Epilepticus and on the Understanding of Drug-Resistant Status Epilepticus
Raman Sankar (USA)

09:15 - 10:45 Unclassified type of seizures in adults: tools and methods for understanding the network
Stefano Meletti (Italy)

The role of unclassified type of seizures in epilepsy syndromes in children: from Epilepsy Syndromes to Epilepsy Sequences
Olivier Dulac (France)

10:45 - 11:00 Coffee break

Chair: ***Hitoshi Yamamoto*** **(Japan)**

11:00 - 12:30 Epileptic spams as a time dependent seizure type: semiology and syndromic value
Nicola Specchio (Italy)

The network of Epileptic spasms, insights from etiology-related patterns and physiological studies
Renzo Guerrini (Italy)

Closing Remarks of the Pre-Congress Meeting

Thursday, September 20th

19th Annual Meeting of Infantile Seizure Society (ISS)
International Symposium on Severe infantile Epilepsies: old and new Treatments

11:00 Registration Desk open

12:30 Lunch (for Pre-Congress Meeting and ISSET Participants)

Aula Magna

13:30 Opening Address

14:00 **Keynote Lecture 1**

Chairs: ***Makiko Osawa*** **(Japan) –** ***Federico Vigevano*** **(Italy)**

Changing paradigms in the development of new treatments for paediatric epilepsies
Emilio Perucca (Italy)

15:00 **Session 1 - Early onset epilepsies**

Chairs: ***Raman Sankar*** **(USA) –** ***Hideo Yamanouchi*** **(Japan)**

Prognosis of early onset epilepsies
Kuang-Lin Lin (Taiwan)

Epileptic network and cognitive decline
Stefano Meletti (Italy)

Treatment strategies
Helen Cross (UK)

16:30 Coffee break

17:00 **Session 2 - Epilepsy and associated disorders**

Chairs: ***Renzo Guerrini*** **(Italy) –** ***Hitoshi Yamamoto*** **(Japan)**

Epilepsy and Movement Disorders
Ingrid Scheffer (Australia)

Epilepsy and inflammation
Tiziana Granata (Italy)

18:00 **Keynote Lecture 2**

Diagnosis CLN2 disease within Childhood epilepsies
Nicola Specchio (Italy)

18:45 Break

19:15 **Opening Ceremony**

19:45 **Concert**

by Mezzosoprano Anna Maria Di Micco

20:30 Welcome Reception
Urbaniana

Friday, September 21st

09:00 **Session 3 - Dravet Syndrome**

Aula Magna

Chairs: ***Charlotte Dravet*** **(France) -** ***Akihisa Okumura*** **(Japan)**

Clinical and Genetics
Norimichi Higurashi (Japan)

Stem cells and gene therapy for “Dravet Syndrome”
Vania Broccoli (Italy)

New perspectives in the treatment
Nicola Specchio (Italy)

Management in adult patients with Dravet Symdrome
Rima Nabbout (France)

10:30 Coffee break

11:00 **Session 4 - Tuberous Sclerosis**

Chairs: ***Paolo Curatolo*** **-** ***Federico Vigevano*** **(Italy)**

Pathogenesis and genetic substrate
Shinichi Hirose (Japan)

Everolimus
Romina Moavero (Italy)

Surgery in patients with tuberous sclerosis
Floor Jansen (The Netherlands)

12:30 **Keynote Lecture 3**

New antiepileptic drugs in development: what is their novelty and potential

Meir Bialer (Israel)

13:30
15:00 Poster Session and lunch

POSTER - ROOM 1

P1 **ACUTE DISSEMINATED ENCEPHALOMYELITIS AND SUBSEQUENT EPILEPSY IN CHILDREN**
Ying-Chao Chang, Chao-Ching Huang (Taiwan)

P2 **CLINICAL CHARACTERISTICS AND RISK FACTORS FOR SEIZURES WITH GASTROENTERITIS IN CHILDHOOD: A COMPARATIVE STUDY OF FEBRILE AND AFEBRILE ATTACKS**
Tai-Heng Chen, Yao-Hua Liu, Wei-Tsun Kao, Yung-Hao Tseng (Taiwan)

P3 **STIMULUS-INDUCED REPETITIVE DISCHARGES (SIRPIDS) IN A NEWBORN WITH TUBULINOPATHY**
Li-Wen Chen (Taiwan)

P4 **USE OF AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY TO PREDICT THE SEIZURE OUTCOME IN INFANTS WITH NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY TREATED WITH THERAPEUTIC HYPOTHERMIA**
Yun-Ju Chen, Ming-Chou Chiang, Jainn-Jim Lin, Kuang-Lin Lin, I-Jun Chou, Huei-Shyong Wang, Shu-Sing Kong, I-Chen Su (Taiwan)

P5 **USING EPILEPSY ONTOLOGY-BASED INTEGRATED DATABASE TOWARD NEW EPILEPSY CLASSIFICATION AND PRECISION MEDICINE**
Kuo-Liang Chiang, Chin-Yin Huang (Taiwan)

P6 **EEG PERFORMED FOR FIRST EPISODE OF FEBRILE SEIZURE IN CHILDREN MIGHT HAVE THE VALUE TO PREDICT SUBSEQUENT EPILEPSY**
Jung Chieh Du, Kun Mei Lee , Hsin Lin Wu,Ya Chi Yang, Min Lee,Ting Fang Chiu (Taiwan)

P7 **EPILEPSY AND ATYPICAL FORM OF STATUS EPILEPTICUS IN FUKUYAMA-TYPE CONGENITAL MUSCULAR DYSTROPHY**
Ryoko Hayashi, Ken Nakajima, Rie Nakai, Taikan Oboshi, Tomokazu Kimizu, Tae Ikeda, Yukiko Mogami, Keiko Yanagihara, Yasuhiro Suzuki (Japan)

P8 **STRONG COUPLING BETWEEN SLOW OSCILLATIONS AND WIDE FAST RIPPLES IN CHILDREN WITH EPILEPTIC SPASMS: INVESTIGATION OF MODULATION INDEX AND OCCURRENCE RATE**
Yasushi Iimura, Hiroshi Otsubo (Canada)

P9 **A STUDY ON THE DIAGNOSTIC VALUE OF CHROMOSOME MICROARRAY ANALYSIS IN PEDIATRIC EPILEPSY WITH COMPLEX PHENOTYPES**
Won Seop Kim, Jon Soo KIM (Republic of Korea)

P10 **TUBB2A MUTATION IN A CHILD WITH EPILEPSY, DEVELOPMENTAL DELAY, AND SIMPLIFIED GYRAL PATTERN**
Young Ok Kim, Yun Young Leeb, Woong Yoonb, Myeong-Kyu Kimc, Young Jong Wooa (Republic of Korea)

P11 IMMUNOTHERAPY FOR ANTI N-METHYL-D-ASPARTATE RECEPTOR ENCEPHALITIS
Shu Sing Kong, Yun-Ju Chen, I-Chen Su, Kuang-Lin Lin, I-Jun Chou (Taiwan)

P12 COGNITION AND EVOLUTION OF MOVEMENT DISORDERS OF FOXG1-RELATED SYNDROME
Wang-Tso Lee, Lee Chin Wong, Yan-Tzu Wu, Wen-Chin Weng (Taiwan)

P13 INFANTILE SPASMS IN A PATIENT WITH MOSAIC MONOCENTRIC AND DUPLICATED SUPERNUMERARY MARKER CHROMOSOME 15
Hiroshi Matsumoto, Kiyotaka Zaha, Kiyotaka Isobe, Keiko Matsubara, Shigeaki Nonoyama (Japan)

P14 RHOBTB2 RELATED ENCEPHALOPATHY: PRECISION MEDICINE SCENARIO SHOULD BE KEPT IN MIND
Gia Melikishvili, Nugzar Sekhniaidze, Lela Lortkipanidze, Sophio Kakabadze, Mariam Melikishvili, Nazi Tabatadze (Georgia)

P15 EPILEPSY IN INFANT WITH DIETARY COBALAMIN DEFICIENCY AFTER SUPPLEMENTARY TREATMENT
Takao Morimune, Jun Matsui, Wataru Saika, Noriko Nishikura, Tatsuyuki Sokoda, Yoshihiro Maruo (Japan)

P16 EPILEPTIC STATUS. EPSTEIN-BARR VIRUS ASSOCIATED ENCEPHALITIS: CLINICAL CASE
Askhat Mukushev, Raushan Kenzhegulova, Assem Khamzina, Gulzhan Moldagalieva (Kazakistan)

P17 QUINIDINE THERAPY IN A GIRL WITH MIGRATING PARTIAL SEIZURES OF I INFANCY CAUSED BY KCNT1 MUTATION
Rie Nakai, Aiko Hirano, Ryoko Hayashi, Tae Ikeda, Sadami Kimura, Yukiko Migami, Keiko Yanagihara, Yasuhiro Suzuki (Japan)

P18 ANALYSIS OF EPILEPTIC SPASMS OF WEST SYNDROME IN 128-CHANNEL DENSE ARRAY ELECTROENCEPHALOGRAPHY
Shingo Oana, Gaku Yamanaka, Yu Ishida, Takamatsu Tomoko, Mika Takeshita, Natsumi Morishita, Shinichiro Morichi, Hisashi Kawashima (Japan)

P19 EPILEPTIC SPASMS IN FIVE CHILDREN CARRYING WDR45 MUTATIONS
Taikan Oboshi, Yukitoshi Takahashi, Shinsaku Yoshitomi, Tokito Yamaguchi, Hiroko Ikeda, Katumi Imai, Mituhiro Katou (Japan)

P20 SEVERE HYPERKINETIC MOVEMENT DISORDER IN GNAO1 ENCEPHALOPATHY-LONG TERM VIDEO CASE REPORT AND REVIEW OF LITERATURE
Oliver Maier, Philip Broser (Switzerland)

P21 HYPSARRHYTHMIA DURING CRITICAL TIME WINDOW OF BRAIN DEVELOPMENT IN THE FIRST YEAR OF LIFE MAY RESULT IN SPECIFIC COGNITIVE DEFICITS
Zvonka Rener-Primec, Vali Glavič Tretnjak, Janez Stare (Slovenia)

P22 DOES THE TITER OF ANTI-GLUTAMIC ACID DECARBOXYLASE (GAD)-ANTIBODY MAKE DIFFERENCE IN PEDIATRIC PATIENTS WITH ENCEPHALITIS OR ENCEPHALOPATHY
I-Chen Su, Kuang-Lin Lin, I-Jun Chou, Jainn-Jim Lin, Huei-Shyong Wang, Yun-Ju Chen, Shu Sing Kong (Taiwan)

P23 TEMPORO-POLAR GRAY/WHITE MATTER BLURRING PRIOR TO FEBRILE SEIZURE STATUS IN TEMPORAL LOBE EPILEPSY
Yuji Sugawara, Takeshi Hasegawa, Toshihiro Nomura, Kengo Moriyama, Tomoko Mizuno, Daisuke Kobayashi, Motoki Inaji, Taketoshi Maehara (Japan)

P24 BROADEN THE PHENOTYPE OF SCN1A CHANNELOPATHIES: RESULTS OF TAIWANESE COHORT STUDY
Y*u Min Syu, Jao-Shwann Liang, Jyh-Feng Lu* (Taiwan)

P25 ELECTROENCEPHALOGRAPHY IN FOLLOW-UP OF CHILDHOOD EPILEPSY
Gabriela Tavchioska (Republic of Macedonia)

P26 SEIZURE AND NEUROIMAGING CHARACTERISTICS OF EPILEPSY IN CHILDREN BORN VERY PRETERM
Yi-Fang Tu, Chao-Ching Huang (Taiwan)

P27 GRANZYME A AS A POTENTIAL BIOMARKER OF ACUTE ENCEPHALOPATHY AND COMPLEX FEBRILE SEIZURES
Gaku Yamanaka, Ryou Takahashi, Shingo Oana, Shinichiro Morichi, Takamatsu Tomoko, Yu Ishida, Natsumi Morishita, Mika Takeshita, Soken Go, Yasuyo Kashiwagi, Hisashi Kawashima (Japan)

15:00 **Session 5 – Platform 1**

Chairs: ***Dana Craiu*** **(Romania) -** ***Luca de Palma*** **(Italy)**

Extending the use of Stiripentol to SLC13A5-related epilepsy
Brahim Melaiki (Saudi Arabia)

ZX008 (Fenfluramine) in Dravet Syndrome: results of a phase 3, randomized, double-blind, placebo-controlled trial
Nicola Pietrafusa (Italy)

Ganaxolone for the Treatment of CDKL5 Deficiency Disorder in an Ongoing Phase 3 Clinical Trial (The Marigold Study)
Nicola Specchio (Italy)

Long-term seizure and developmental outcomes of Ohtahara Syndrome: surgical vs medical treatment
Kenji Sugai (Japan)

16:00 **Session 6 - Epilepsy Surgery**

Chairs: ***Carlo Efisio Marras*** **(Italy) –** ***Kensuke Kawai*** **(Japan)**

Drug-resistance and guidelines (in the first 3 years)
Alexis Arzimanoglou (France)

Memory issues in epilepsy surgery of temporal lobe epilepsy
Kensuke Kawai (Japan)

Long-term prognosis of treated patients: where do we are?
Laura Tassi (Italy)

17:30 **End of the session**

18:30 Departure from the Congress Venue to the Residence of the Ambassador of Japan to the Holy See

19:30 Farewell Reception “A Tasting of Japanese Cuisine” hosted by the Ambassador of Japan to the Holy See

21:30 Return to Congress Venue

Saturday, September 22nd

08:45 **Session 7 - Alternative treatments**

Aula Magna

Chairs: ***Kai-Ping Chang*** **(Taiwan) -** ***Katsuhiro Kobayashi*** **(Japan)**

Ketogenic diet
Effectiveness for specific epilepsy syndromes
*Hirokazu Oguni (*Japan)

Neurostimulation
Lieven Lagae (Belgium)

Steroids and hormones: what we learned?
Federico Vigevano (Italy)

10:15 Coffee break

10:45 **Keynote Lecture 4**

Chairs: ***Oriano Mecarelli*** **(Italy) -** ***Takao Takahashi*** **(Japan)**

Mechanism and Treatment of Status Epilepticus
Hideo Yamanouchi (Japan)

11:30 **Session 8 - Platform 2**

Chairs: ***Lucia Fusco*** **(Italy) -** ***Hideaki Shiraishi*** **(Japan)**

Study of 15 patients with early infantile epileptic encephalopathy treatable Neurometabolic causes
Harshuti Shah (India)

The risk for epilepsy during childhood after neonatal seizures: a long-term follow-up study
Ruzica Kravljanac (Serbia)

Characteristic surface EMG in a case of epileptic spasms with nodding/obeying manner
Kaori Sassa (Japan)

Genetic diagnosis in children with Epileptic Encephalopathies using Targeted Gene Panel Analysis
Jao-Shwann Liang (Taiwan)

KCNT1-related Epileptic Encephalopathy: the first case series in Taiwan
Ming-Tao Yang (Taiwan)

Fatal status epilepticus in Dravet Syndrome: a multicenter survey
Paola De Liso (Italy)

13:00
14:30 Poster Session and lunch

POSTER - ROOM 1

P28 THERAPEUTIC HYPOTHERMIA FOR PEDIATRIC REFRACTORY STATUS EPILEPTICUS - A SINGLE CENTER EXPERIENCE
Pi-Lien Hung, Mei-Hsin Hsu, Hsuan-Chang Kuo, Ming-Yi Chou, Jui-Ying Lin (Taiwan)

P29 ACUTE ENCEPHALOPATHY IN DRAVET SYNDROME
Sarah Bompard, Maria Luigia Gambardella, Serena Sivo, Ilaria Contaldo, Chiara Veredice, Elisabetta Ferraroli, Massimo Apicella, Domenica Battaglia, Charlotte Dravet (Italy)

P30 GAIT DISTURBANCE OF DRAVET SYNDROME
Yurika Numata-Uematsu, Marie Yoshida, Tomoko Kobayashi, Mitsugu Uematsu, Shigeo Kure (Japan)

P31 EPILEPTIC FEATURES IN 34 TEENAGERS WITH DRAVET SYNDROME
Ida Turrini, Giorgia Olivieri, Daniela Chieffo, Ilaria Contaldo, Valentina Arcangeli, Elisa Musto, Simona Lucibello, Domenica Battaglia, Charlotte Dravet (Italy)

P32 DE NOVO MISSENSE MUTATION OF X-LINKED SMC1A GENE CAUSES A SEVERE EARLY ONSET EPILEPSY AND INTELLECTUAL DISABILITY IN A FEMALE PATIENT
Ching-Shiang Chi, Hsiu-Fen Lee, Chi-Zen Tsai (Taiwan)

P33 COMPOUND HETEROZYGOTE OF NOVEL ALDH7A1 MUTATIONS
Yuri Dowa, Tomoyuki Akiyama, Kosei Hasegawa, Fumitaka Inoue, Takashi Shiihara (Japan)

P34 SCN2A MUTATION IN AN INFANT PRESENTING WITH MIGRATING FOCAL SEIZURES AND INFANTILE SPASM RESPONSIVE TO A KETOGENIC DIET
Kun-Long Hung, Da-Jyun Su, Jyh-Feng Lu, Li-Ju Lin, Jao-Shwann Liang (Taiwan)

P35 ATYPICAL PYRIDOXINE-DEPENDENT EPILEPSY: A RARE CAUSE OF FAMILIAL EPILEPSY
Hsiu-Fen Lee, Chi-Zen Tsai, Ching-Shiang Chi (Taiwan)

P36 KCNQ2 MUTATIONS IN CHILDHOOD NON-LESIONAL EPILEPSY: VARIABLE PHENOTYPES AND NOVEL MUTATIONS IN A CASES SERIES
Inn-Chi Lee, Jiaznn-Jou Yang, Shuan-Yow Li (Taiwan)

P37 THE SAFETY OF ACTH THERAPY FOR INFANTILE SPASMS ASSOCIATED WITH HYDROCEPHALUS
Jun Matsui, Takao Morimune, Noriko Nishikura, Tatsuyuki Sokoda, Yoshihiro Maruo (Japan)

P38 SCALP HIGH-FREQUENCY OSCILLATIONS IN A SPECTRUM OF PEDIATRIC EPILEPSIES CHARACTERIZED WITH SLEEP-ACTIVATED SPIKES IN EEG
Yuji Ohuchi, Katsuhiro Kobayashi (Japan)

P39 OHTAHARA SYNDROME IN KCTN1-RELATED ENCEPHALOPATHY

Marco Perulli, Leonardo Lapenta, Sarah Bompard, Maria Luigia Gambardella, Michela Quintiliani, Francesca Sini, Domenico Romeo, Claudia Brogna, Domenica Immacolata Battaglia (Italy)

P40 EARLY-ONSET GENETIC EPILEPSIES AND EPILEPTIC/DEVELOPMENTAL ENCEPHALOPATHIES: A SINGLE-CENTRE EXPERIENCE IN REGGIO EMILIA, ITALY

Carlotta Spagnoli, Elena Pavlidis, Daniele Frattini, Grazia Gabriella Salerno, Carlo Fusco (Italy)

P41 THE GENETIC LANDSCAPE OF EARLY ONSET EPILEPSY/EPILEPTIC ENCEPHALOPATHIES IN SAUDI ARABIA AND THE IMPACT ON THE TREATMENT

Brahim Tabarki Melaiki, Xena AlQahtani (Saudi Arabia)

P42 EFFECTIVENESS OF VITAMIN B6 FOR WEST SYNDROME

Noboru Yoshida, Fumiko Ushimaki, Tomoyuki Nakazawa, Shinichi Niijima (Japan)

P43 PRELIMINARY RESULTS OF 1 AND 2 YEARS FOLLOW-UP STUDY IN PATIENTS WITH WEST SYNDROME IN GEORGIA

Ana Kvernadze, Nino Nana Tatishvili (Georgia)

P44 IN VITRO CELL DIFFERENTIATION ANALYSIS OF INDUCED PLURIPOTENT STEM (IPS) CELLS FROM LEIGH-LIKE ENCEPHALOPATHY PATIENT WITH DNM1L MUTATION INTO NEURONAL AND MUSCULAR CELLS

Kiyotaka Zaha, Hiroshi Matsumoto, Yasuko Nakamura, Kenji Uematsu, Megumu K. Saito, Shigeaki Nonoyama (Japan)

P45 GOOD OUTCOME OF EARLY HEMISPHERECTOMY OR MODIFIED HEMISPHERECTOMY FOR REFRACTORY EPILEPSY DUE TO FOCAL ABUSIVE HEAD TRAUMA AND STROKE IN INFANCYS AND TODDLERS

Chih-Wei Lin, Ting-Rong Hsu, Hsin-Hung Chen, Mu-Li Liang, Kai-Ping Chang (Taiwan)

P46 INCREASED SUBCORTICAL OLIGODENDROGLIA-LIKE CELLS IN PHARMACO-RESISTANT FOCAL EPILEPSY IN CHILDREN CORRELATE WITH EPILEPTIC SPASMS

Satoru Sakuma, Hiroshi Otsubo (Japan)

P47 EFFICACY OF VIGABATRIN THERAPY FOR TUBEROUS SCLEROSIS: SEIZURE AND NEUROPSYCHIATRIC OUTCOMES

Mitsugu Uematsu, Yurika Numata-Uematsu, Sato Suzuki-Muromoto, Shigeo Kure, Takashi Shiihara, Ayako Hattori, Shinji Saito (Japan)

14:30 **Session 9 - SUDEP**

Chairs: ***Ching-Shiang Chi*** **(Taiwan) -** ***Hideo Yamanouchi*** **(Japan)**

Risk in infancy
Marina Trivisano (Italy)

SUDEP: pathogenesis and possible prevention using wearable seizure-detection devices
Sándor Beniczky (Denmark)

Seizure detection
Satsuki Watanabe (Japan)

16:00 **Closing Remarks and... Arrivederci!**

BIOSKETCH
Invited Lecturers

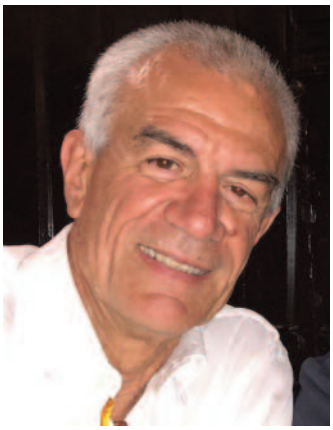
Ingrid SCHEFFER

Laureate Professor Ingrid Scheffer is a physician-scientist whose work as a paediatric neurologist and epileptologist at the University of Melbourne has led the field of epilepsy genetics over more than 25 years, in collaboration with Professor Samuel Berkovic and molecular geneticists.

Together they identified the first epilepsy gene and many genes subsequently.

Professor Scheffer has described many novel epilepsy syndromes and refined genotype–phenotype correlation of many disorders. Her major interests are genetics of the epilepsies, epilepsy syndromology and classification, and translational research. She collaborates on research on the genetics of speech and language disorders, autism spectrum disorders, cortical malformations and intellectual disability. She led the first major reclassification of the epilepsies in three decades for the International League Against Epilepsy.

She has received many awards: 2007 American Epilepsy Society Clinical Research Recognition Award, ILAE Ambassador for Epilepsy Award, 2013 Australian Neuroscience Medallion, and the 2012 L'Oréal-UNESCO Women in Science Laureate for the Asia-Pacific region. In 2014, she was a co-recipient of the Prime Minister's Prize of Science, and awarded the Order of Australia. In 2014 she became the inaugural Vice-President of the Australian Academy of Health and Medical Sciences.



Federico VIGEVANO

Federico Vigevano holds the role of Director of the Neuroscience Department at Bambino Gesù Paediatric Hospital and he is adjunct professor of Neurology in postgraduate course in Paediatrics and in Infantile Neurology and Psychiatry respectively at “La Sapienza” and “Tor Vergata” University in Rome.

Dr. Federico Vigevano has focused on studies, using video-EEG monitoring systems, in the field of childhood epilepsy, with particular attention to seizures in the first years of life. He studied the electroclinical patterns of various types of epileptic seizures, especially epileptic spasms.

Together with Japanese authors, he identified an epileptic syndrome, called Benign Infantile Familial Seizures. Studies on focal dysplasia and hemimegalencephaly led to the definition of surgical indications for these cases and in general for pharmacoresistant paediatric patients. Data regarding non epileptic paroxysmal disorders in childhood have been collected for years with the use of video-EEG monitoring and presented at the most important international epilepsy congress.

Dr. Vigevano has been a member of various ILAE Commissions for epileptic syndromes classification and diagnostic strategies. In 1996 he was elected Secretary of the Lega Italiana Contro l’Epilessia and has been President since 1999 to 2002. Since 2001 to 2005 has been Chair of European Advisory Council. He has been the Chair of the Scientific Committee of the International Congress on Epilepsy (Rome 2011). Since 2014 he organize the international residential course on Resistant Epilepsy in Tagliacozzo (Italy). Federico Vigevano in 2016 received the European Epileptology Award by the European ILAE Commission.

Paolo TINUPER

Paolo Tinuper graduated from the University of Bologna (Italy) and trained at the Neurological Institute of Bologna under Prof. E. Lugaresi. He gained further expertise at the Marseille School with Prof. H. Gastaut and at the Montreal Neurological Institute with Dr. F. Andermann.

He is Associate Professor of Neurology at the University of Bologna, in charge of the Epilepsy Center and the EEG laboratory of the Department of Neurological Sciences.

Past-President of the Italian League against Epilepsy, Certified Trainer of the European Epilepsy Academy and Ambassador for Epilepsy.

He is involved in teaching epileptology and clinical neurophysiology in undergraduate and postgraduate university courses and in national courses.

Author of many scientific papers in international peer-reviewed journals, his main scientific interests include semeiological and neurophysiological aspects of epileptic seizures, prognosis of the epileptic syndromes, prognosis of epilepsy after drug withdrawal, epilepsies with seizures during sleep and presurgical evaluation in drug-resistant epilepsies.

Floor JANSEN

Floor Jansen specialised in pediatric neurologist in 2007, and in the same year she obtained her PhD degree on a thesis entitled “identification of epileptogenic sources in patients with TSC”.

Her clinical and scientific areas of expertise are: refractory paediatric epilepsy, epilepsy surgery, tuberous sclerosis, electrical status epilepticus in sleep (ESES of CSWS), and genetic epilepsy.

She coordinates the TSC center of excellence, for children, in the UMC Utrecht (one of two in the Netherlands).

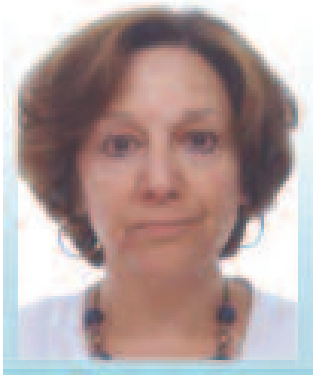
She takes part in the European multicentre EPISTOP consortium. She coordinates a European multicenter RCT in children with new onset ESES syndrome: the RESCUE ESES trial. She is a member of the national and international (Utask) epilepsy surgery program working groups.

Francesca BISULLI

Francesca Bisulli, MD, PhD, 46 years, is a neurologist and neurophysiologist with strong research interests in genetics of epilepsy. She has always combined clinical epilepsy care with academic epilepsy research. She is currently working in the Epilepsy Centre directed by Prof. Tinuper at the Institute of Neurological Sciences in Bologna, Italy.

In 2011 she obtained a PhD on the topic of sleep-related epilepsies, specifically on Sleep-related Hypermotor Epilepsy. Since 2006, she is Assistant Professor at the University of Bologna.

Her research has focused on various epilepsy-related topics over the years, although lately she is concentrating on the genetics of focal epilepsies, being involved in many international projects and obtaining research grants from Italian Ministry of Health and Telethon, among others. Dr. Bisulli has acted as an editor and tutor within the editions of the VIRPA course on Clinical Pharmacology & Pharmacotherapy. She is currently member of the directive board of LICE, Italian chapter of ILAE.



Lucia FUSCO

Dott. Fusco is an Associate Professor in Pediatric Neurology since 1988, at Bambino Gesù Children's Hospital, Vatican City, Rome, Italy.

She is specialized in clinical Neurophysiology and is the Coordinator of Long Term video/EEG Monitoring in Epilepsy. She is also highly specialized in drug refractory epilepsy. Dr. Lucia Fusco trained as neurologist and epileptologist.

Her main area of clinical expertise and research is epilepsy in childhood, and in video/EEG monitoring.

She is an expert in the differential diagnosis between epilepsy and other paroxysmal manifestations, in both patients at onset of disease and patients with drug-resistant epilepsy and candidate for surgery.

The clinical activity is carried out in the in and out -patients clinic and she is the reference neurology for Status epilepticus in the Intensive Care ward.

Clinical research includes electroclinical, etioapthogenetic and therapeutic aspect of childhhod epilepsy.

She participated as invited speaker in several national and international congress, and meetings, and acted as teacher and tutor in National and International courses and masters dedicated to epilepsy

Dana CRAIU

Dana Craiu is Professor of Pediatric Neurology at “Carol Davila” University of Medicine, Bucharest, Romania.

She graduated in 1993 the same University and since then she constantly improved her knowledge in Pediatric Neurology with a special interest in Epilepsy and EEG.

She is the Head of Pediatric Neurology Discipline, and has been since 2007. After a brief fellowship in the tertiary Epilepsy Center Heemstede (2000), The Netherlands – under the supervision of Walter van Emde Boas, she presented her Ph.D. thesis in Bucharest at “Carol Davila” University of Medicine on “Frontal epilepsies” in 2004. She developed the first video-EEG lab and started presurgical evaluation in children and adults in Romania (2001), with the first successful surgeries for epilepsy after 2007. Dana has been developing annual Romanian teaching courses on EEG, in children and adolescents since 2004 and has organised numerous courses on epilepsy for different levels starting in 2001.

Over 400 physicians and nurses were trained by her team. Dana is involved in ILAE (International League Against Epilepsy) activity since 2009, as member of the Pediatric Commission – Infantile Seizures Guidelines Task Force, and Autism and Epilepsy Task Force and member of the ILAE-Europe (former CEA –ILAE – Commission of European Affairs of the League) since 2013. She is a member of EPNS (European Pediatric Neurology) Board, Chair of European Training Advisory Board for Pediatric Neurology (TAB). She was actively involved in organisation of EPNS 2009-2011 Training Courses in Romania and of the EPNS Research Conference in Bucharest in 2014. The main research interest of Dr. Craiu is EEG and epilepsy. She is involved in research in Epilepsy Genetics (European consortium EuroEPINOMICS), cognition in epilepsy, quality of life in epilepsy, etc. She leaded the Romanian research group joining E-pilepsy pilot project involved in Epilepsy Surgery and since 2016 she leads the Romanian team joining Epi-CARE (the European Reference Network of rare and complex epilepsies).

She is author or coauthor of over 60 publications in the field of Pediatric Neurology and Epilepsy.

Raman SANKAR

Raman Sankar, MD, PhD is Professor of Neurology and Pediatrics and Chief of Pediatric Neurology at the David Geffen School of Medicine at the University of California, Los Angeles.

He holds the Rubin Brown Distinguished Chair in Paediatric Neurology. Dr. Sankar is a graduate of the University of Bombay, India. He obtained his PhD from the University of Washington in Medicinal Chemistry and his PhD from Tulane Medical School. He completed his training in neurology and pediatric neurology at UCLA.

Dr. Sankar has authored more than 250 research articles, reviews and book chapters. He has also made editorial contributions to several books on epilepsy.

He has been a member of the Commission on Neurobiology of the International League Against Epilepsy (ILAE) and presently serves on the Commission's Task Force for the Workshop on the Neurobiology of Epilepsy (WONOEP). Professor Sankar will receive the prestigious Founder's Award (formerly the William Lennox Award) of the American Epilepsy Society at the 2018 annual meeting.

Stefano MELETTI

I was born in Bologna, Italy, August 12th, 1969.

At present I work at the University Hospital in Modena, Italy. Chair of the Clinical Neurophysiology Unit and associate Professor in Neurology at the University of Modena and Reggio Emilia.

My background and research activities comprise epilepsy, sleep disorders and neuroimaging. My clinical works concern both out-patients visits, as well as the responsibility of neurological patients that needs hospitalization for epileptic disorders and presurgical epilepsy monitoring. We have developed a functional imaging centre with regional-national relevance for advanced neuroimaging studies in epilepsy patients. I coordinate a group of clinicians dedicated to epilepsy diagnosis and treatment, as well as residents in Neurology, and PhD students.

Olivier DULAC

Professor of Pediatrics, founder and prior head of the Neuropediatric Department and of the reference Centre for Rare Epilepsies in the Paris V University Hospital Necker-Enfants Malades, in Paris.

I contributed to found the Inserm U663/1129 Research Unit. I chaired the Pediatric Commission, and contributed to Drug treatment and Classification Commissions of ILEA.

Research of my team focused on Epilepsy syndromes including neurophysiological espects, Pediatric Epilepsy Imaging and Surgery, Genetics of Pediatric Epilepsies, Neuropsychology, the indications of the Ketogenic Diet in children, and the development of Antiepileptic Drugs for children with epilepsy, including Ethics of drug trials in children.

Presently retired from Hospital and University, my time is devoted to playing with my grand-children, teaching in various countries in Europe, Africa, America and Asia, and contributing to the development of new antiepileptic compounds dedicated to Pediatric Epilepsy, namely epileptic encephalopathy, in AdPueriVitam.

Nicola SPECCHIO

Nicola Specchio is Head of the Epilepsy Unit in the Department of Neuroscience at Bambino Gesù Children's Hospital, Rome, Italy, where within his role, he is responsible for the diagnosis and treatment of patients with paediatric epilepsy. This includes the pre-surgical evaluation of patients with drug resistant epilepsy and the selection of patients with genetic epilepsies.

Dr Specchio's main interest lies with seizure semiology and the classification of epileptic seizures and syndromes. He has published papers in many international journals including *Epilepsia, Epilepsy Research, Epilepsy and Behavior* and is currently responsible for several clinical studies regarding the invasive monitoring of patients with epilepsy and the genetic aetiology of epileptic encephalopathy in the first three years of life.

Dr Specchio is a representative of International League Against Epilepsy (ILAE) Europe and of the Italian Chapter of the ILAE.

Renzo GUERRINI

Renzo Guerrini is a Professor of Child Neurology and Psychiatry, Director of the Neuroscience Department, Children's Hospital Anna Meyer, University of Florence, Italy.

He has authored over 600 Articles in peer reviewed journals, 10 books on epilepsy and served in the Editorial board of several journals.

Prof. Guerrini was awarded Ambassador for Epilepsy ILAE in 2003 and the American Epilepsy Society Award for Research in Clinical Science in 2012. He has been principal investigator of numerous research projects and is now coordinating DESIRE (Development and Epilepsy – Strategies for Innovative Research to improve diagnosis, prevention and treatment in children with difficult to treat Epilepsy), a major EU Research funded project

Emilio PERUCCA

Prof. Emilio Perucca trained as a neurologist and clinical pharmacologist at the National Hospital for Nervous Diseases, London.

He is currently Past President of the International League against Epilepsy (ILAE , Professor at the University of Pavia and Director of the Clinical Trial Centre at the C. Mondino National Neurological Institute in Pavia. He is a member of the Editorial Board of several journals, including *Lancet Neurology*, and *CNS Drugs*.

Dr. Perucca's research activities have focused on the clinical pharmacology of antiepileptic drugs, the drug treatment of seizure disorders, clinical trial methodology and assessment of outcome in people with epilepsy.

He is the recipient of the 2018 ILAE European Epileptology Award. He co-edited several textbooks and authored over 400 Pubmed-listed publications, with an H-Index of 75 and a Citation Index of over 20,000.

Kuang-Lin LIN

Dr. Lin had been the Director of Pediatric Neurology, the Deputy Minister of Pediatrics, Chang Gung Children's Hospital, the Director of Taiwan Tourette Syndrome Association and the General Secretary of Taiwan Child Neurology Society.

He had completed his research in the Laboratory for Brain Magnetic Stimulation, Beth Israel Deaconess Medical Center (July 2000 to 2001, Harvard Medical School, Boston).

He did the research of transcranial magnetic stimulation for the correlation of musician training and language process in the plasticity of brain. His current and future research direction is mainly on the immunological pathogenesis and treatment of pediatric encephalitis/encephalopathy, with special emphasis on the encephalitis related status epilepticus and epilepsy. He is the leader of CHEESE study group (Chang Gung Children's Hospital Study Group for Children with Encephalitis/Encephalopathy Related Status Epilepticus and Epilepsy, Taoyuan, Taiwan).

The study group has several important publications about antineuronal antibodies and pediatric encephalitis with status epilepticus

Helen CROSS

Professor Helen Cross is The Prince of Wales's Chair of Childhood Epilepsy and Head of the Developmental Neuroscience Programme at University College London-Great Ormond Street Institute of Child Health, as well as Honorary Consultant in Paediatric Neurology at Great Ormond Street Hospital for Children NHS Foundation Trust, London and Young Epilepsy, Lingfield, UK.

Her major research interest is improving outcomes in early onset epilepsies. Her initial research was into the improvement of brain imaging in the presurgical evaluation of children with complex epilepsy, increasing the number of children who were to be considered for surgical treatment. In establishing one of the largest epilepsy surgery programs in the world, she has worked on the utilisation of advanced imaging techniques, but also in determining short and long term outcomes from early surgery demonstrating the benefits to those who remain seizure free and who wean from medication.

She has also contributed significantly to the evidence base of both newer and older medical treatments, leading the first randomised controlled trial of the ketogenic diet in childhood epilepsy. She has edited 7 books, written 47 chapters and has >250 peer reviewed publications. She is elected Treasurer of the International League Against Epilepsy (2017-2021), Coordinator of the European Reference Network (ERN) EpiCARE (an ERN for rare and complex epilepsies), Clinical Advisor to the National Children's Epilepsy Surgery Service for England, Chair of the British Paediatric Neurology Association Research Committee, and is a member of the Board of the International Child Neurology Association (ICNA). She was awarded the ILAE/IBE Ambassador for Epilepsy in 2007, an OBE in the Queens Birthday Honours 2015 for her services to children with epilepsy, the AAN Sidney Carter award in 2017 and the ICNA Frank Ford Award for services to Child Neurology in 2018.

Tiziana GRANATA

Tiziana Granata is the head of the Epilepsy Unit in the Department of Pediatric Neuroscience at the Neurological Institute C.Besta in Milan, Italy.

Main areas of interest are rare genetic epilepsies of childhood, including those resulting from metabolic and degenerative diseases, and inflammation-related epilepsies.

She has published more than 130 papers in international journals, and is currently responsible for clinical studies on diagnosis and treatment of rare epilepsies.

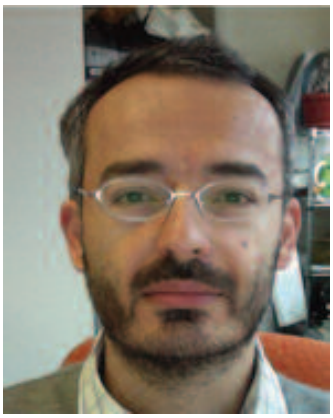
Norimichi HIGURASHI

Dr. Higurashi graduated and obtained his MD (2001) and PhD (2013) degrees at Jikei University School of Medicine. He has spent most of his career taking care of sick children, particularly with neurological diseases.

In 2009, he started research on the genetics and cellular/molecular pathomechanisms of early onset epilepsies at Fukuoka University (Prof. Shinichi Hirose) in collaboration with Keio University (Prof. Hideyuki Okano).

In a groundbreaking study, he succeeded in replicating the pathology of Dravet syndrome by using patient-derived induced pluripotent stem cells in 2013. He also contributed to the current understanding of many clinical aspects of PCDH19-related epilepsy.

Now, he continues basic research on pediatric epilepsies by obtaining research grants mainly from the Japan Society for the Promotion of Science and Japan Agency for Medical Research and Development. He also served as a taskforce member for ILAE and was involved in the establishment of the 2017 seizure type classification.



Vania BROCCOLI

Head of Unit, Division of Neuroscience, San Raffaele Scientific Institute, Milan;
Senior Scientist, Institute of Neuroscience, CNR, Milan, Italy.

Education

1997 Ph.D. in Genetic Science - University of Ferrara, Italy
1993 Master degree in Biological Sciences (highest grade) - University of Bologna, Italy.

Training And Professional Experience

2011-present Senior Scientist, Institute of Neuroscience, CNR, Milan, Italy
2011- present Head of Unit, Division of Neuroscience, San Raffaele Scientific Institute, Milan, Italy
2002-2010 Group Leader, Stem Cell Institute (SCRI), San Raffaele Scientific Institute, Milan, Italy
2003 Guest scientist, UCSF San Francisco, Superv. Prof. J. Rubinstein
2001 Staff Scientist, Telethon Institute of Genetics and Medicine (TIGEM), Milan, Italy
1998-2000 Post-doctoral Fellow, Neurogenetics Dept., Helmholtz Centre, Munich, Germany
1994-1997 San Raffaele Scientific Institute, Ph.D. Student, Superv.: Prof. Boncinelli.

Honours And Awards

■Human Frontier Science Program, Short Term Fellowship ■ EMBO, Short Term Fellowship ■ Advanced ERC Fellow ■Editorial board of Frontiers in Pharmacology ■ Armenise Foundation's Italian Scholarship Advisory Committee – Armenise Harvard Foundation ■ Member of the evaluating committee for the Consolidator European Research Council (ERC) awards, Panel LS7. ■ Member of the Reviewer Scientific Panel of the California Institute of Regenerative Medicine (CIRM) USA ■ Member of the European Scientific Advisory Board of the FP7-ERANET Neuron-II program ■Member of the external Scientific Advisory Board of the University of Lund (Sweden) Excellence Centre in Parkinson and Huntington ■ Research proposal reviewer for MRC (UK), ANR (France), FRM (France), FRC (France), University College London (UK), FWO (Belgium), DFG (Germany), et al.

Current And Recent Grants (Since 2007)

■Advanced Grant European Research Council (ERC) 2014-2019 ■European Project DESIRE 2013-2018 ■ Target Advancement Grant, Michael J. Fox Foundation (USA) 2017-2018 ■ Annual Grant, Italian Dravet Association 2017-2018 ■Telethon Grant 2014-2017 ■ Ordinary Grant, Health Ministry, Italy, 2013-2016 ■Lombardia Regional Grant, Italy 2013-2016 ■ Young Investigator Grant, Health Ministry, Italy 2009-2013 ■ Lombardia Regional Grant, Italy 2013-2016 ■ Cariplo Foundation, Italy, 2011-2013.

Research Fields

Developmental neurobiology, stem cell biology, cell reprogramming, gene therapy, gene editing, CRSIPR/Cas9-related technologies, AAV technology, neurodegeneration.

Rima NABBOUT

Rima Nabbout is Professor of Paediatric Neurology at Paris Descartes University and Director of the French centre for Rare Epilepsies at Necker Enfants Malades, Imagine Institute, Paris, France.

She is a member of the steering committee of EPICARE (European reference network on rare epilepsies) and of scientific committees of patient associations on rare epilepsies.

She is leading a research group at Inserm U1163 dedicated to translational research on developmental rare epilepsies. She received her medical degree from Saint Joseph University, Beirut, Lebanon; her paediatric board from Descartes University, Paris; and a PhD in Neurosciences from University Pierre et Marie Curie, Paris, France.

Dr Nabbout areas of research include electro clinical delineation and genetics of rare epilepsies, new end points and trials methodologies in rare epilepsies and transition from childhood into adulthood.

She is member of the editorial board of Epilepsia open and she has authored more than 160 peer-reviewed papers.

Shinichi HIROSE

Shinichi Hirose, MD, PhD is Professor of Pediatrics and Head of Department of Pediatrics and Research Institute for the Molecular Pathomechanisms of Epilepsy, Fukuoka University.

His interests are in molecular genetics of epilepsies.

He has worked extensively in the area of causative mutations and their molecular consequences in the neuroscience mechanisms underlying epilepsies and has published extensively on molecular pathomechanisms of epilepsies.

He is principal investigator on numerous clinical studies and has directed various research projects examining metabolic as well as inherited childhood disorders resulting in a prolific record of publication.

Romina MOAVERO

Romina Moavero is a child neurologist and psychiatrist working in Rome, both in a hospital and academic setting.

Since the medical degree she mainly focused her clinical research on refractory epilepsy and tuberous sclerosis, as well as on neuropsychiatric comorbidities of early onset epilepsy, such as intellectual disability, autism spectrum disorder and attention deficit hyperactivity disorder.

She is also greatly interested in developmental trajectories of infants and children at high risk for neurodevelopmental disabilities. She also deals with most of neurological disorders of childhood, including migraine, cerebral palsy, neurogenetic diseases, vascular diseases and so on.

She participated to different international trials evaluating the efficacy and safety of everolimus on different manifestations of tuberous sclerosis complex (subependymal giant cell astrocytomas an renal angiomyolipomas) and is now local study coordinator for long-term prospective study evaluating clinical and molecular biomarkers of epileptogenesis in a genetic model of epilepsy - tuberous sclerosis complex (EPISTOP).

Meir BIALER

Meir Bialer, PhD, MBA, is the David H. Eisenberg Emeritus (active) Professor of Pharmacy at the School of Pharmacy, Faculty of Medicine of The Hebrew University of Jerusalem. He received his B. Pharm (with distinction), M.Sc. (with distinction), M.B.A. and Ph.D. degrees from The Hebrew University of Jerusalem. Dr. Bialer completed a postdoctoral fellowship in pharmacokinetics at the University of Florida and spent an additional year at the College of Pharmacy at the University of Kentucky.

Since 1980 he has been a member of the faculty of the School of Pharmacy of The Hebrew University of Jerusalem and from 1994-1997 served as Head of the Department of Pharmaceutics in the School of Pharmacy. Professor Bialer has been awarded the Fellow (1992) of the American Association of Pharmaceutical Scientists (AAPS), Kaye Innovation Award (2000) of The Hebrew University of Jerusalem, an Ambassador for Epilepsy Award (2001) of The International League Against Epilepsy (ILAE) and The International Bureau for Epilepsy (IBE) and was (2009-2017) the Chair of the ILAE-Commission on European Affairs (CEA). He is also the co-founder and member of the Organizing Committees of the fourteen (1992-2018) EILAT Conferences on New Antiepileptic Drugs, the seven Eilat International Educational Courses on the Pharmacological Treatment of Epilepsy (2005-2017) and the four (1988-1999) Jerusalem Conferences on Pharmaceutical Sciences and Clinical Pharmacology.

He is a former president of the Israeli Society of Clinical Pharmacy and Biopharmaceutics (1989-1999) and of the Israeli League Against Epilepsy (1996-2002). He has served or is currently serving as a member of the editorial board of the following international journals: Biopharmaceutics & Drug Disposition (1988-2012), CNS Drugs (1994-present), Epilepsia (2000-2010), Epilepsy & Behaviour (2002-present), Epilepsy Research (2007-present), European Journal of Pharmaceutical Sciences (1992-1998), Journal of Pharmaceutical Sciences (1990-1995) and Therapeutic Drug Monitoring (1999-present).

Dr. Bialer's research interests include: a) Pharmacokinetics of new antiepileptic drugs (AEDs) and pharmacokinetic-based design of new antiepileptics and CNS drugs. In this regard he has been utilizing structure pharmacokinetic pharmacodynamic relationship (SPPR) studies to deign and develop new CNS drugs with better potency, lack of teratogenicity and a wide safety margin; b) Pharmacokinetic analysis of new drugs, sustained release dosage forms and novel drug delivery systems (DDS); c) Stereospecific pharmacokinetic and pharmacodynamic analysis of chiral drugs; d) Pharmacogenetics of CNS drugs; and e) Pharmacoresistance to AEDs. In these areas, he has 245 peer reviewed publications and is an author of numerous book chapters.

Alexis ARZIMANOGLOU

Director of the Department of Paediatric Clinical Epileptology, Sleep Disorders and Functional Neurology, University Hospitals of Lyon, France

Visiting Professor, Universitat de Barcelona, Spain

Coordinator Epilepsy Research Program, Hospital San Juan de Déu, Barcelona, Spain

Member of the Steering Committee of the European Reference Network EpiCARE & Coordinator of the Lyon EpiCARE centre

Member of the Executive Committee of the International League Against Epilepsy (ILAE)

Editor-in-Chief of the journal EPILEPTIC DISORDERS _ Educational Journal of the ILAE

Associate Editor of the European Journal of Child Neurology_ Journal of the EPNS

Awarded as Ambassador for Epilepsy – International League Against Epilepsy

Aicardi Award for Excellence in Paediatric Neurology – European Paediatric Neurology Society (EPNS)

Authored several books and has 165 peer-reviewed publications

Past President of the French Chapter of the ILAE

Past chair of the European Academy of Neurology Child Neurology Scientific Panel

Past Chair of the Scientific & Research Committee of the EPNS

Kensuke KAWAI

Professor & Director, Department of Neurosurgery, Jichi Medical University

Dr. Kawai graduated from the University of Tokyo and earned M.D. and Japanese medical license in 1987.

He had clinical training in the fields of neurosurgery in the University of Tokyo Hospital and associated hospitals.

He started basic research in the fields of stroke and epilepsy in 1990 as a visiting fellow in National Institutes of Health, U.S.A. He continued his clinical and research works in epilepsy and epilepsy surgery in the University of Tokyo and Tokyo Metropolitan Neurological Hospital. In the latter, he developed a new surgical technique, multiple hippocampal transection, with his mentor, Dr. Hiroyuki Shimizu.

He established epilepsy surgery program in the University of Tokyo Hospital, NTT Medical Center Tokyo and Jichi Medical University. He was a president of the Epilepsy Surgery Society of Japan and have been a vice president of Japan Epilepsy Society for 4 years.

Hirokazu OGUNI

Current Position: Consultant at Epilepsy center in TMG Asaka Medical Center, Part-time lecturer at Tokyo Women's Medical University

Educational Background: 1971-1977 Faculty of Medicine, Yamaguchi University

Professional Experiences:1977-1983 Medical residence: Department of Pediatrics in Tokyo Women's Medical University (under Prof. Yukio Fukuyama)

1988-1990: Postdoctoral fellow in Montreal Neurological Institute and Hospital, McGill University, (under Prof. Frederick & Eva Andermann), 2005–2018 Professor of Pediatrics (retire on March 2018) in Tokyo Women's Medical University

Professional Organizations: former executive board member of Japan Epilepsy Society and Japan Child Neurology Society

Main Scientific Interesting:

Clinical and EEG characteristics of specific childhood epileptic syndromes

Neurophysiological characteristics of epileptic seizures (especially myoclonic seizures, atonic seizures and epileptic spasms) and non-epileptic involuntary movement disorders

Lieven LAGAE

Lieven Lagae is Full Professor at the University of Leuven, Belgium (KUL), Head of the Paediatric Neurology Department of the KUL University Hospitals, and Director of the Childhood Epilepsy Program at the KUL University Hospitals.

Lieven Lagae is the immediate past President of the European Pediatric Neurology Society and serves as an elected Board Member of the International Child Neurology Association (ICNA).

He chairs the Finance Committee of the ICNA board and the Taskforce on Medical Treatment of Childhood Epilepsy of the International League against Epilepsy (ILAE). From 2004 to 2015, he was the Editor-in-Chief of the European Journal of Paediatric Neurology. In 2017, he was the recipient of the 'Cures within Reach patient impact Clinical Award'.

Current epilepsy research projects include: 1/ translational research in Zebrafish models of epilepsy; 2/ new anti-epileptic drugs in childhood epilepsy and especially in Dravet syndrome; 3/ brain stimulation in childhood epilepsy; 4/ preventive treatment of epilepsy in tuberous sclerosis complex He published >200 papers in peer reviewed scientific journals and is the editor of the book: Cognition and Behaviour in Childhood epilepsy (Mac Keith Press 2017). He serves in many editorial boards of epilepsy and neurology journals

Hideo YAMANOUCHI

Hideo Yamanouchi, MD, is the Professor of Pediatrics and the Director of Comprehensive Epilepsy Center, Saitama Medical University Hospital, Japan.

He is a member of board of directors, Japanese Society of Child Neurology as well as Japan Epilepsy Society.

He was the president of International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders, the 18th ISS meeting in 2016. He had served as the secretary general of ISS for over 7 years. He was elected as a chairperson of Infantile Seizure Society for 2018-2012 term.

His main objective during this term is to promote international friendships to understand, diagnose and treat infantile/pediatric epilepsy. Also, he puts a high priority on the education of young investigators to foster international leaders in the field of infantile/pediatric epileptology and child neurology in the future. His research field has focused on acute infantile encephalopathy as well as management of status epilepticus.

Marina TRIVISANO

Marina Trivisano has been working since 2014 as Paediatric Neurologist in the Unit of Rare and Complex Epilepsy of Neuroscience Department at Bambino Gesù Children's Hospital, IRCCS in Rome, Italy.

She received Medical Degree in 2008, Neurology Specialization in 2014, and PhD in 2017.

Her main area of expertise is clinical and EEG characterization of rare genetic epilepsies as well as of other epileptic syndromes. She is member of the Italian League Against Epilepsy.

She is actively involved in research of genetic epilepsies and author of more than 50 peer-reviewed papers and many book chapters and has been involved in numerous clinical trials on drug-resistant epilepsy.

Sándor BENICZKY

Sándor Beniczky is board-certified neurologist, clinical neurophysiologist and epileptologist.

He is professor of Clinical Neurophysiology at Aarhus University Hospital, and the head of the Clinical Neurophysiology Department at the Danish Epilepsy Centre. He is the chair of the joint EEG taskforce of the IFCN and ILAE, member of the ILAE commission on diagnostic methods, ILAE education taskforce and the executive committee of the Europe. Professor Beniczky has recently been appointed editor-in-chief of Epileptic Disorders.

The main research interest of Dr. Beniczky is EEG and epilepsy, focusing on electromagnetic source imaging, seizure detection, standardisation and quality-assurance in clinical neurophysiology. He has supervised eight Ph.D. students. He is author of 112 peer-reviewed papers and 18 book chapters.

Satsuki WATANABE

Satsuki Watanabe obtained her medical degree at Yamanashi University in Japan and became a designated psychiatrist under the Japan Mental Health and Welfare Law in 2000.

During her residency with the National Center Hospital of Neurology and Psychiatry (NCNP), she completed two Epilepsy Programs in the Psychiatry Division and the Neurosurgery Division.

She obtained a board certification as a clinical epileptologist from the Japan Epilepsy Society and an EEG specialist from the Japanese Society of Clinical Neurophysiology.

From 2012 to 2014, Dr. Watanabe has worked in Dr. Gotman's research laboratory in Montreal Neurological Institute as a postdoctoral fellow.

She got PhD at Tokyo Medical and Dental University in 2014 and started to work in the Psychiatry ward specialized in epilepsy in NCNP. In 2017, she moved to Saitama Medical University Hospital to start a new epilepsy center with her colleagues. Her current research focuses on seizure detection using video-analysis.

ABSTRATCS

Invited Lectures

CLASSIFICATION OF EPILEPSIES: NEW INSIGHTS FROM THE RECENT REPORT OF THE ILAE COMMISSION

Ingrid E Scheffer

University of Melbourne, Austin and Royal Children's Hospital, Melbourne, Australia

The first major revision of the classification of the epilepsies in almost three decades was published in 2017. This classification introduced more transparent terminology, designed to use words that both patients and clinicians alike could understand. The overall framework of classification was simplified with renewed emphasis on the aetiology of the patient's epilepsy, which requires consideration from the time of initial presentation.

Seizure types are classified according to onset, be it focal, generalized or unknown. From seizure type, the next step is to make an epilepsy type classification, and now includes combined generalized and focal epilepsy, as well as focal epilepsy, generalized epilepsy and unknown. The final step is to endeavor to make an epilepsy syndrome classification.

A key issue is the concomitant importance of both diagnosis of aetiology and co-morbidities. These aspects both impact on treatment selection and recognition of potential accompanying disorders such as learning difficulties, psychiatric issues, autism spectrum disorder, sleep problems, gait abnormalities, gastrointestinal problems to name a few. Six major aetiological groups have been recognized, selected because of their impact on management. Implementation of the new classification promises to improve patient care for people living with epilepsy.

HOW TO CLASSIFY EPILEPTIC SEIZURES: DEVELOPMENT OF A NEW ALGORITHM

Federico Vigevano (Italy)

The ILAE Commission for Classification and Terminology in 2017 choose to produce an operational system, not a true scientific classification of seizure types.

The main goal was to develop an algorithm predominantly for clinicians. This new classification is based on how seizures present to people with epilepsy and their families, carers and doctors. An important new concept is that *the first symptom classifies the seizure.*

This is always valid with the exception of the focal impaired awareness seizures, so classified if awareness is impaired at any time during the seizure. Focal seizures are again classified on the basis of awareness impairment, but the concept of *focal impaired awareness seizures* does not exactly coincide with old term of *complex partial seizures.*

To properly analyze the impairment of consciousness the document provides clear definitions for awareness, memory, responsiveness and sense of self. The generalized seizures are so classified only if the seizure is generalized at the onset; the secondarily generalized tonic-clonic seizure is now called *focal to bilateral tonic-clonic seizure*.

This new algorithm allows some seizure to be either focal or generalized onset and to have an unknown onset, include previously unclassified seizure types, define in details old and new terms.

SEIZURES WITH EITHER FOCAL OR GENERALIZED ONSET IN ADULTS

Paolo Tinuper (Italy)

IRCCS Institute of Neurological Science of Bologna

Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

In 2017, the ILAE Commission for Classification and Terminology published the Operational Classification of seizure types. According to this official document epileptic seizures should be classified in seizures with focal onset, seizure with generalized onset and seizures with unknown onset.

Each category my include different type of seizures (spasms, tonic seizures, clonic or myoclonic seizures, and so on).

In this lesson, video-polygraphic recordings of seizures presenting with the same typology (i.e. tonic seizures) but with focal or generalized onset will be shown to the audience. Particular cases will be discussed interactively with the participants in order to improve their knowledge of seizure semeiology and their skills in classifing epileptic phenomena.

FOCAL AND GENERALISED SEIZURES IN CHILDREN

Floor Jansen

Pediatric neurologist UMC Utrecht, The Netherlands

In 2017 the ILAE published the new operational classification of seizure types. An operational seizure type is defined as a useful grouping of seizure characteristics to improve unambiguously communication, in daily care, teaching and research. In the new classification a number of seizures can have both a focal or a generalised onset. Examples of these seizure types will be presented.

THE CONCEPT OF "IMPAIRMENT OF CONSCIOUSNESS" IN ADULTS

Francesca Bisulli

IRCCS Institute of Neurological Science of Bologna

Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Among many possible behaviors during an epileptic attack, impairment of consciousness has always had a key role in classifying the seizure. In adults it has practical importance for seizure self-reporting and management of therapy, driving and employability.

Over the years, seizure classifications have used various terms to describe impairment of consciousness. Seizures characterized by this feature were originally referred to as complex partial, then dialeptic and dyscognitive have been proposed as alternative nomenclatures.

Finally, the ILAE Task Force adopted state of awareness as a surrogate marker for consciousness. Awareness is operationally defined as knowledge of self and environment. When this is impaired for any portion of the episode, then the seizure is classified as a focal impaired awareness seizure.

To establish whether or not consciousness is impaired during a seizure is a challenging task, particularly when considering the differential diagnosis with language disturbances. It is therefore important to ask the patient whether awareness for events occurring during the seizures was retained or impaired, even when the patient was unresponsive or unable to understand language. As a practical issue, retained awareness usually implies that the person having the seizure later can recall and validate having retained awareness; otherwise, impaired awareness may be assumed. Awareness may be left unspecified when the extent of awareness cannot be ascertained. On the other hand, exceptional seizures may present with isolated transient epileptic amnesia in clear awareness, but classification of an amnestic seizure as a focal aware seizure would require clear documentation by meticulous observers.

HOW TO DEFINE THE IMPAIRMENT OF CONSCIOUSNESS IN CHILDREN

Lucia Fusco (Italy)

In pediatric age, impairment of consciousness may accompany many types of seizures with both focal and generalized onset, with or without some motor components. Focal seizures in posterior temporal lobe and absence seizures with 3 Hz spike and wave discharges are the seizures most frequently associated with impaired consciousness.

In the first year of life, an impairment of consciousness could be recognized by a halt of the motor activities, a stare modification with blank or vacant stare, or a behavioral disorder. Sometimes, when the child has a developmental encephalopathy, it can be very difficult to understand if the consciousness is compromised as a clinical counterpart of sustained epileptic discharges.

On the contrary, many apparent generalized convulsive seizures can manifest with preserved consciousness expressed by persistence of crying, which imply the persistence of consciousness, suggesting a bilateral motor involvement more than a true generalized one. Despite clinical and EEG differences in the different type of seizures associated to an impairment of consciousness, there are many evidence that these epileptic discharges converge on a common set of structures including the fronto-parietal association cortex, and the subcortical arousal system in the thalamus and upper brainstem.

The precuneus/posterior cingulate, the medial frontal and lateral parietal cortices are the primary nodes of the default mode network (DMN) of the brain, which has been demonstrated consistently activated during the resting state and deactivated during engagement with task. This same network has been shown to be selectively impaired during epileptic seizures associated with loss of consciousness.

The failure of the DMN could be the basis of cognitive deficits sometimes associated with drug resistance epilepsy in children.

REFINING THE CONCEPT: EPILEPTIC ENCEPHALOPATHIES VERSUS EPILEPSIES WITH DEVELOPMENTAL ENCEPHALOPATHY – THE ROLE OF THE ETIOLOGY

Dana Craiu (Romania)

The sintagm “Epileptic encephalopathy” has been used for the cases who develop cognitive and comportamental impairment as a result of the seizures and epileptic discharges (described on EEG).

In many cases, although epilepsy is fully controlled and epileptic discharges „whipped out” with the help of anti-epileptic drugs, the cognitive and behavioral status of the patient continues to deteriorate. In these cases, it is the etiology who provokes epilepsy and epileptic discharges, but also cognitive impairment and behavioral disturbances.

The encephalopathy is considered in these cases „developmental encephalopathy” considering that the genetic mutation will disturb the normal developmental processes and lead also to epilepsy. Mutations of the SCN1A, CDKL5, STXPB1 genes are just a few examples of genetic causes followed by developmental encephalopathy and epilepsy.

The encephalopathy may be agravated also by the epilepsy and the epileptic discharges, on top of the results of the genetic cause. In many cases of genetic developmental encephalopathy with epilepsy, the patients may also develop in time motor disabilities, one example being the motor chaneges in patients with Dravet syndrome with SCN1A mutation, which progresses late even if the epilepsy is controlled, or, in some cases, even before the onset of epilepsy. These concepts are presented based on cases examples.

EMERGING CONCEPTS ON THE CLASSIFICATION OF STATUS EPILEPTICUS AND ON THE UNDERSTANDING OF DRUG-RESISTANT STATUS EPILEPTICUS

Raman Sankar (USA)

The task force of the International league Against Epilepsy (ILAE) on the classification of status epilepticus published its report in 2015.

This definition conceptualized two important mechanistic dimensions, one involving failure of seizure termination mechanisms leading to prolonged seizures, and the other where enough time in seizures has elapsed that neuronal injury, plasticity and long-term consequences ensue.

The new diagnostic system also proposed that classification be undertaken in a frame work of 4 axes, based on: (1) semiology; (2) etiology; (3) EEG Correlates; and (4) age.

This presentation will familiarize the audience with this new classification scheme, provide some comparisons to the classic approach and its implication for pediatric practice. Mechanistic discussion will address both failure of termination of seizures involving pre- and post-synaptic mechanisms, as well as factors involved in seizure-induced neurodegeneration which may involve both excitotoxic as well as inflammatory mechanisms.

Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, Shorvon S, Lowenstein DH. A definition and classification of status epilepticus—Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015;56:1515-23.

Rossetti AO, Trinka E, Stähli C, Novy J. New ILAE versus previous clinical status epilepticus semiologic classification: Analysis of a hospital-based cohort. Epilepsia. 2016;57:1036-41.

UNCLASSIFIED TYPE OF SEIZURES IN ADULTS: TOOLS AND METHODS FOR UNDERSTANDING THE NETWORK

Stefano Meletti (Italy)

Seizures that cannot be classified represent a challenge.

From a clinical point of view, they cause limitation on treatment choices, both in terms of the choice of the most appropriate antiepileptic drug than in the choice of other possible alternative treatments (i.e. surgery).

The first and actually the best tool to resolve and classify 'unclassified seizure' is of course a direct video-EEG recording of the event.

However, this is not always possible, as in the case of seizures that occurs rarely. Moreover, there are situation in whom the clinical semeiology and the EEG correlates of the seizure itself are difficult to categorize in the actual concept of 'focal' or 'generalized'.

In these situations, the diagnostic process relies on the in deep evaluation of the interictal EEG and of the structural brain MRI of the patient. Also PET imaging can be particularly useful to understand brain regions that show metabolic alteration, either focal or more diffuse.

Finally, to get information on the epileptic network advanced EEG analysis technique, as well as the combination of EEG and functional MRI recordings can add relevant information to the understanding of networks involved by epileptic activities.

THE ROLE OF UNCLASSIFIED TYPE OF SEIZURES IN EPILEPSY SYNDROMES IN CHILDREN: FROM EPILEPSY SYNDROMES TO EPILEPSY SEQUENCES

Olivier Dulac (France)

The 2017 ILAE seizure classification fails to include all seizure types presently documented: the age at which seizure incidence is the highest, the neonatal period, and seizures of the most frequent epilepsy syndromes, i.e. Benign epilepsy with Rolandic syndrome and Absence Epilepsy of Childhood, are not considered.

On the other hand, many seizure types are included in 2-3 chapters of the classification. This paradox results mainly from “classificomania”. Indeed, one major question is “why should we classify epilepsy seizures instead of just listing them?” There is typically a “lost origin”.

Classification is eventually necessary when specific items need to be found among a lot of them. For instance, words can easily be found in a dictionary among thousands of them because there is an alphabet classification.

However, classifying the letters is not the aim but the method. Regarding epilepsy syndromes, the description included in the 1989 ILAE classification is transversal. Although some syndromes remain unchanged throughout the course of the disease, this is far from being always the case, namely in neonates, infants and small children.

Description of the sequence – how it started, not only the age of onset, and the course – may give the clue to efficiently find the aetiology which may require specific and urgent treatment.

EPILEPTIC SPASMS AS A TIME DEPENDENT SEIZURE TYPE: SEMIOLOGY AND SYNDROMIC VALUE

Nicola Specchio (Italy)

Studying infantile spasms is challenging because there are so many aspects of variation that introduce potential bias. These might relate to the many underlying etiologies, and variations in clinical semiology and electroencephalographic features that relate more to age or timing of investigation than to the underlying epilepsy or seizures type. New gene defects associated with the CDKL5/STK9, ARX, GAMT, ALG, SCN2A, STXBP1, ALG13, GABRB3, DNM1, SCN8A, MAGI2, ACADS, WDR45, and GABRA10 genes are associated with infantile spasms, but these illustrate that, when studying neurodevelopmental outcomes, it is necessary to deal also with heterogeneity at the level of genotype–phenotype correlation.

Semiology is the science that deals with signs or sign language. In the context of epilepsy it is used to describe the way in which we classify the clinical features of a seizure. This helps us to determine the likely seizure type. As with many seizure types, infantile spasms are associated with many clinical features and the challenge is to discern which of these features actually provide a signal that relate to underlying etiology, biological mechanism, or prognosis. In studying the signs associated with infantile spasms, there are many features to choose from.

Subtle spasms include such features as yawning, gasping, isolated eye movements, and transient focal motor activity. The clinical significance of subtle spasms is unclear, but they are known to occur in the context of the classical interictal EEG pattern of infantile spasms—hypsarrhythmia. However, even though they are sometimes found to occur periodically in clusters that resemble infantile spasms, in some cases they might represent focal seizures, particularly if the duration of the movement longer than 2 s. The term “mixed spasms” can be used in two senses: to indicate that the trunk and limb movements are discordant: for example, truncal flexion with predominantly extension limb movements; or to indicate that within or between clusters there are spasms with variably truncal flexion or truncal extension movements.

At the present time, none of these factors considered in isolation are recognized to have any fully sensitive or specific associations with underlying etiology, mechanisms of spasms, or prognosis, but detailed analysis of large cohorts is lacking. However, there are features of semiology that might be important and that, when considered as part of a semiological construct and in particular when considered in association with EEG findings, may relate to underlying etiology and mechanisms. For example, features such as lateralized cortical dysplasia and agenesis of the corpus callosum are associated with asymmetry and asynchrony during the clinical attack of spasms. And it is recognized that there are associations between focal seizures and spasms that can be quite complex, and which indicate an underlying cause that is likely to be associated with a focal cortical abnormality. However, it should be borne in mind that the most characteristic EEG feature is generally found interictally rather than during the attack of spasms and that information gathered from ictal recordings might be more useful for classification.

THE NETWORK OF EPILEPTIC SPASMS, INSIGHTS FROM ETIOLOGY-RELATED PATTERNS AND PHYSIOLOGICAL STUDIES

Renzo Guerrini

Neuroscience Department
Children's Hospital A. Meyer-University of Florence

Infantile spasms represent the response of the infant brain to multiple etiologies. It has been recognized that different etiologies can underlie different electroclinical patterns and different outcomes. In a clinical perspective this is an obviously important aspect, as it might help predicting outcome and, to some extent, guiding treatment strategies. In a more treatment oriented perspective anatomoelectroclinical correlations can provide useful insights into the pathohysiology of the disorder.

Relatively specific electroclinical patterns have been associated with spasms that are symptomatic of focal cortical dysplasia, tuberous sclerosis hemimegalencephaly and the lissencephaly pachygyria spectrum.

Also relatively characteristic is the experession of spasms in some specific genetic disorders such as for example CDKL5 encephalopathy or even Down syndrome.

Recent acquisitions on etiological diagnosis, should prompt e reevaluation of the electroclinical feature in order to provide a better understanding of any possible difference between those patterns that are characteristic of the immature brain from those that are characteristic of the functionally impaired brain. Overall, the pathophysiology of spasms remains to be fully elucidated.

Earliest studies suggested brainstem dysfunction as a trigger for both spasms and the hypsarrhythmic EEG. Based on PET studies showing focal cortical hypometabolism and electroclinical demonstrations of co-occurring partial seizures and spasms, abnormal functional interactions between brainstem and a focal or diffuse cortical abnormality were hypothesized.

A predominant role of either the cortical abnormality or the subcortical structures has always been a divisive argument. Uncertainties on pathophysiology have prompted caution in proposing surgery as a viable therapeutic approach for spasms with subsequent limited surgical referral rates.

However, in many cases, spasms have a focal cortical origin as suggested by invasive EEG recordings as well as the favourable outcome following removal of discrete epileptogenic lesions.

CHANGING PARADIGMS IN THE DEVELOPMENT OF NEW TREATMENTS FOR PAEDIATRIC EPILEPSIES

Emilio Perucca

Clinical Pharmacology Unit, Department of Internal Medicine and Therapeutics, University of Pavia, and Clinical trial Centre, Institute of Neurology IRCCS C Mondino Foundation, Pavia Italy

Developing antiepileptic drugs for children involves special challenges, not least because epilepsies with onset in infancy and childhood include a wide variety of syndromes which are often drug resistant or difficult to treat.

In the past, drug discovery and development of novel antiseizure drugs were based on utilization of animal models with limited specificity, and focused on traditional targets such as excitatory or inihibitory neurotransmitters.

During the last decade, however, impressive advances have been made in understanding the etiology of many epilepsies, including epilepsies which have a genetic, metabolic, and immune cause. In particular, a wide array of gene defects responsible for epileptic encephalopathies have been identified. Identification of the gene defect led to elucidation of the underlying molecular mechanisms involved in epileptogenesis in the individual patient.

Novel models such as the HEK293 cell line or the zebrafish permit to replicate the specific gene defects and associated functional abnormalities, and to utilise these systems for high throughput screening. These strategies permit rational design of new molecules which target no longer the symptoms, but the etiology of the disease.

Novel compounds being developed as precision medicines for severe pediatric epilepsies include orally active chemicals as well as peptides and antisense oligonucleotides intended for intrathecal delivery.

Screening models are also revealing that many drugs already marketed for non-epilepsy indications could serve as potential precision medicines against specific forms of epilepsy, offering unprecedented opportunities for repurposing. Examples of these approaches, including pathways for clinical validation, will be discussed.

PROGNOSIS OF EARLY ONSET EPILEPSIES

Kuang-Lin Lin

Pediatric Neurology, Chang Gung Children's Hospital, Taoyuan, Taiwan

The natural history of early onset epilepsy has good or poor outcomes. The underlying etiologies are diverse. They may be the manifestation of a genetic predisposition associated with a benign course and good prognosis for neurodevelopment. In some situations, they may present as'epileptic encephalopathy', which is rare but potentially treatable metabolic conditions.

On the other hand, brain structural abnormalities with poor development outcomes and intractable seizures may occur. Early onset epilepsies have wide range of underlying causes. Specific treatments may avoid preventable neurodevelopmental damage.

A complete evaluation of the child presenting with early onset epilepsy is necessary, since seizure outcome can be early predicted after obtaining neuro-radiological, metabolic/genetic and neurodevelopmental information. Early onset epilepsy is significantly associated with intellectual disability, especially when seizures are drug resistant.

Neuro-behavioral complications could be prevented or better addressed by routine screening for psychiatric disorders. Moreover, mortality in pediatric epilepsy is higher in children with early onset epilepsy. Children with epilepsy onset in the first year of life were over six times more likely to die than children with later onset epilepsy.

EPILEPTIC NETWORK AND COGNITIVE DECLINE

Stefano Meletti (Italy)

Epilepsy related cognitive impairment and decline affects several epileptic disorders, spanning from childhood epileptic encephalopathies to adult onset focal epilepsies.

Cognitive deficits can sometimes be subtle and affects also 'benign' conditions.

Considering the several mechanisms that can lead to epilepsy-related cognitive impairments these can be due to the effects of interictal epileptic discharges (IEDs) on physiological cognitive networks, to alteration of cortical and white matter connection, to the effects of anti-epileptic drugs.

In recent years, advances in EEG and neuroimaging has expanded our knowledge about the relationships and the detrimental effects of the epileptic network on physiologic cognitive networks, both in focal and generalized epilepsies.

In particular, I will focus on the consequences of the interactions between epilepsy-related networks and the networks subserving, executive, attentive, and emotional/social competences.

TREATMENT STRATEGIES

J Helen Cross (UK)

Early onset epilepsies are a complex group, with many having a poor prognosis for both seizure control and neurodevelopmental outcome.

Evidence base for effective treatments, particularly as second line has essentially been lacking. Recognition of the epilepsy syndrome remains key to determining treatment strategy.

Infantile spasms and Dravet syndrome on recognition have a clear treatment path.

Other syndromes may be clear, but few successful treatment options remain.

That aside determination of cause may lead to a more targeted approach. Children with unilateral or lateralised structural abnormalities should be referred early for assessment of possible curative epilepsy surgery.

Dravet syndrome provides a model whereby careful delineation of the epilepsy syndrome has led to improved treatment strategies, and specific trials of innovative treatments.

Further as we gain further insights into genetic mechanisms in this and other epilepsies other more targeted medical treatments become a real possibility.

EPILEPSY AND MOVEMENT DISORDERS

Ingrid E Scheffer

University of Melbourne, Austin and Royal Children's Hospital, Melbourne, Australia

The increasing recognition of movement disorders in patients with epilepsy is intriguing at a mechanistic level and it highlights the need for accurate diagnosis and different management of these disorders. Movement disorders occur in individuals with both severe and mild epilepsies.

In the self-limited familial epilepsies of infancy, the syndrome of infantile convulsions choreoathetosis (ICCA) begins in infancy and can be followed in childhood, adolescence or adult life with paroxysmal kinesigenic dyskinesia. This movement disorder is often brief and subtle and may escape diagnosis. It is readily treated with low doses of sodium channel blockers such as carbamazepine. ICCA is typically due to mutations in *PRRT2*, with many families sharing a common mutation. Rare families with *SCN8A* mutations have been reported with a similar clinical picture.

Glucose transporter 1 deficiency, due to mutations of *SLC2A1*, has a broad phenotypic spectrum ranging from a developmental and epileptic encephalopathy, to mild genetic generalized and focal epilepsies. The archetypal movement disorder seen in patients with GLUT1 deficiency is paroxysmal exercise-induced dyskinesia where quite prolonged dyskinesia can occur following 15 minutes of exercise. In patients with GLUT1 encephalopathy, ataxia is also common.

A range of movement disorders is seen with the developmental and epileptic encephalopathy which are highly genetically heterogeneous. These include dyskinetic movements, stereotypies and hyperkinetic movements. Differential diagnosis is critical in order to optimize management.

EPILEPSY AND INFLAMMATION

Tiziana Granata (Italy)

Since 1958, when brain inflammation in the epileptic brain was first demonstrated in Rasmussen's encephalitis, the presence of inflammatory mediators in epileptogenic brain areas has been increasingly recognized in several epileptic disease not linked to autoimmune dysfunctions or active infections. Markers of inflammation have been demonstrated in surgically-resected specimens from patients with various drug-resistant forms of epilepsy, including hippocampal sclerosis, malformations of cortical development, low grade tumors, and tuberous sclerosis.

Moreover, circulating auto-antibodies against neuronal components have been detected in systemic or neurological autoimmune disorders associated with epilepsy. While induction of innate immunity and activation of brain resident cells leading to neuroinflammation is commonly found in structural epilepsies, a prominent role of adaptive immunity in triggering or perpetuating the inflammatory response more specifically relates to epileptic encephalitis and autoimmune conditions associated with epilepsy.

The identification of inflammatory mediators involved in epileptogenesis may contribute to identify potential targets for treatment, and the choice of drugs. Several "non- conventional" anti-epileptic treatment, such as steroids, ketogenic diet, vagal nerve stimulation, and cannabinoids, display anti-inflammatory mechanisms of action which may mediate their therapeutic effects.

Moreover, the anticonvulsive and anti-epileptogenic properties of some anti-inflammatory drugs already in use for auto-inflammatory or autoimmune diseases has been demonstrated in experimental models of epilepsy. Clinical trials with these drugs, that are known to target specific inflammatory molecules or lymphocyte trafficking, may speed up clinical translation of laboratory findings.

DIAGNOSIS CLN2 DISEASE WITHIN CHILDHOOD EPILEPSIES

Nicola Specchio (Italy)

To increase understanding of the conditions that present with seizures and/or cognitive delay/disturbance and provide an overview and raise awareness of potential differential diagnoses of CLN2. Aim of the presentation is to identify CLN2 disease within early-onset epilepsies based on clinical observations, language delay and clinical/laboratory testing.

The disease onset is around the age of 2 years and first symptoms are language delay and epileptic seizures. Other symptoms soon after appearing as ataxia, cognitive deterioration, loss of ambulation and visual loss.

Seizures are mainly myoclonic, even if focal to bilateral tonic-clonic and atonic seizures might be evident. Highlight the importance of early diagnosis of CLN2 within early-onset epilepsies is crucial in order to start an enzymatic replacement therapy the earliest the possible. It will be discussed the differential diagnosis of early-onset epilepsies (including Dravet syndrome, myoclonic-astatic epilepsy, Lennox-Gastaut syndrome).

Moreover, will be included general principles of EEG and MRI in diagnosis of CLN2. The role of intermittent photic stimulation (IPS) in differential diagnosis of early-onset epilepsies is critical, as in patients affected by CLN2 disease a specific photoparoxysmal response is evident in more than 80% of cases: at low frequency of stimulation is evident a flash per flash response which is typical of CLN. Diagnosis is time critical in genetic epilepsies, and an appropriate evaluation and differential diagnoses might speed up the process.

CLINICAL AND GENETICS

Norimichi Higurashi

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Central Research Institute for the Pathomechanisms of Epilepsy
Fukuoka University, Fukuoka, Japan

Dravet syndrome is a developmental and epileptic encephalopathy that affects previously healthy infants.

This syndrome is best characterized by a unique sequential evolution of several electroclinical features during the early phase of the disease.

Recurrent generalized and/or unilateral convulsive seizures, which are often triggered by hyperthermia and tend to be prolonged, appear in the first year of life.

Multiple types of seizures, interictal epileptic discharges on electroencephalography, cognitive and behavioral impairments, and motor disorders develop later. All types of seizures are resistant to currently available antiepileptic drugs.

Patients are also at a risk of serious complications, including acute encephalopathy and premature mortality. Thus, many clinical issues remain to be solved.

Dravet syndrome is, in most cases, caused by genetic defects in *SCN1A*, a gene encoding the voltage-gated sodium channel α1-subunit, $Na_V1.1$. Until now, over 1,200 pathogenic variants have been identified. While clinical phenotypes have also been thoroughly described, it is no simple to reveal the full spectrum of genotype-phenotype correlations.

Recent unrelenting efforts have, however, identified some correlations as well as various genetic and environmental factors that can modify the clinical phenotype. In particular, a significant involvement of somatic mosaic variants has become more evident in the inheritance, development, and clinical severity of this disease.

Furthermore, clinical application of whole genome sequencing has increasingly identified alternative genes that could be associated with the Dravet syndrome phenotype or its mimics. In this presentation, I will comprehensively review and discuss key clinical and genetic issues of Dravet syndrome, especially highlighting the updated topics as stated above.

STEM CELLS AND GENE THERAPY FOR “DRAVET SYNDROME”

Vania Broccoli (Italy)

Dravet syndrome (DS) is an incurable infantile encephalopathy with a devastating prognosis with kids suffering of daily clusters of epileptic seizures that are only marginally controlled by pharmacological agents.

Hence, there is an urgent need for new therapies that can control epileptic crises and reverse the subsequent poor development and acquisition of cognitive and motor skills. DS is mostly caused by loss-of-function mutations in one S*cn1a* gene encoding for the Nav1.1 voltage-gated sodium channel alpha-subunit.

These data imply that a reduced amount of Nav1.1 channel impairs neuronal activity and function and underlying the disease pathophysiology. Gene-therapy approaches for neurodevelopmental disorders are in rapid development thanks to the introduction of novel serotypes of recombinant adeno-associated viruses (AAVs) supporting a large diffusion in the brain parenchyma.

Moreover, the recent introduction of the CRISPR/Cas9 system offers a flexible technology for editing the sequence or modulate the expression of a given gene. We equipped therapeutic AAVs with a modified Cas9 system to stimulate the expression of the Scn1a gene and transduced them into Dravet mice. We showed that this treatment can significantly stimulate *Scn1a* gene expression in primary neurons and brain tissues.

Furthermore, this strategy exerted a clinical amelioration of the temperature-induced epileptic crises characteristic of this DS mouse strain. These results establish a strong prove-of-concept for the therapeutic impact of regulating gene activation through the dCas9 activation system.

NEW PERSPECTIVES IN THE TREATMENT

Nicola Specchio (Italy)

Dravet syndrome is an infantile epilepsy syndrome with intractable polymorphic seizures (myoclonic, atypical absences, drops), cognitive impairment, and a number of comorbidities including ataxia/gait abnormalities and behavioral issues. There is a high likelihood of recurrent status epilepticus; seizures are medically refractory; and patients have multiple co-morbidities, including intellectual disability, behaviour and sleep problems, and crouch gait. Additionally, they are at significant risk of sudden unexplained death.

This review will focus predominantly on the prophylactic medical management of seizures, addressing mainly second-line therapies such as stiripentol, ketogenic diet or later options (levetiracetam, bromides, vagus nerve stimulation). Drug on pipeline which have been shown efficacy are fenfluramine and cannabidiol. Both of them are promising therapies for Dravet syndrome, and their efficacy has been documented in randomized controlled studies. Sodium channel agents-including carbamazepine, oxcarbazepine, phenytoin and lamotrigine-should be avoided, as they typically exacerbate seizures.

While many medications are used in treating the seizures associated with DS, these patients typically have medically refractory epilepsy, and polytherapy is often required.

Nonpharmacologic therapies (such as neurostimulation or surgery) are understudied in DS. Vagus nerve stimulation appears to reduce seizure frequency in patients with DS in some open label studies.

Status epilepticus is a recurring problem for patients with DS, particularly in their early childhood years. All patients should be prescribed a home rescue therapy (usually a benzodiazepine) but should also have a written seizure action plan that outlines when rescue should be given and further steps to take in the local hospital if the seizure persists despite home rescue therapy.

Families must be counselled on non-pharmacologic strategies to reduce seizure risk, including avoidance of triggers that commonly induce seizures (including hyperthermia, flashing lights and patterns). In addition to addressing seizures, holistic care for a patient with Dravet syndrome must involve a multidisciplinary team that includes specialists in physical, occupational and speech therapy, neuropsychology, social work and physical medicine.

MANAGEMENT IN ADULT PATIENTS WITH DRAVET SYNDROME

Rima Nabbout (France)

The delineation of the phenotype of patients with Dravet syndrome will help to establish the best follow-up for patients diagnosed in childhood and to better diagnose this syndrome in adulthood.

The adult phenotype comprises multiple seizures types, mainly nocturnal Tonic clonic or tonic, mild to severe intellectual disability, psychiatric disorders and various motor abnormalities. Tonic-clonic and tonic seizures are frequently observed, but are less frequent than in childhood. Seizures are mostly nocturnal with possible focal origin. Myoclonic seizures, atypical absences and complex focal seizures are less common in adulthood. Although the fever sensitivity persists, the incidence of status epilepticus decreases and seizures tend to become less frequent and less prolonged. Cognitive impairement and lack of autonomy becomes the predominant burden of the disease in many patients. Autism spectrum disorder is reported in over one third of them with possible agressive behavior mainly during late adolescence and early adulthood. Sleep disturbances are frequently reported and might be multifactorial.

Motor abnormalities often exceed gait disturbance. Crouching is frequent with orthopedic deformities and patients often present with different levels of bradykinesia and hypomimia mimicking early onset parkinson feartures. These features are often worsened by the lack of continuity in the educational and rehabilitation more available for pediatric patients in many countries.

This picture emphasizes the need for a multidisciplinary care program beyond the anti epiletic drugs and encompassing psychiatric, motor and cognitive continuous rehabilitation and the burden of the disease on ageing parents should be carefully considered. This multidisciplinary care program might increase the difficulty faced by adult epileptologists and could partly explain the delayed transfer to adult care.

This presentation will address the adult phenotype of Dravet syndrome and the current knowledge on management.

PATHOGENESIS AND GENETIC SUBSTRATE

Shinichi Hirose

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Tuberous Sclerosis Complex (TSC) is an autosomal dominant multisystemic disorder, characterized by tumors and lesions in multiple organs.

Individuals with TSC often suffer neurological complications such as epilepsy, mental retardation, and autism spectrum disorders. Various pathological variants of two genes, *TSC1* and *TSC2*, have been identified as the causes of TSC. *TSC1* and *TSC2* encode proteins called hamartin and tuberin, respectively.

Complexes of hamartin and tuberin control the activity of mechanistic or mammalian target of rapamycin complex 1 (mTORC1). mTORC1 plays a central role in cell proliferation and growth. Pathological variants of *TSC1* or *TS2* allow overactivity of mTORC1 in the mTOR pathway, which is subject to complex controls. Rapamycin or sirolimus exerts its pharmacological effect on TSC to inhibit the mTORC1 overactivity. Thus, TSC may be considered an mTORopathy or a disease caused by dysregulation of the mTOR pathway.

Recently, mTORopathy has drawn attention not only for its role in TSC but also in other disorders that result in epilepsy. For example, pathological variants of the gene *DEPDEC5* cause focal epilepsy. The protein DEPEC5 forms a complex called GATOR1, which also controls the mTORC1 activity. Homozygous variants of the gene *STRADA* cause polyhydramnios, megalencephaly and symptomatic epilepsy (PMSE) due to mTORC1 dysregulation.

Furthermore, somatic mutations in *TSC1* and *TSC2*, as well as in the gene encoding mTOR, are associated with focal cortical dysplasia. Examinations of mTORopathies, including TSC, can reveal new pathomechanisms of epilepsy and other neurological abnormalities and suggest novel therapeutic measures targeting the mTOR pathway.

EVEROLIMUS

Romina Moavero

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Everolimus is an inhibitor of the mTOR (mechanistic/mammalian target of rapamycin) complex, initially developed as an antitumoral agent, but it later became evident that it could serve as a targeted drug for tuberous sclerosis complex (TSC)-related manifestations.

Preclinical research demonstrated that everolimus could exert both an antiseizure and an antiepileptogenic effect in models of genetic and acquired epilepsy.

A phase I/II clinical trial evaluating the efficacy of everolimus in medically refractory TSC related epilepsy reported a >50% seizure frequency reduction in 12/20 patients. The 4-year final analysis of this first prospective open label human clinical trial for individuals with TSC related refractory epilepsy treated with everolimus adjusted for a target serum range of 5-15 ng/mL provided evidence that improved seizure control is maintained in 72% of patients.

A phase III randomized, double-blind, placebo-controlled study (EXIST3) evaluated the efficacy and safety of two trough-ranges of everolimus (3-7 ng/ml and 9-15 ng/ml) given as adjunctive therapy for patients with refractory partial-onset seizures. This consisted of an 8 week baseline phase, 6 week titration phase, and 12 week maintenance phase, followed by an extension phase of 48 weeks. 366 patients aged 2-65 years have been enrolled in this multicentre study. The response rate at the end of the maintenance phase, appeared to be 15.1% in the placebo group, 28.2% in the low-exposure everolimus group, and 40% in the high exposure everolimus group.

Overall adverse events, including mouth ulcerations, upper respiratory tract infections and stomatitis, were usually mild and self-limited. Grade 3 or 4 adverse events were reported with placebo vs low-exposure/high-exposure in 10.9% vs 17.9/23.8%; serious adverse events were reported in 2.5% vs 13.7/13.8%. Adverse events led to treatment discontinuation in 1.7% vs 5.1/3.1%. Preliminary evidence from the extension phase revealed a sustained seizure reduction over time with acceptable safety profile. Taking into consideration the positive results of the EXIST3 study, everolimus was approved by both FDA and EMA for refractory epilepsy related to TSC in patients aged at least 2 years.

SURGERY IN PATIENTS WITH TUBEROUS SCLEROSIS

Floor Jansen

Pediatric neurologist UMC Utrecht, The Netherlands

A diagnosis of tuberous sclerosis complex (TSC) confronts patients, caregivers, and their treating clinicians with a high risk of intractable epilepsy and mental retardation. Although tuber load and genotype are related to cognitive outcome to a certain extent, early onset of seizures has been proven the only independent risk factor of cognitive deficits. Seventy % of children have seizure onset before the second birthday, 5% in the neonatal period. Infantile or epileptic spasms are frequent seizure types.

Epilepsy surgery has been shown to be effective in some patients with drug-resistant epilepsies in several retrospective series. Selection of good surgical candidates amongst children with TSC remains difficult with subsequent delays in surgical decision making. Given the complexity of epilepsy in patients with TSC and its precarious prognosis, different surgical strategies, sometimes including invasive investigations, are justified. However these investigations are not always feasible in very young children.

In selected case series, postsurgical seizure freedom rated vary from 50-80% and overall positive effect on neurodevelopment are reported. An overview of data on epilepsy surgery in infants and young children will be presented.

NEW ANTIEPILEPTIC DRUGS IN DEVELOPMENT: WHAT IS THEIR NOVELTY AND POTENTIAL

Meir Bialer

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Between 1993 and 2018 nineteen new antiepileptic drugs (AEDs) have been approved. These AEDs offer appreciable advantages in terms of their favorable pharmacokinetics, improved tolerability and lower potential for drug interactions. In addition, the availability of old and new AEDs with various activity spectra enables clinicians to better tailor drug choice to the characteristics of individual patients. Nevertheless 30% of patients with epilepsy are still not seizure-free and thus, there is a substantial need to develop new AEDs.

The new AEDs in development or recently approved can be divided into three categories: a) completely new chemical structures such as, cannabidiol, fenfluramine, ganaxolone, padsevonil or XEN1101 (KCNQ2-5 enhancer); b) derivatives of existing AEDs such as: brivaracetam, cannabidivarin, OV329 (a follow up compound to vigabartin) and the valproic acid (VPA) derivatives of octanoic acid and valnoctamide; c) novel epilepsy treatments emerging from drug repurposing such as: anakinra, everolimus or quinidine. Valnoctamide has the potential to be non-teratogenic, more potent valproic acid derivative. Cannabidiol, a non-psychoactive major component of Cannabis Sativa, was approved on 25/6/2018 by the FDA for Lennox-Gastaut and Dravet syndromes, in patients (>2 years). This is the first FDA-approved drug that contains a purified drug substance derived from marijuana. It is also the first FDA approval of a drug for the treatment of patients with Dravet syndrome. Subsequently, the FDA approved on 25/8/2018 stiripentol concomitantly with clobazam for Dravet syndrome.

Target-based drug design or Targephilia's mantra of: "one gene, one protein, one function" is not useful in the development of antiepileptics or CNS drugs. This is because all successful AEDs have multiple mechanisms of action (MOA) and the two single-mechanism AEDs developed by mechanism-based design are not widely used due to side effects related to their single MOA. In addition, CNS drugs with multiple MOAs have a better probability of being efficacious in refractory epilepsies and other CNS disorders.

Thus, new AEDs should be better than existing drugs in efficacy, safety or active in refractory animal models where existing AEDs are inactive. A new MOA might be an incentive if it is the drug's only (major) MOA. PK-based design can increase potency and minimize toxicity of existing AEDs. Small chemical changes "do big" (e.g. brivaracetam *vs*. levetiracetam, and ganaxolone *vs.* allopregnanolone. Pharmacokinetics (PK) is secondary to pharmacodynamics (efficacy and safety). PK-based design of VPA derivatives circumvents VPA teratogenic structural requirements. Most new AEDs have better PK, tolerability and safety profile, however they did not significantly helped refractory patients but only a subset of patients (e.g. CBD).

EPILEPSY SURGERY: DRUG RESISTANCE AND GUIDELINES (IN THE FIRST 3 YEARS)

Alexis Arzimanoglou

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Surgery is now a well-established treatment approach for selected children with focal epilepsy. Data per aetiology are available, mainly focusing on control of seizures.

There are many aspects to very young children, however, that can be particularly challenging and deserve special consideration in the evaluation of surgery and planning of surgical strategy. The following are just examples:

- Early recurrent seizures have an extremely poor prognosis for neurodevelopmental outcome and behaviour;

- it is assumed that in young children immaturity of brain development is at the origin of substantial differences in seizure expression, as compared to older children. As a result, focal seizures may present as epileptic spasms, drop-attacks, absence-like manifestations etc., often associated to generalized EEG abnormalities.

- Magnetic Resonance Imaging may be misleading with incomplete myelination in the very young;

- Possibilities for relocalization of function decrease with age;

- Pre-surgical investigations, such as implantation of depth electrodes or functional neuroimaging techniques, may not be feasible in infants and very young children.

The adverse long-term psychosocial outcome from ongoing seizures through childhood is well established. Cure from seizures, or partial control, following early epilepsy surgery is also known for a number of aetiologies. What remains to be answered is whether social, behavioural and cognitive outcomes can be improved in the long term with early cessation of seizures through surgery.

Specific guidelines for very young children may still be lacking but all experts agree upon one major point: the time to act is now. All young children with epilepsy should be referred to specialized centres and assessed early in their clinical course. Considering the highly variable types of epilepsies and related aetiologies in very young children and the complexity of the corresponding pre-surgical evaluations, early referral offers a unique chance for a better outcome. This is also a prerequisite for the realization of long-term cohort studies per aetiology, still needed.

MEMORY ISSUES IN EPILEPSY SURGERY FOR TEMPORAL LOBE EPILEPSY

Kensuke Kawai (Japan)

Mesial temporal resection for drug-resistant mesial temporal lobe epilepsy achieves favorable seizure outcome, but carries the risk of postoperative memory decline, particularly in those patients in whom hippocampal sclerosis is not apparent on the verbally dominant side.

I will present the long-term outcome of a novel surgical technique, multiple hippocampal transection (MHT), and review the current less invasive procedures for treatment of TLE.

Radiosurgery and laser ablation are regarded as less invasive but they destroy medical temporal structures disrupting the memory circuit. Their memory outcomes are not as good as expected when the target hippocampus is normal and pretreatment memory is preserved.

Electrical stimulation is expected to preserve memory function in cases with normal MRI, but seizure free rate is not as high as surgical resection. MHT is a hippocampal counterpart to multiple subpial transection. Intermittent incisions perpendicular to the longitudinal axis of the hippocampal formation from its ventricular surface at 4–5 mm intervals without ablation of fimbria are expected to inhibit abnormal longitudinal synchronization and thus abolish epileptic activity, while preserving the intrahippocampal neural circuitry and, ultimately, memory function.

The long-term outcome for complex partial seizures after MHT + MST/L was comparable to that seen after anterior temporal lobectomy. The long-term cognitive outcome was favorable, even for patients with a high risk of severe postoperative memory decline.

KETOGENIC DIET - EFFECTIVENESS FOR SPECIFIC EPILEPSY SYNDROMES -

Hirokazu Oguni

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We conducted a survey on the efficacy of ketogenic diet (KD) therapy for pharmaco-resistant childhood epileptic syndromes in our hospital.

We retrospectively reviewed the effectiveness of KD therapy from 1984 to 2018. More than 75%, 50-75% and less than 50% reduction of seizures were rated as excellent, good and poor responses, respectively. Result: 108 patients underwent KD therapy including MCT2:1 in 42, classical 4:1 or 3:1 in 38, Modified Atkins in 18 and 3:1 ketone milk in 10 patients.

They consisted of symptomatic generalized epilepsy in 26, Dravet syndrome (DS) in 20, West syndrome in 12, Glucose transporter type 1 deficiency syndrome (GLUT1DS) in 11, Myoclonic-atonic epilepsy (MAE), Symptomatic focal epilepsy (SFE), Lennox-Gastaut syndrome (LGS) in each 9, Transitional state from West to LGS (TWSLGS) in 7 and Atypical benign partial epilepsy of childhood (ABPE) in 5 patients. At 1 year after KD therapy, 20 (19%) and 35(34%) children maintained excellent and good responses, respectively. KD therapy was initiated in 71% of all patients between 1 and 6 years of age and 50% of them achieved more than good effects (>50%) at this age range. As for the effectiveness on the specific epileptic syndromes, more than good effects were shown in the following order at 1 year follow-up period ; GLUT-1DS (100%), ABPE (80%), TWSLGS (57%), LGS(55%) , MAE (50%), Dravet syndrome (45%), West syndrome (42%).

KD therapy is effective for pharmaco-resistant specific epilepsy syndromes in childhood and worth-while trying from infants to adolescents regardless of age.

NEUROSTIMULATION

Lieven Lagae (Belgium)

Considerable progress has been made in understanding the working mechanisms and the optimal indications for neurostimulation in pharmacoresistant epilepsy, also in children.

Deep Brain Stimulation is not yet commonly used in childhood epilepsy, but Vagus Nerve Stimulation is now more frequently considered for the treatment of refractory childhood epilepsy. Efficacy of VNS is comparable to the effect of adding a new AED in refractory epilepsy, with responder rates between 30 and 40%, 6 months after implantation.

Few children (5-8%) become seizure free on VNS Therapy, but also this is comparable to the effect of adding a new AED. Studies have shown a better response in younger children than in adolescents and adults.

Most likely, this is due to a combined effect of younger age and shorter duration of the epilepsy. The efficacy of the newer cardiac rhythm based responsive VNS device (Aspire) in childhood epilepsy is not yet very well studied, but adult studies show a higher efficacy.

The side effect profile is favorable with a seizure frequency independent positive effect on alertness and mood. VNS Therapy should be considered as a valid and earlier treatment option in pharmacoresistant childhood epilepsy.

STEROIDS AND HORMONES: WHAT WE LEARNED?

Federico Vigevano (Italy)

In 1958, Sorel and Dusaucy-Bauloye discovered almost serendipiditously that adrenocorticotropic hormone (ACTH or corticotropin) was efficacious in controlling seizures and improving electroencephalogram (EEG) abnormalities as well as neuropsychological performance in patients with infantile spasms.

The importance of this finding is noteworthy, since infantile spasms represent a severe epileptic condition which is associated with encephalopathic symptoms and an unfavorable cognitive outcome. Since then, several other publications have confirmed the efficacy of ACTH and corticosteroids in the treatment of spasms.

These agents have also been applied – and continue to be applied – to the treatment of other severe forms of childhood epilepsy, even though there is a paucity of high-quality studies demonstrating their efficacy in these conditions. An update on the efficacy, side effects and mechanism of action of the Steroids and hormones will be presented

MECHANISM AND TREATMENT OF STATUS EPILEPTICUS

Hideo Yamanouchi

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Status epilepticus (SE) is one of the most common neurological emergencies in infancy and childhood.

The mortality rate of children is lower than adults, however SE exhibits various degrees of neurological sequelae, such as neurological impairments, intractable epilepsy and developmental disorders. Thus, child neurologist/ epileptologist have a crucial role of optimal and prompt management to treat this emergency condition.

SE is classically defined as persistent seizure status for “a sufficient length of time”, ordinally over 30min. This reflects irreversible neuronal damages, such as neuronal death or neuronal injury as well as alteration of neuronal networks, although the degree of which may be dependent on causative etiologies and the age of the onset. ILAE recently defined SE as concepts from operational aspects: an initial time point (t1) when a seizure is less likely to stop spontaneously as well as a second-time point (t2), after which it may lead long-term consequences. Studies have shown several mechanisms for drug resistance of SE including neurotransmitter receptor trafficking, i.e., the internalization of $GABA_A$ receptor which causes decrease of $GABA_A$ receptor on the synaptic cell wall sites leading reduced $GABA_A$ mediated synaptic inhibition. Increased glutamatergic neuronal excitation is induced by the externalization of NMDA receptor moved from the interior sites to the synaptic cell wall in the condition of prolonged seizure. Altered subunit composition of GABA and glutamate receptors may play a role for susceptibility of prolonged seizures, at least in the neuropathological conditions such as tuberous sclerosis or cortical dysplasia.

These mechanisms help to understand the clinical data that the longer a seizure lasts, the less likely it is to stop. Prompt drug choice should be determined appropriately based on the timing after provocation of seizures.

RISK IN INFANCY

Marina Trivisano (Italy)

Sudden unexpected death in epilepsy (SUDEP) refers to the sudden death of a seemingly healthy individual with epilepsy, usually occurring during, or immediately after, a tonic-clonic seizure.

The frequency of SUDEP varies depending on the severity of the epilepsy, but overall the risk of sudden death is more than 20 times higher than that in the general population. Several different mechanisms probably exist, and most research has focused on seizure-related respiratory depression, cardiac arrhythmia, cerebral depression, and autonomic dysfunction.

Various neuro-cardiac ion channel genes associated with epilepsy and SUDEP are expressed in both neuro-cardiac and respiratory control pathways and indicates that some variants might predispose to sudden death through neurocardiac or sole cardiac mechanisms. SUDEP risk assessment should be integral to the care of individuals with epilepsy.

The most important risk factor was frequency of generalised tonic-clonic seizures (GTCS). Patients on combination therapy (polytherapy) with antiepileptic drugs (AEDs) had a three times higher risk of SUDEP than did those on monotherapy. When the frequency of GTCS and AED treatment were studied together in an interaction analysis, both GTCS and polytherapy contributed to a risk of SUDEP, although a high frequency of GTCS had greater risk.

The use of evidence-based risk assessment tools may provide an opportunity to communicate identified risks in a person-centred holistic way.

SUDEP: PATHOGENESIS AND POSSIBLE PREVENTION USING WEARABLE SEIZURE-DETECTION DEVICES

Sándor Beniczky (Denmark)

Sudden unexpected death in epilepsy (SUDEP) is defined as sudden, unexpected, non-traumatic, non-drowning death in an individual with epilepsy, witnessed or unwitnessed, in which post-mortem examination does not reveal an anatomical or toxicological cause of death.

SUDEP is one of the major causes of death related to epilepsy. Its incidence is estimated at 1 / 10,000 patient-years in newly diagnosed epilepsy, and 1-2 per 1,000 patient-years in patients with chronic epilepsy. Recent studies suggested that various mechanisms may be involved in the development of SUDEP.

The vast majority of SUDEPs occur after generalized tonic-clonic seizures (GTCS). Cardiorespiratory dysfunction with failure of arousal occur following a prolonged postictal generalized EEG suppression. The risk is especially high in unattended patients with a history of GTCS, living alone.

Therefore, wearable seizure detection devices, targeting GTCS have potential role in preventing SUDEP. Recent prospective studies demonstrated the accuracy of wearable devices based on surface electromyography and of accelerometry for automatically detecting GTCS.

SEIZURE DETECTION

Satsuki Watanabe

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Seizure detection has the potential to improve treatment of patients with epilepsy or prevent sudden unexpected death in epilepsy (SUDEP). Variety of modalities have been applied to detect epileptic seizures. Electroencephalogram is the most traditional tool for seizure detection based on analysis of epileptiform discharges. Electrocardiography, respiratory monitors, pulse oximetry are applied to measure physiological data. Surface electromyography, accelerometer, mattress sensor and video analysis detect motor manifestations of seizures.

Real time seizure detection is now capable because of the advance in computer technology. Small devices such as smartphones and tablet personal computers are wildly used among general citizens nowadays. Therefore, seizure detection system at home will be the future goal. If we apply the at-home system, not only high accuracy but also a stress-free system for patients is needed. Although contactless method is ideal for patients, there is no perfect modality so far to detect seizures because of many different types of seizures. Combination of detection technologies and personalized detection system might solve this problem.

In this talk, I will introduce previous studies related to seizure detection methods and discuss possible systems to protect patients with epilepsy from SUDEP.

ABSTRATCS
Oral Presentation

EXTENDING THE USE OF STIRIPENTOL TO SLC13A5-RELATED EPILEPSY

Brahim Tabarki Melaiki

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SLC13A5-related epilepsy/epileptic encephalopathy is a recently described autosomal recessive disorder that is characterized by infantile epilepsy and developmental delay. Seizures are markedly drug resistant and often induced by fever; they mainly occur in clusters, sometimes evolving into status epilepticus.

We report the use of Stiripentol as an adjunctive therapy in five patients with drug-resistant SLC13A5-related epilepsy. The five patients showed remarkable improvement in the severity and frequency of seizures, status epilepticus, emergency department visits, and alertness. These observations extend the use of Stiripentol beyond the classical Dravet syndrome, and further studies on the use of this drug in drug-resistant epilepsy, mainly of genetic origin, are warranted.

ZX008 (FENFLURAMINE) IN DRAVET SYNDROME: RESULTS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Dravet syndrome (DS) is a rare, severe, treatment-resistant epileptic developmental encephalopathy. Fenfluramine (FFA) has been reported to have sustained anti-convulsive activity in a small cohort of patients with DS. Here we describe the results of a Phase 3 clinical trial comparing two doses of ZX008 vs placebo for the change in convulsive seizure frequency (CSF) in DS patients.

Patients 2-18 years old with a diagnosis of DS and in whom convulsive seizures were not completely controlled by their current anti-epileptic drug regimen were enrolled. Patients who had ≥6 convulsive seizures during the 6-week baseline period were randomized in a 1:1:1 ratio to ZX008 0.8 mg/kg/day, 0.2 mg/kg/day, or placebo. Daily doses were administered BID with a maximum dose not to exceed 30 mg/day. After a 2-week titration period patients were maintained on their randomized dose for an additional 12 weeks. The number and type of seizures were recorded daily in an electronic diary by caregivers. The primary efficacy endpoint was the change in mean monthly CSF between ZX008 0.8 mg/kg/day and placebo during the 14-week treatment period compared to the 6-week baseline observation period.

A total of 119 patients with DS enrolled in the study and were randomized to treatment (n=40, 0.8 mg/kg/day; n=39, 0.2 mg/kg/day; n=40, placebo). The mean age of the patients was 9 years (range: 2-18 years). 110 patients (92%) completed the study (85% 0.8 mg/kg/day; 100% 0.2 mg/kg/day; 93% placebo).

Baseline mean CSF across treatment groups was ~40 seizures/month. For the primary endpoint, ZX008 0.8 mg/kg/day showed a 63.9% greater reduction in mean monthly CSF vs placebo ($p<0.001$) (Fig. 1). The median percent reduction from baseline in monthly CSF was 72.4% for ZX008 0.8 mg/kg/day patients vs 17.4% for placebo patients ($p<0.001$). A significantly greater proportion of patients in the ZX008 groups achieved a ≥50% or ≥75% reduction in CSF and a longer median seizure-free interval vs placebo, with 0.8 mg/kg/day exceeding 0.2 mg/kg/day on all endpoints, suggesting a dose-response relationship (Fig. 2).

Results have been also evaluated within patients who previously withdrawn Stiripentol. A total of 58 subjects met the criteria for this analysis with a mean age 9.7 years (range, 2-18). ZX008 0.8 mg/kg/day showed a 60.8% greater reduction in mean monthly FCS vs placebo ($p=0.002$) (Fig. 3). Seventy-three percent of subjects in the ZX008 0.8 mg/kg/day group achieved ≥50% reduction in FCS ($p=0.006$) and 50% achieved ≥75% reduction in FCS ($p=0.036$). Longest median seizure-free intervals were 24.5 days (0.8 mg/kg/day, $p=0.003$), 18 days (0.2 mg/kg/day, $p=0.012$), and 9 days (placebo) (Fig. 4).

The most common non-cardiovascular adverse events reported in ZX008-treated subjects were decreased appetite, diarrhea, nasopharyngitis, lethargy, somnolence, and pyrexia. No clinical or echocardiographic evidence of cardiac valvulopathy or pulmonary hypertension was observed.

Patients treated with ZX008 experienced statistically significant, clinically meaningful reductions in CSF compared with patients treated with placebo, a sub-group analysis of patients who previously failed treatment with Stiripentol showed comparable efficacy and tolerability to the entire study population. ZX008 was generally well tolerated, with no clinical and/or echocardiographic signs of valvulopathy or pulmonary hypertension. ZX008 may represent an important and effective new treatment option for patients with DS.

GANAXOLONE FOR THE TREATMENT OF CDKL5 DEFICIENCY DISORDER IN AN ONGOING PHASE 3 CLINICAL TRIAL (THE MARIGOLD STUDY)

Nicola Specchio (Italy)

Ganaxolone (GNX) is an investigational synthetic neurosteroid that acts as a positive allosteric modulator of synaptic and extrasynaptic GABAA receptors and has known anticonvulsant activity.

GNX is a rationally designed 3β methyl analog of allopregnanolone with similar biological activity. The addition of the methyl group allows the compound to be orally bioavailable and prevents back-conversion to hormonally active compound.

GNX has been extensively studied in pediatric populations (>165 children dosed), including rare genetic epilepsies. In an open-label Phase 2 study, children with CDKL5 Deficiency Disorder (CDD) demonstrated a median 43% reduction in seizure frequency and a median 78% increase in seizure-free days following 26 weeks of treatment.

These findings in a current treatment refractory patient population led to the initiation of the first Phase 3 pivotal study in CDD (The Marigold Study). The design of this multicenter clinical trial will be presented during this session

LONG-TERM SEIZURE AND DEVELOPMENTAL OUTCOMES OF OHTAHARA SYNDROME: SURGICAL VS MEDICAL TREATMENT

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Ohtahara syndrome (OS) is one of most severe infantile epileptic encephalopathy and its seizure and developmental outcomes are usually quite poor. Long-term seizure and developmental outcomes were compared between surgical and medical treatment. METHODS: 26 surgical cases and 15 non-surgical cases of OS, followed up for one to 16 years after surgical or medical treatment, were studied.

Surgical cases of OS had hemimegalencephaly in 21, multilobar dysplasia in 3, and no cortical dysplasia in 2 cases. All the surgical cases underwent surgery after non-invasive evaluations. Surgical procedures included hemispherotomy in 22, multilobar disconnection in 2, and callosotomy in 2 cases.

Surgery was done at 2 and under 10 months. At the last evaluation aged 1-year-9-month and 16-year-5-month. Medical treatment included VPA, PB, ZNS, KBr, CLB and/or ACTH. Seizure outcome of surgical/medical treatment included seizure (Sz) free in 20/6, monthly Sz in 0/0, weekly Sz in 1/1, and daily Sz in 5/8. Developmental outcome consisted of IQ/DQ= 70-79 in 2/0, 50-69 in 3/0, 35-49 in 4/1, 20-34 in 9/0, and < 20 in 8/24 cases. Motor function included delayed death in 2/2, bed-ridden in 4/12, sit in 7/0, stand with support in □/1, and walk in □/0. Conversation was obtained in 5/0 cases, words in 5/1, jargon in 12/0, and no words in 4/11.

For OS, surgical treatment, if posible, brings far better long-term seizure and developmental outcomes.

STUDY OF 15 PATIENTS WITH EARLY INFANTILE EPILEPTIC ENCEPHALOPATHY TREATABLE NEUROMETABOLIC CAUSES

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Neonatal seizures are usually symptomatic as a result of perinatal insult like HIE hypoglycemia,ICH etc. Early infantile epileptic encephalopathy presents either in late neonatal period or early in infancy. IEM in few cases is one of the treatable cause of EIEE.To identify treatable etiology like IEM for EARLY INFANTILE EPILEPTIC ENCEPHALOPATHY assessment of neurodevelopment in treated infants with IEM.

All EIEE in clinics were included Patients with perinatal insults were excluded. Seizure semiology was recorded in all patients with video EEG. Metabolic workup included Blood glucose,lactate,ammonia,ABG.CSf glucose sugar carried out in few,followed by TMS and Urine GCMS.

Dietary management included low protein food combined with commercial formula in few cases. Biotinidase assay done in indicated cases. Those who responded with metabolic cocktail and could not be established by TMS and GCMs were subjected to exome sequencing .

All patients were followed up for 6months -3 years for neurodevelopmental assessment. Total 4 patients had biotinidase deficiency. 1patient had GLUt1 transporter defect, 1patient had multiple carboxylase deficiency responded to biotin and 1 died during treatment, 3patient had MMA, 1patient had MTHFR deficiency. 2patients had pyridoxine dependency and one lost to follow up. One patient with abnormal parameters had multiple gene defect. All treated patients had near normal neurodevelopment on follow up

Total 15 patients were included in study.

Cofactor like biotin and pyridoxine has dramatic effect on supplementation in deficient cases Organic acidemias responded to low protein diet combined with hydroxycobalamin and carnitine. EIEE may have few treatable IEM conditions which if diagnosed in time leads to near normal outcome but if diagnosed late in infancy leads to permanent sequalae. This insight is useful even for future generation hence,screening for IEM should be mandatory in developing countries like INDIA.

THE RISK FOR EPILEPSY DURING CHILDHOOD AFTER NEONATAL SEIZURES: A LONG-TERM FOLLOW-UP STUDY

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To determine the risk and predictors for epilepsy in children after neonatal seizures (NS).

The retrospective study included full-term and pre-term newborns: (1) with seizures clinically observed by a physician in Institute (2) with ictal electroencephalographic pattern of seizures, (3) with EEG recording within the first 48 hours after seizure onset, (4) follow-up duration for at least 12 months. The predictive value was evaluated for parameters: (1) characteristics of the patients (gender, gestational age, birth BW, Apgar score) (2) etiology, (3) characteristics of seizures (type, onset, resistance to tretment) (4) EEG background activity and paroxysmal discharges. Univariate and multivariate logistic regression analyses were used to assess the predictors for epilepsy at the end of follow-up period.

The epilepsy was diagnosed in 12 (7.4%) of 168 children after NS. The follow-up, period ranged 1-12 (med 5.2, iqr 6.7, mean 5.6, SD 3.5) years. Most of the cohort had normal development 131/168 (77.9%), neurological abnormalities – 31/168 (18.5%), intellectual disability – 28/168 (16.7%), and seven patients (4.2%) had lethal outcome. Abnormal EEG background activity, electrographic and resistant seizures to AEDs have the high predictive value for epilepsy.

The newborns with abnormal EEG background activity, electrographic and resistant seizures are at the high risk for epilepsy. So, the long-term EEG monitoring is important in order to assess the background activity and identify subtle or electrographic seizures. The infants with the risk for epilepsy have to be followed and education of thair caregivers about rescue anticonvulsive medication is essential.

CHARACTERISTIC SURFACE EMG IN A CASE OF EPILEPTIC SPASMS WITH NODDING/OBEYING MANNER

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The aim of this case report is to show the negative EMG discharge simultaneously with positive EMG discharge at epileptic spasms with nodding and/or obeying manner on VTR-EEG recording.

This 1-year-2-month-old boy was admitted to our hospital for cluster-formed epileptic spasms. He was born after normal gestation and delivery. Karyotype of chromosome was normal. Metabolic screening tests including tandem mass screening tests as well as work-up tests for congenital fetal infections were all negative. MRI exhibited age-matched myelination of the cerebral white matters with normal structural configuration of the brain. His developmental milestones were delayed such as sitting alone at 11 months, when he was poorly reactive to the mother's calling, inactive to fix his eyes and lost social smile. Cluster-formed spasms developed at 1 year and 1 month old. They were comprised of sudden elevations of bilateral upper limbs as well as nodding anteriorly or obeying repeatedly at his sitting position. Hypsarrhythmia was recorded on interictal EEG. Ictal VTR-EEGs at spasms with nodding/obeying exhibited positive-negative biphasic high-voltage slow wave discharges. Surface EMG recording showed the attenuation of EMG discharges on the erector spine muscles as well as simultaneous positive EMG discharge on the deltoid muscle.

The evidence of co-existing of negative contraction in the erector spine muscles and positive contraction in the proximal limb muscles were shown as spasms with nodding/obeying manners, and were suggestive for the mechanisms of variable manifestations of epileptic spasms.

GENETIC DIAGNOSIS IN CHILDREN WITH EPILEPTIC ENCEPHALOPATHIES USING TARGETED GENE PANEL ANALYSIS

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Epileptic encephalopathies (EEs) are phenotypically heterogeneous disorders with different underlying genetic defects and always accompanied with developmental delay/mental retardation and behavior problems. Finding the genetic basis of EEs with developmental delay/mental retardation can be valuable not only for diagnosis but also for guiding treatment and providing disease prognosis.

A customized panel of 90 genes related to epileptic encephalopathies was utilized to screen for potential genetic variants via targeted next generation sequencing (NGS). A total of 78 children with EEs were analyzed with an average read depth of 265.3±68.3X.

Mutations were found in 23 (9 boys and 14 girls) probands, and the overall mutation identification rate was 29.5%. Fifteen (65.2%) mutations involve ion channels, including SCN1A, KCNT1, SCN2A, SCN8A, KCNB1 and KCNQ2. The other (34.8%) mutations involve CDKL5, ALG13, GFAP, PCDH19, SNAP25, STXBP1 and SYNGAP1. Seventeen (69.6%) of the identified mutations were confirmed to be de novo and one (4.3%) was found to be paternal mosaicism. Channelopathies were found to be the major cause of both early onset (≤6 months) and later onset unclassified EE as well as febrile seizure cases. On the contrary, patients with infantile spasms were mainly caused by mutations in non-ion channel proteins.

NGS is a valuable diagnostic tool to detect the gene mutation in children with EEs. This cost-effective method shortens the course from seizure onset to genetic diagnosis. By understanding the gene mutations and genotype-phenotype correlation better, clinical practitioners could provide the optimal anticonvulsant and treatment.

Keywords: Epileptic encephalopathies (EEs), Developmental delay (DD), Infantile spasms (IS), Targeted next generation sequencing (NGS).

KCNT1-RELATED EPILEPTIC ENCEPHALOPATHY: THE FIRST CASE SERIES IN TAIWAN

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Mutations in the sodium-gated potassium channel subunit gene KCNT1 have recently emerged as a cause of several different epileptic disorders. Here we reported the first case series of KCNT1-related epileptic encephalopathy in Taiwan. Molecular genetic methods: Mutational screening was performed using targeted next generation DNA sequencing of a custom-designed panel containing 100 selected genes that are reported to cause epileptic encephalopathies.

Four male and one female patients were confirmed. The ages of seizure onset ranged from 14 days to 1 year. Most initial seizure pattern was focal seizure. Fever-sensitive seizures were noted in one patient. The EEGs of the two patients in the same family revealed burst suppression pattern, and the others' showed multifocal spikes. All of them had severe developmental delay or mental retardation, while autistic features were noted in three. Lacosamide improved the seizure control in two patients whom previous treatment with standard antiepileptic therapies failed.

Our case series of KCNT1-related epileptic encephalopathy expanded the knowledge of this disorder. The seizure onset was often in early infancy, and the prognosis was poor. Except quinidine, lacosamide is a potential anticonvulsant to treat KCNT1-related epileptic encephalopathy.

FATAL STATUS EPILEPTICUS IN DRAVET SYNDROME: A MULTICENTER SURVEY

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Status epilepticus (SE) occurs commonly in patients with Dravet syndrome (DS) and few of them could be followed with acute encephalopathy and death. Causes of death has still poorly defined and their risk factors as well. We describe a cohort of children with DS who died after SE.

We launched an international call through the European Reference Network on rare and complex epilepsies (Epicare). A questionnaire was sent by mail to the 7 hospitals who reported cases of death after SE to obtain information on the following items for each patient: gender, SCN1A mutation, age at death, results of cardiological screening, relevant clinical comorbidities, previous SEs, frequency of seizures and ongoing therapies during the last 6 mounths before death, treatment of the SE, autopsy findings. Data were collected at the Pediatric Neurology Unit, Bambino Gesù Children's Hospital, Rome, Italy.

So far, we received feedback from 5 hospitals; data from 4 SCN1A patients were analyzed. None has other relevant comorbidities, 1 have cortical dysplasia. All underwent cardiological screening with ECG, referred normal. Just 1 patient has seizures control, 2 have different type of seizures and none have myoclonic seizures. 2 have previous SE and 2 have fever as trigger of the SE. Only 1 post mortem examination has been performed.

Our survey results are consistent with the assumption that unexpected death in DS patients could be related to SE, even with a negative cardiological screening and no other relevant comorbidities. The role of SCN1A mutation and antiepileptic drugs will be discussed.

ABSTRATCS

Poster Presentation

P1

ACUTE DISSEMINATED ENCEPHALOMYELITIS AND SUBSEQUENT EPILEPSY IN CHILDREN

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To analyze the range of demographic, clinical, MRI, and CSF features of children with acute disseminated encephalomyelitis (ADEM), a rare, typically monophasic demyelinating disorder, and analyze long-term outcomes.

We performed a retrospective study in a tertiary medical centers of all patients clinically diagnosed with ADEM.

Of 31 patients (11 female, follow-up 8±4.4 years), eight (29%) experienced at least one relapse and 9 (31%) had subsequent epilepsy. A majority of patients had preceding events including upper respiratory infection (40%) or trauma (11.1%). The clinical manifestations included fever (74.3%), lethargy (68.6%), encephalopathy (65.7%), motor weakness (60%), and seizures (45.7%). The MR images showed lesions over white matter (82.9%), basal ganglia/thalamus (80%), infratentorium (31.4%), and cortex (20%). Sixteen patients (45.7%) did not receive treatments, 8 (22.9%) treated with steroids, 8 (22.9%) IVIG, and 5 (13.9 %) both. Among the patient with subsequent epilepsy, seven were on remission and 2 were AED-dependent. Patients with subsequent epilepsy were more likely to have seizures in acute phase, severe cognitive impairments in nadir, and cortical involvements by MR images than those without epilepsy. Those with relapsing demyelinating disease were less often presented with pain, severe neurological dysfunction in nadir and had shorter ICU stay than those with monophasic course. Those children with relapsing course or subsequent epilepsy had a non-significant trend of long-term neuropsychological deficits and learning difficulties.

The long-term outcome suggested that the neurological deficits and neurocognitive impairments were not so rare in childhood-onset ADEM.

P2

CLINICAL CHARACTERISTICS AND RISK FACTORS FOR SEIZURES WITH GASTROENTERITIS IN CHILDHOOD: A COMPARATIVE STUDY OF FEBRILE AND AFEBRILE ATTACKS

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Benign convulsions with mild gastroenteritis (CwG) occur in infants during the course of mild acute gastroenteritis(AGE). We analyzed the clinical characteristics of febrile and afebrile seizures associated with mild gastroenteritis, and attempted to determine the influence of fever in these two groups.

Retrospective analysis was performed on pediatric patients admitted with mild AGE combined with convulsions to Kaohsiung Medical University Hospital between January 2008 and December 2017.

We reviewed the medical records of 79 infants and young children presenting with seizures during a mild AGE episode. All patients had no past history of epilepsy or febrile seizures who experienced first convulsions of their lifetime. The median age was 13.5 months (range, 6-56 months), with 68% younger than 18 months. 48 cases were afebrile. Seizures were generalized tonic-clonic (65%), followed by generalized tonic (28%), and hypotonic (4.7%), with 2 (2.3%) partial. Twenty-two patients (25.3%) presented single episode of convulsion, and in 42 patients (48.3%), the seizures were in clusters from 2 to 6. 34 epidoses (39%) presented 2 different types of convulsion. More afebrile patients experienced □2 seizures/day than did febrile ones (68% vs. 40%, P = 0.03). Electroencephalograms, obtained from 52 patients, showed abnormal discharges in 8. Rotavirus was the main infectious agent in the AGEs, found in 20 patients.

The presence of fever may influence the clinical characteristics of CwG. Despite some differences in seizure characteristics, both febrile and afebrile seizures associated with mild AGE were mostly benign with a favorable prognosis.

P3

STIMULUS-INDUCED REPETITIVE DISCHARGES (SIRPIDS) IN A NEWBORN WITH TUBULINOPATHY

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Stimulus-induced repetitive discharges (SIRPIDs) could be observed in critically ill patients. However, SIRPIDs could be confusing in neonatal EEG. Identification of SIRPIDs in neonates could lead to a better clinical care by elimination of stimuli and avoidance of unnecessary antiepileptic medications.

The report demonstrated SIRPIDs in a newborn video EEG and managements after diagnosis of SIRPIDs. Survey of underlying etiology of SIRPIDs is crucial for prognosis prediction.

A female newborn was referred for medication-refractory seizures since birth. Physical examinations showed microcephaly (30.5cm) but without growth restriction. The seizures were very frequent once on acoustic or tactile stimuli. EEG showed generalized low-attenuated background. On tactile stimuli, high-amplitude rhythmic ictal discharges over bilateral parietal-occipital areas occurred, when the patient had generalized clonic movements at the same time. SIRPIDs were diagnosed according to the somatosensory provocation and video EEG findings. Neuroimaging studies showed agyria, corpus callosum agenesis, cerebellar hypoplasia, dysmorphic basal ganglia, and right olfactory nerve hypoplasia, suggesting features of tubulinopathy. Exon-wide sequencing analysis of Tubulin-α1A (TUBA1A) was performed, which confirmed a c.629A>G (p.Tyr210Cys) mutation. Although phenobarbital and levetiracetem were applied for seizure control, a limited clinical care by minimizing examinations and procedures led to a dramatic decrease of seizure frequency.

Diagnosis of SIRPIDs in neonates is critical for clinical managements, that elimination of stimuli greatly reduces seizure frequency. Since SIRPIDs result from cortical hyper-excitability, SIRPIDs in our patient could be explained by the genetically determined cortical malformation.

P4

USE OF AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY TO PREDICT THE SEIZURE OUTCOME IN INFANTS WITH NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY TREATED WITH THERAPEUTIC HYPOTHERMIA

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The aim of this study is to examine the predictive value of amplitude-integrated electroencephalography (aEEG) parameters to seizure outcomes at 6 months.

This was a single-center, retrospective cohort study. Between May 2012 and September 2017, neonates with hypoxic-ischemic encephalopathy (HIE) received both therapeutic hypothermia (TH) and aEEG throughout TH were enrolled. Clinical data were reviewed via electronic medical records. The aEEG parameters were analyzed and classified as background patterns and seizure activities. We determined the trend of seizure activity burden to be increased or decreased. The definition of epilepsy at 6 months was classified as clinical seizures and the usage of antiepileptic drugs (AEDs).

A total of 23 infants (14 boys, 9 girls) with the mean gestational age of 38.9 weeks were enrolled. Fifteen (65%) patients had moderate HIE and 8 (35%) severe HIE (modified Sarnat staging). The mean recording time of aEEG was 107.5 hours. At 6 months, 5 (22%) patients had clinical seizures with regular use of AEDs. No difference of demographic data was shown between infants with epilepsy or not. The presence of epilepsy at 6 months related to the increased trend of seizure activities by aEEG records during TH (Fisher's exact test, $p = 0.037$).

The study shows that the increased trend of seizure activities by aEEG during TH can predict epilepsy at 6 months for the survivors of neonatal HIE.

P5

USING EPILEPSY ONTOLOGY-BASED INTEGRATED DATABASE TOWARD NEW EPILEPSY CLASSIFICATION AND PRECISION MEDICINE

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In this new era of genomic medicine, personalized and precision medicine become increasingly focusing in epilepsy research and practice, also drives the development of new epilepsy classification. However, excessively derived knowledge and information make it difficult for clinicians and related researchers to quickly find the right aetiology, diagnosis and treatments for patients, especially those with rare or intractable epilepsy. In current study, we try to build up an epilepsy ontology-based integrated database for assisting physicians to diagnosis and treat patients with epilepsy rapidly and accurately

Initially we used Protégée 5.2 to build up an epilepsy ontology-based integrated database, in which including seizure types, classification of epilepsy, Various epilepsy syndromes, aetiologies, genetic database, antibody database for epilepsy, medical term database for symptoms and signs, comorbidities, treatments, based on ILAE 2017 classification and associated literatures. Add protégé plugin in Eclipse and try to access and read from the file. Then we use clinical cases to evaluate the accuracy rate.

This study uses the epilepsy ontology-based integrated database to reach a user-friendly and adaptable complete diagnostic and treatment solution for clinicians approaching epilepsy.

With this module, the expense of epilepsy diagnoses and treatments can be greatly reduced, but the quality care would be improved. The experience of this system development will provide a good illustration of the development of intelligent health care systems for other diseases.

P6

EEG PERFORMED FOR FIRST EPISODE OF FEBRILE SEIZURE IN CHILDREN MIGHT HAVE THE VALUE TO PREDICT SUBSEQUENT EPILEPSY

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The value of electroencephalography (EEG) for evaluation of febrile seizure (FS) remains controversial. We investigated the EEG characteristics as predictors for subsequent epilepsy or developmental delay in children.

We've enrolled children with FS from the pediatric outpatient clinics for EEG study within 7~14 days after their first FS episode and follow up for 5~10 years. EEGs were classified as abnormal based on the presence of focal or generalized epileptiform discharges and/or background slowing.

From Jan, 2007 to Dec, 2017, we've enrolled 92 children with FS and 32 (34.8%) revealed paroxysmal abnormality on EEG. Children with abnormal EEG were obviously older than those with normal EEG (3.4±1.39 v.s. 2.4±1.26 yr, p=0.01). Of 17 patients (18.5%) with complex febrile seizure, 12(70.6%) revealed EEG abnormality. Within those 32 children with abnormal EEG, 8 (25%) developed epilepsy later and 3 (9.3%) had global developmental delay. However, of 60 children with normal EEG, no one developed epilepsy. As to the abnormality on EEG, 26 patients (81.3%) had focal spikes or sharp waves and most commonly seen foci were frontal regions (n=16, 61.5%)□7 patients (21.9%) revealed generalized epileptiform discharges and only 3 (9.4%) showed focal background slowing. Compared with all EEG foci, patients with frontal spikes/sharp waves had higher risk for developing epilepsy (OR=1.67, 95%CI: 1.06-2.62, p=0.03).

Patients with first FS episode presenting with frontal paroxysmal EEG abnormalities may have higher risk for developing epilepsy later. EEG performed for first FS episode still have the value to predict subsequent epilepsy.

P7

EPILEPSY AND ATYPICAL FORM OF STATUS EPILEPTICUS IN FUKUYAMA-TYPE CONGENITAL MUSCULAR DYSTROPHY

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Fukuyama-type congenital muscular dystrophy (FCMD) is an autosomal recessive disorder, characterized by congenital muscular dystrophy and brain malformation. Little is known about epilepsy associated with FCMD. The aim of this study is to clarify the epilepsy in patients with FCMD.

Between 1981 and 2016, nine patients (6 male) were diagnosed with FCMD in our center. All six patients tested carried a homozygous founder mutation, a 3kb insertion in a 3'-untranslated region. Muscle biopsy was examined for six patients, including three of which genetic testing was not available. We retrospectively studied the clinical manifestations from their medical records.

The follow-up period ranged from 3 to 27 years (mean 15.4 years). Three patients died of respiratory failure after the age of 20 years. Neuroimaging revealed migration anomalies in all patients.

Two patients had neonatal seizures caused by intracranial hemorrhage. Febrile seizures were observed in two other children. During follow-up, six (4 homozygote, 2 not examined) of nine patients developed epilepsy. Except for one girl (2 years of age), the remaining five patients developed epilepsy between 13 and 22 years of age. The most common seizure type was CPS, followed by (s)GTC. With progression of muscle weakness, the convulsive movements of their seizures became less prominent. Three patients exhibited convulsive SE, including peculiar one, characterized by impaired consciousness and autonomic symptoms with no convulsive movements, which may be overlooked without EEG. At the last evaluation, all but one patient had uncontrolled seizures despite antiepileptic drug treatment.

Epilepsy was observed in two-thirds of patients with FCMD. In contrast to the previous reports, epilepsy developed after adolescence in the majority of our subjects. Of note, some patients developed atypical forms of SE, which required EEG monitoring for detection.

P8

STRONG COUPLING BETWEEN SLOW OSCILLATIONS AND WIDE FAST RIPPLES IN CHILDREN WITH EPILEPTIC SPASMS: INVESTIGATION OF MODULATION INDEX AND OCCURRENCE RATE

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Epileptic spasms (ES) often become drug-resistant. To reveal the electrophysiological

difference between children with ES (ES+) and without ES (ES-), we compared occurrence rate (OR) of high-frequency oscillations (HFOs) and modulation index (MI) of coupling between slow and fast oscillations.

We reviewed 24 children who underwent multilobar resections. We measured OR of HFOs and determined the electrodes with a high rate of HFOs by cluster analysis. We calculated MI, which reflects the degree of coupling between HFO (ripple/fast ripple [FR]) amplitude and 5 different frequency bands (0.5-1, 1-2, 2-3, 3-4, 4-8 Hz).

In ES+ (n = 10), OR(FR), the number of electrodes with high-rate FRs, and MI(FR & 3-4 Hz) in all electrodes were significantly higher than in ES- (n = 14). In both ES+ and ES-, MI(ripple/FR & 3-4 Hz) was the highest among 5 frequency bands. Within the good seizure outcome groups, OR(FR) and MI(FR & 3-4 Hz) in the resected area in ES+ were significantly higher than in ES-.

In ES+, the larger number of high-rate FR electrodes indicates more widespread epileptogenicity than in ES-. High values of OR(FR) and MI(FR & 3-4 Hz) in ES+ compared to ES- are a signature of the severity of epileptogenicity. We proved that ES+ children who achieved seizure freedom following multilobar resections exhibited strong coupling between slow oscillations and FR.

P9

A STUDY ON THE DIAGNOSTIC VALUE OF CHROMOSOME MICROARRAY ANALYSIS IN PEDIATRIC EPILEPSY WITH COMPLEX PHENOTYPES

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To evaluate the role of copy number abnormalities detectable using chromosomal microarray (CMA) and diagnostic value of CMA in pediatric epilepsy patients with complex phenotypes.

From January 2014 to October 2017, we retrospective studied children with unexpected epilepsy and complex phenotypes such as developmental delay, intellectual disability, dysmorphic features, and autism spectrum disorder. The CMA was conducted with CytoScan®750K array (Affymetrix, USA) with an average resolution of 100 kb.

9 patients 9mle 3 and female 6 patients) with performing CMA were studied. Mean age at exam was 10.5 5.0 years. All patients were taking anticonvulsant medications. Six of them were able to with two or more anticonvulsants. All patients had developmental or intellectual disabilities, and 88.9% (8/9) had dysmorphic features such as facial dysmorphism and 66.7% (6/9) with clinical symptoms of autistic spectrum disorder. Total 8 copy number variants (CNVs) in 6 patients were detected. Among them, 6 6 CNVs were considered pathogenic (diagnostic yield 66.7%). One patient occurred by uniparental disomy (15q) and 5 patients showed microdeletion; 14q11.2(57 Mb), 2q31(6.iMb), 1q44(4Mb), 6q26(7.6Mb). All 2 size of benign CNVs were below 500 kb.

The efforts to identify the various pathogenic CNVs in Korean patients furnish variable materials to establish the cause of disease. Our data suggest that CMA is useful diagnostic tool for detecting clinically significant CNVs in children with epilepsy, especially in combination with complex phenotypes.

P10

TUBB2A MUTATION IN A CHILD WITH EPILEPSY, DEVELOPMENTAL DELAY, AND SIMPLIFIED GYRAL PATTERN

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Among the numerous genes reported in cortical malformation, the genes encoding alpha- or beta-tubulin isotypes give new insights into tubulinopathies. Differently from other tubulin genes, mutations of TUBB2A cause simplified gyral patterning that was first reported in 2014. In a 5-year-old girl with simplified gyral pattern, we tried to find genetic etiology.

The patient's data were retrospectively collected and her brain magnetic resonance imaging (MRI) was reviewed by two radiologists independently. Whole-exome sequencing (WES) was performed on samples from the proband and her mother. The variants were prioritized, referring different single nucleotide polymorphism (SNP) databases.

The proband and her mother had developmental delay, intellectual disability, and mildly dysmorphic features such as a round and flat face, hypertelorism, and strabismus. At 2 years and 7 months, the proband presented prolonged generalized tonic-clonic seizures. Brain MRI showed a mildly simplified gyral pattern with normal cortical thickness and partial dysgenesis of the corpus callosum in addition to dysplastic basal ganglia and thalami. Electroencephalograms showed diffuse slowing. Her seizures have been well controlled by carbamazepine. Chromosomal analysis and chromosomal SNP array were normal. WES found rare cis-heterozygous variants of TUBB2A (NM_001069.2; NP_001060.1): c.[223T>G;224C>T] (p.Ser75Val). These variants were confirmed in the proband and her mother by Sanger.

This case is the second report of a rare TUBB2A variant causing simplified cerebral gyral patterning, epilepsy, developmental delay, intellectual disability, and a mild dysmorphic features.

P11

IMMUNOTHERAPY FOR ANTI N-METHYL-D-ASPARTATE RECEPTOR ENCEPHALITIS

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Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an antibody-mediated inflammatory brain disease causing severe psychiatric and neurological deficits in previously healthy patients. The aim of this study was to demonstrate the clinical characteristics of the patients diagnosed with anti-NMDAR encephalitis and to compare the different treatment strategies among these patients.

Patients presenting with newly acquired psychiatric and/or neurologicdeficits were studied retrospectively from year 2009 to 2017. Patients who had confirmatory evidence of anti-NMDAR antibodies in the serum and/or cerebrospinal fluid (CSF) were selected. The modified Rankin scale (mRS) was used to assess the initial status and the outcome of those patients. Details of clinical presentation and results of investigations were reported.

26 patients were enrolled in this study. 25 patients received first-line immunotherapy (steroids, and/or immunoglobulins, and/or plasma exchange) and 16 patients received second line immunotherapy (Rituximab and/or Cyclophosphamide). Median time between the first line and second line treatment was 13 days. During the first 6 months, 21 of 26 patients (80.8%) achieved a good outcome (mRS ≤2) and 15 of 26 patients (61.5%) achieved complete recovery (mRS=0). 4 patients (17.7%) relapsed, and 3 patients (12.5%) were noted to have associated tumor.

Rituximab and/or Cyclophosphamide may be another treatment option for those who do not tolerate or respond to first line immunotherapy. The present study highlights the need for clinical trials to determine the optimal treatment of anti-NMDAR encephalitis. HSV encephalitis is a poor prognostic factor for those with anti-NMDAR encephalitis.

P12

COGNITION AND EVOLUTION OF MOVEMENT DISORDERS OF FOXG1-RELATED SYNDROME

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We aimed to investigate a series of children presenting with postnatal microcephaly, epilepsy, and movement disorders.

We performed trio whole exome sequencing on children presenting with postnatal microcephaly, movement disorders and severe encephalopathy.

Three children with de novo FOXG1 mutations were detected. All patients were males, aged 1.1, 1.8 and 16.9 years. All of them had normal head girth since birth and had evidence of microcephaly at the age of 2-4 months old, and hypogenesis of corpus callosum. All presented with dyskinesia (chorea & dystonia), hypotonia, and severe mental retardation. All had epilepsy, with focal and generalized seizures. The onset of seizures was at the ages of 8 months, 1.5 years, and 2.5 years. They can be well controlled under anti-epileptic drugs. In contrast to literature review that failed to identify specific facial features in FOXG1 syndrome, all the patients showed consistent facial dysmorphism (strabismus, pointed chin, bulbous upturned nose and tented upper lip).

Epilepsy is not uncommon in children with FOXG1 mutation, but can be well controlled by anti-epileptic drugs. Children with FOXG1 mutation can present with chorea or dystonia before the onset of seizures.

P13

INFANTILE SPASMS IN A PATIENT WITH MOSAIC MONOCENTRIC AND DUPLICATED SUPERNUMERARY MARKER CHROMOSOME 15

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To report detail of a patient with infantile spasms whose cytogenetic analysis revealed mosaic monocentric and duplicated supernumerary marker chromosome 15.

A 13-month-old girl with infantile spasms and delayed developmental milestones. Chromosomal analysis with G-band showed the presence of supernumerary marker chromosome in mosaic. Further investigations using in situ hybridization, methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA), microsatellite marker, and SNP array analysis were performed.

Her karyotype was noted as mosaic 47,XX,+mar[26]/46,XX[4], ish der(15)(D15Z1+, SNRPN++, PML–) de novo. MS-MLPA analysis showed that the Prader–Willi syndrome/Angelman syndrome critical region is highly methylated, and microsatellite marker analysis proved that the 15q11.2 region of the patient comprises three kinds of alleles: one paternal and two maternal origins. SNP array analysis suggested an asymmetric structure of SMC(15) composed of 15q11-q13 recombination at breakpoints (BP) 4:BP5. Treatment with ACTH was quite effective and the patient was seizure free for 6 years, but tonic and complex partial seizures relapsed when she is 7 years of age.

This is the first report of SMC(15) with monocentric and duplicated proximal 15q. The clinical presentations are quite similar to those of idic(15) syndrome. The results of microsatellite and SNP array analysis suggests two possibilities regarding the timing of the mosaic SMC(15) formation. One possibility is that it occurred during maternal meiosis, and the other possibility is formation during a very early stage of embryo that was initially trisomic of chromosome 15.

P14

RHOBTB2 RELATED ENCEPHALOPATHY: PRECISION MEDICINE SCENARIO SHOULD BE KEPT IN MIND

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Until two years ago a little was known about a RHOBTB2, a gene encoding Rho-related BTBdomain-containing protein 2, role in neurodevelopment.

A recent studies (Lopes et al 2016) identified it's possible causative role in Rett like phenotype, papers by Straub et al 2018; Belal et al 2018 designated it as a causative gene for developmental and/or epileptic encephalopathies.

The most constant symptoms of RHOBTB2 encephalopathy includes early-onset seizures, severe to profound intellectual disability (ID), postnatal microcephaly, and movement disorders, a phenotype also observed in CDKL5-, FOXG1-, or SLC2A1- related encephalopathies.

Therefore, diagnosis of RHOBTB2-related developmental and epileptic encephalopathy might rely on whole exome sequencing rather than on a specific clinical suspicion.

However, paper by Straub et al highlights (post-ictal) hemiparesis and secondary MRI anomalies that might be more specifically related to RHOBTB2.

Here we present a case of 6 y.o. boy with RHOBTB2 (c.1532G>A p.(Arg511Gln) related encephalopathy with early (infantile) onset epilepsy, ID, acquired microcephaly and frequent disabling dystonic (non-epileptic) attacks accompanied by hemiparesis as main and constant feature.

Dystonic attacks and hemiplegia were similar to the attacks sometimes observed in Familial Hemiplegic Migraine (FHM).

Moreover the case we present has excellent response to Acetazolamide (AAA), frequently observed in FHM.

Along with ID, epilepsy and postnatal microcephaly, dystonia attacks with hemiplegia could be the most disabling feature of some cases with RHOBTB2 encephalopathy.

AAA treatment dramatically reduced the attacks.

RHOBTB2 gene should be included in early onset epilepsies as well as dystonia/microcephaly and ID panels.

P15

EPILEPSY IN INFANT WITH DIETARY COBALAMIN DEFICIENCY AFTER SUPPLEMENTARY TREATMENT

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Dietary cobalamin (vitamin B12) deficiency in infants often manifests as neurological abnormalities such as seizure, involuntary movement, and retardation. In rare cases these symptoms appear after initiation of treatment. In this report, we describe a case of infantile cobalamin deficiency in which epilepsy manifested after treatment initiation.

An 8-month-old male being fed only breast milk was referred to our hospital with pancytopenia, failure to thrive, and developmental retardation. His serum cobalamin was under 50.0 pg/mL. Bone marrow examination revealed megaloblastic changes. Cranial MRI showed cerebral atrophy. Additionally, his mother had not been taken cobalamin after total gastrectomy for gastric cancer. He was diagnosed with dietary cobalamin deficiency, and oral cobalamin was initiated. On the 10th day of treatment, generalized tremors and myoclonus were observed in his hands, feet, and tongue, but his electroencephalography (EEG) was normal. After the 15th day of treatment, impaired consciousness and generalized tonic-chronic seizures were observed several times a day. His ictal EEG showed diffuse multifocal spikes and rhythmic slow waves dominantly propagated to one side hemisphere. Cobalamin treatment was stopped, and oral clonazepam was initiated for involuntary movement and epilepsy.

Although several cases of involuntary movements after cobalamin initiation have been reported, the underlying mechanism remains unclear. Epilepsy and involuntary movements may be due to increased excitability of cortical neurons accompanied by metabolic changes due to rapid cobalamin saturation. In infants, clinical findings associated with cobalamin deficiency vary, and epilepsy could be observed during cobalamin therapy.

P16

EPILEPTIC STATUS. EPSTEIN-BARR VIRUS ASSOCIATED ENCEPHALITIS: CLINICAL CASE

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Epileptic status is a life-threatening neurological and medical emergency. The cause of epileptic status may be various etiological factors, such as cerebral circulation disorders, intoxications, encephalitis and also post traumatic and other causes. The purpose of this clinical case is to investigate the features of epileptic status in encephalitis of an unknown genesis and to determine the etiological factor of encephalitis on the basis of the clinical picture, laboratory tests, neuroimaging and electrophysiological examination methods.

This article presents a clinical case of a 7-year-old child who had fever, seizures with the development of epileptic status, behavioral changes.

Objective evidence indicated the presence of acute encephalitis. Magnetic resonance imaging examinations and electroencephalography did not show any specific changes. The diagnosis was made on the basis of a clinical picture, an anamnesis, and also on the basis of molecular research.

Considering the multiple causes of epileptic status diagnostic searches can be difficult. This clinical case shows that in the absence of specific neuroimaging data for organic lesions in the brain, the presence of representative clinical signs of encephalitis is not sufficient to establish a definitive diagnosis, and requires comprehensive diagnostic measures, including molecular diagnostics.

P17

QUINIDINE THERAPY IN A GIRL WITH MIGRATING PARTIAL SEIZURES OF INFANCY CAUSED BY KCNT1 MUTATION

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Migrating partial seizures of infancy (MPSI) is one of the early-onset epileptic encephalopathies. The most common genetic cause is a gain of function mutation of KCNT1, which encodes voltage dependent sodium activated potassium channels. Herein, we report a case of MPSI with a de novo heterozygous missense mutation in KCNT1 (c.1283G>A; p.R428Q) treated with quinidine, a partial antagonist of KCNT1.

The female patient was born normally at 39 weeks of gestation, weighing 3152 g. She required tube feeding because of poor sucking due to hypotonia. She developed focal motor seizures at the age of 1 month. As seizures became very frequent, occurring in clusters, she was referred to our center. Initial interictal EEG showed normal background activity with focal spikes. At 2 months, seizures evolved to a series of several types of focal seizures, manifesting with motor and autonomic symptoms. A diagnosis of MPSI was made based on ictal EEG, which revealed shifting foci on ictal onset in consecutive seizures. She exhibited episodic involuntary movements (dyskinesia and chorea) starting at the age of 3 years. Seizures were intractable to antiepileptic drugs. After informed consent was obtained, a starting dose of quinidine (2 mg/kg/day t.i.d.) was added to PHT, PB and GBP at 5 years of age. The doses were gradually titrated upwards to 50 mg/kg/day (serum level 0.3g/mL), when ECG revealed prolonged QT intervals. During the quinidine treatment, the frequency of seizures did not decrease, and EEG demonstrated no improvement. Psychomotor development remained markedly delayed.

To date, five reports have studied the efficacy of quinidine therapy, but yielded conflicting results. Although our patient carried an identical KCNT1 mutation to that in the first quinidine-effective case (Ann Neurol 2014), quinidine was ineffective. Further studies are necessary to clarify the efficacy of quinidine treatment in KCNT1-positive epilepsy.

P18

ANALYSIS OF EPILEPTIC SPASMS OF WEST SYNDROME IN 128-CHANNEL DENSE ARRAY ELECTROENCEPHALOGRAPHY

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This study evaluated the features of epileptic spasms in West syndrome buy using128-channel dense array electroencephalography (dEEG).

We performed video electroencephalography dEEG) using NetStation GES400 (NS5.1.2; Electrical Geodesics Inc.) for epileptic spasms in three cases of West syndrome. We analyzed 20 ictal EEG recordings were of the spasms. Electrode recordings were obtaining using the 128-channel EEG Hydrocell Geodesic Sensor Net (HCGSN).The wave pattern in the 128-channel EEG montage was examined using the international 10-20 method-derived Cz as the system reference, Furthermore, we performed electroencephalographic mapping during an epileptic attack and analyzed the change in EEG amplitude over time.

Just before an epileptic seizure, a slightly negative wave in the 128-channel pattern was noted which shifted to a positive wave; thereafter, a high-amplitude multiphasic (five components) wave pattern was observed. The epileptic spasms began when a generalized positive waveform the initial shift segment transitioned to a high-amplitude negative wave. Fast were not recognized by the record of the bucca of both sides, and it was unclear, and the origin was only a slow negative-positive-negative wave.

Herein, analysis of the 128-channel dEEG suggested the epileptic spams originate from the cerebral cortex.

P19

EPILEPTIC SPASMS IN FIVE CHILDREN CARRYING WDR45 MUTATIONS

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WDR45 mutations are causally related to beta-propeller protein-associated neurodegeneration (BPAN), a subtype of neurodegeneration with iron accumulation. Although BPAN is characterized by adult-onset dementia and dystonia, little is known about its clinical phenotypes during childhood. The aim of this study was to clarify the clinical manifestations, including epilepsy, in children with WDR45 mutations.

We retrospectively examined the clinical features, laboratory data, MRI and EEG of five epileptic children (2 boys) with WDR45 mutations.

All five patients developed epileptic spasms (ES) before three years of age (West syndrome 3 and late-onset spasms 2); four children had epilepsy onset with ES, and one had complex partial seizures. ES were subtle, accompanied by fast, diffuse low-voltage waves on ictal EEG. Initial MRI revealed no abnormalities. All patients had elevated serum NSE (32.8 to 93 ng/ml) and AST values (62 to 82 IU/ml). Seizures were refractory to treatment, including ACTH therapy. At the final evaluation (2 to 8 years of age), seizures were controlled with ZNS in only one boy. The remaining four patients had daily seizures; persisting ES in two, partial seizures in one, and a combination of ES and other atonic, atypical absence seizures in one. On follow-up MRI, T2*-weighted scans detected symmetrical hypointensity in the globus pallidus after 6 years of age.

If subtle ES combined with elevated serum NSE and AST values are present, epilepsy due to WDR45 mutations should be considered.

P20

SEVERE HYPERKINETIC MOVEMENT DISORDER IN GNAO1 ENCEPHALOPATHY-LONG TERM VIDEO CASE REPORT AND REVIEW OF LITERATURE

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Severe hyperkinetic movement disorder in GNAO1 encephalopathy-long term video case report and review of literature

Heterozygous mutations in the GNAO1 gene (MIM 139311), encoding the subunit of the heterotrimeric guanine nucleotide-binding proteins (G protein) were first described as a cause of early infantile epileptic encephalopathy (EIEE) in 2013. Subsequent reports have broadened the spectrum of clinical presentation including prominent dyskinesia and intellectual disability with few or no seizures.

We report a now 6 year old girl that presented at the age of 1 year with severe muscular hypotonia and developmental delay. After the age of 2 years she developed severe dyskinetic movement disorder with paroxysmal life-threatening episodes of choreoathetoid crisis induced by fever and emotions. She has only mild epilepsy. We present a video case report from the age of – 6 years and give a review of the literature.

GNAO1 encephalopathy can cause involuntary movements and severe developmental delay with or without seizures including various types of early-onset epileptic encephalopathy.

P21

HYPSARRHYTHMIA DURING CRITICAL TIME WINDOW OF BRAIN DEVELOPMENT IN THE FIRST YEAR OF LIFE MAY RESULT IN SPECIFIC COGNITIVE DEFICITS

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Developmental arrest after the onset of infantile spasms (IS) is known since the first description by dr.West.

To study the impact of hypsarrhythmia on cognitive development in infants with IS.

The following data were retrospectively collected from medical records: age at IS onset, treatment delay, the hypsarrhythmia duration in weeks, aetiology and the response to treatment. Good outcome was considered in cases of complete spasms and hypsarrhythmia remission and favourable neurodevelopment. At follow up study, ≥3 years after the onset of IS all children were psychologically tested and results analyzed according to the age at IS onset and duration of hypsarrhythmia ≤ 3 weeks or longer. Visual problems, language development, fine motor skills and signs of autistic features were evaluated.

The remission of spasms was achieved in 23 out of 48 infants; hypsarrhythmia resolved in only 18 cases. Treatment delay from IS onset was 1 to 4 weeks in 35 (73 %), longer in 13 infants. At follow-up normal/ borderline mental development was found in 14 children (29 %), mild intellectual disability in 6 children, moderate in 10 and severe in 14 children (29 %). The outcome was statistically significantly related to etiology ($p = 0.001$); The correlation between duration of hypsarrhythmia, the age at onset in months and the specific cognitive deficits later was noted: for visual tasks children with vision disturbances had earlier onset (average age 4M versus 6 M in children without visual deficits), while autistic behaviour was more frequent in later onset group (6,4M) compared to children without autistic behaviour (IS onset at 5,4M). Higher risk was noted for infants with longer duration of hypsarrhythmia.

Hypsarrhythmia may interact with the period of intensive cortical maturation thus demonstrating influence of epileptic activity during the critical time window of specific cognitive function development.

P22

DOES THE TITER OF ANTI-GLUTAMIC ACID DECARBOXYLASE (GAD)-ANTIBODY MAKE DIFFERENCE IN PEDIATRIC PATIENTS WITH ENCEPHALITIS OR ENCEPHALOPATHY

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Anti-glutamate decarboxylase (anti-GAD) antibody has been associated with encephalitis. However, few studies investigated the correlation between anti-GAD antibody titers to clinical severity and outcome. Thus, this study aims to evaluate whether the level of serum titers relates to disease presentation or outcome in pediatric population.

This was a single-center, retrospective cohort study. Between February 2010 and September 2016, we enrolled consecutive hospitalized patients who had encephalitis or encephalopathy and had positive anti-GAD antibodies. We divided patients into two groups: patients with anti-GAD > 100 (U/mL) and those with anti-GAD < 100 IU/ml. Clinical severity assessment during hospitalization includes the Glasgow Coma Scale, need of intensive care or endotracheal tube, duration of hospital stay, use of antiepileptic medications, electroencephalography and neuroimaging. The outcome measure includes Modified Rankin scale (MRS), epilepsy and use of antiepileptic medications.

A total of 42 patients (18 boys, 24 girls) with positive anti-GAD antibody encephalitis or encephalopathy was enrolled(Age: 7.8 ± 6.5 year olds, follow-up duration: 1 month to 8 years). Eighteen patients with anti-GAD antibody were above 100 U/ml (range, 100-2000U/mL), and 24 patients were below 100 U/ml (range, 50-100 U/mL). No correlation was found between antibody titers and either measurement regarding clinical severity during hospitalization or outcome.

In pediatric patients with anti-GAD encephalitis or encephalopathy, the study showed that there was no significant difference between serum titers and either clinical severity or outcome.

P23

TEMPORO-POLAR GRAY/WHITE MATTER BLURRING PRIOR TO FEBRILE SEIZURE STATUS IN TEMPORAL LOBE EPILEPSY

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This study aimed to elucidate the pathogenesis of temporo-polar gray/white matter blurring in temporal lobe epilepsy.

A 6-year-old boy was operated for right temporal lobe epilepsy with hippocampal sclerosis. Radiological evaluation of the four serial cranial magnetic resonance imaging (MRI) scans and pathological study of the surgical specimen were performed.

MRI was performed 1 month after birth for suspected macrocephaly, at an age of 11 months in the acute phase of a prolonged febrile seizure (the unique febrile seizure episode of his life), at an age of 5 years, when discognitive seizures occurred, and at the age of 6 years, when right temporal lobectomy was performed. The appearance of the right hippocampus changed chronologically: high signal in diffusion-weighted images at 11 months, then atrophic, and high signal in T2-weighted images at 5 years. Conversely, the right temporo-polar gray/white matter boundary was blurred in all serial MRIs. Pathological studies of the resected specimen revealed typical hippocampal sclerosis but did not reveal disturbed cortical architecture or atypical cells.

The epileptogenesis of temporal lobe epilepsy could be a long-lasting process initiated even before febrile seizures. However, it could not be explained by anomalous cortical migration. Further investigations on the “insidious” period are warranted, for example, investigating the role of repetitive subclinical electrical firing in maturing cortex and subcortical white matter.

P24

BROADEN THE PHENOTYPE OF SCN1A CHANNELOPATHIES: RESULTS OF TAIWANESE COHORT STUDY

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The SCN1A gene which encodes the voltage-gated sodium channel alpha 1 subunit (Nav1.1) was reported associating with a spectrum of GEFS+. However, correlating genotypes and phenotypes of SCN1A variants was still challenging. We investigated ten patients with identified SCN1A mutations in Taiwan. By evaluating clinical and genetic relevance of the mutations and correlating them with the clinical significance, we provide a further insight to broaden clinical spectrum associated with SCN1A mutations.

We enrolled patients with identified SCN1A variants. Patients underwent clinical evaluations for factors related to phenotypes. A panel of 90 epileptic related genes was used to identify previously reported potential SCN1A modifier genes.

We enrolled ten children with identified SCN1A mutations including a pair of monozygotic twins. There were two frameshift, one deletion and six missense mutations. Four patients had Dravet syndrome. Two patients had family history of seizure. Two patients had identified potential modifier gene. One patient had focal seizure without temperature sensitivity and a point mutation on exon 1 of SCN1A. The monozygotic twins without family history had discordant presentations. One of them had Dravet syndrome while the other remained asymptomatic.

SCN1A variants can cause focal seizures without fever triggering. A broader spectrum than GEFS+ should be taken into consideration and management should differ from the traditional practice. In the monozygotic twins, we excluded several factors contributing to genotype-phenotype inconsistency. Our study showed there were possible epigenetic factors affecting the phenotypes of familial patients with same genotypes.

P25

ELECTROENCEPHALOGRAPHY IN FOLLOW-UP OF CHILDHOOD EPILEPSY

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The aim is to demonstrate the usefulness and importance of electroencephalography (EEG) as part of the therapeutic strategy in the follow-up of children with epilepsy.

Data for this prospective study were collected from medical documentation of patients at the unit for pediatric neurology within the department of pediatrics in General Hospital in Prilep. This study included 38 children with newly diagnosed epilepsy following electrophysiological, biochemical and neuroimaging investigations and initiated therapy.

Out of 38 children from 1 to 5 years old 4 (10,5%) had epileptic encephalopathy, 14 (36,8%) had focal epilepsy and 20 (52,6%) had generalized epilepsy. The study group is followed for three years and EEG was performed 2 to 4 times per child yearly. During the investigated period in 28 (73,6%) EEG changes disappeared due to appropriate therapy. In 8 children (21%) there was a reduction in the changes. 2 children (5,2%) with epileptic encephalopathy had no improvement on EEG changes. According to changing in EEC features therapy was corrected in 7 children.

Electroencephalography is of great importance in the monitoring of the therapeutic effect in children with epilepsy. Also it gives directions in case of need for change of therapy and self-confidence to clinicians in discontinuation of therapy.

P26

SEIZURE AND NEUROIMAGING CHARACTERISTICS OF EPILEPSY IN CHILDREN BORN VERY PRETERM

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To investigate the seizure and neuroimaging characteristics of epilepsy after neonatal brain injury in children born very preterm.

Using a prospective registry data of the very preterm population in Southern Taiwan, this study investigated the seizure and neuroimaging characteristics of epilepsy in children who are born very prematurely.

Totally 686 very preterm infants were available for follow up till the age of 5 years. Of them, 19 patients had epilepsy: 12 (63.2%) had the generalized seizures and 7 (36.8%) had focal impaired awareness seizures. In total, 6 patients (31.6%) exhibited status epilepticus, whereas 8 patients (42%) had drug-resistant epilepsy. Electroencephalographic assessments revealed that epileptic discharges were distributed equally in the frontal and temporal lobes.

Of the 686 infants, 60 (8.7%) had experienced significant neonatal brain injury, including 34 infants with high-grade intraventricular hemorrhage and 33 with cystic periventricular leukomalacia. Of these 60 infants, 33 received MRI examination: 13 infants exhibited epilepsy and 20 reported no seizure events before the age of 5 years. The MRI characteristics significantly associated with epilepsy after neonatal brain injury were cortical and deep gray matter lesions, persistent white matter cyst, and asymmetric cerebral lesions (all $P < .001$).

Children born very preterm are at high-risk for epilepsy, particularly status epilepticus and drug-resistant epilepsy. Characteristic gray matter and white matter lesions are associated with epilepsy occurrence after neonatal brain injury.

P27

GRANZYME A AS A POTENTIAL BIOMARKER OF ACUTE ENCEPHALOPATHY AND COMPLEX FEBRILE SEIZURES

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Although the precise mechanisms behind acute encephalopathy (AE) remain unclear, it has been suggested that not only inflammation but also apoptosis is involved in the pathogenesis of AE. Granzymes are known to induce apoptosis in virus-infected cells, the participation with inflammation is currently being discussed. Here, we focused on whether granzymes are implicated in the pathogenesis of AE. We assessed the role of apoptosis in the pathology of AE through measuring cerebrospinal fluid (CSF) as well as granzyme and TNF-α levels in AE and complex febrile seizures (cFS) patients.

A total of 31 Japanese pediatric patients with AE (n = 13), including 6 sequelae, and cFS (n = 18) were included. Granzyme A and B levels were measured by ELISA and TNF-α was assessed using the Bio-Plex suspension array system. CSF samples were collected after obtaining informed consent.

CSF granzyme A levels in AE patients were significantly higher than in the cFS group, while no significant difference was found between granzyme B levels in AE and cFS groups. Cytokine TNF-α levels in the CSF of AE patients were significantly lower than in cFS patients. In a comparison of patients with and without sequelae, no significant differences were detected for CSF levels of granzymes A and B and TNF-α.

These results suggest that granzyme A may be a valid predictive biomarker for distinguishing between AE and cFS and that apoptosis or inflammation in AE may be mediated through granzyme A.

P28

THERAPEUTIC HYPOTHERMIA FOR PEDIATRIC REFRACTORY STATUS EPILEPTICUS-A SINGLE CENTER EXPERIENCE

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Refractory status epilepticus (RSE) is a life-threatening emergency defined as persist seizure more than 60 minutes despite of aggressive management. Super-refractory status epilepticus (SRSE) is status epilepticus lasted for more than 24 hours. Treatment of RSE/SRSE requires anesthetic agents and anticonvulsants to achieve burst- suppression background on electroencephalography (EEG). Hypothermia has been reported as an adjuvant therapy to anticonvulsants in RSE/SRSE treatment. We introduce therapeutic hypothermia (TH) for childhood with RSE/SRSE since 2014. Herein, we evaluated the effect of hypothermia on status epilepticus and assessed the long-term outcome.

This was a retrospective and case- control study from Jan 2014 to Dec 2017. We reviewed medical records of whom admitted to the Pediatric Intensive Care Unit (PICU) at Kaohsiung Chang Gung Memorial Hospital for status epileptic with TH management. Only 6 children were enrolled in the study group. Another 12 patients encountered RSE/SRSE without TH was categorized into control group. The selective endpoints were seizure duration in acute stage, PICU admission days, and Glasgow Outcome Score (GOS). The TH was achieved by Artic Sun® temperature management system in this study.

Six patients with RSE/SRSE who received TH with target temperature 34~35°C for 48 or 72 hours in acute stage. Two patients were Febrile Infection-Related Epilepsy Syndrome (FIRES),one was Dravet syndrome and another three patients were traumatic brain injury . The patients with TH had significantly shorter seizure duration than those without TH (32.67±14.20 v.s 89.5±17.15 hours, $P < 0.05$). Two patients in TH group finally died of pulmonary embolism and extremely brain edema. TH did not shorten the ICU stay between groups (29.25±5.63 v.s 33.67±9.51 days, $P=0.673$). The patients received TH had significantly better long -term outcome compared to those without TH (GOS score 2.67±1.09 v.s 2.08±0.6, $P<0.01$). In addition, we provided the evidences that patients with RSE/ RSE receiving TH significantly decrease incidence of later chronic refractory epilepsy.

The therapeutic hypothermia is effective in decreasing seizure burden during acute stage in patients with RSE/SRSE. Our results provided evidences that TH performance in acute stage of RSE/SRSE would shorten seizure duration in the acute phase which led to decreasing occurrence of post-status epilepticus epilepsy and improving long-term survival outcome and morbidity.

P29

ACUTE ENCEPHALOPATHY IN DRAVET SYNDROME

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Acute encephalopathy (EA) is defined as a sudden onset of neurological symptoms, with seizures followed by a long-term unconsciousness until coma, preceded by a febrile infectious episode, associated with non-inflammatory cerebral edema. It is already described in patients with Dravet syndrome (SD). Etiopathogenesis is unknown. We describe two clinical cases, comparing them literature. The aims are to help identify pathogenetic mechanisms, evaluate the role of drug treatment on outcome, design algorithm for the diagnostic and therapeutic management of febrile SE in DS.

We describe the clinical, neuroradiological and eegraphic features of two DS patients with SCN1A mutation.

Almost all cases of EA in DS are characterized by high fever before the onset of symptoms, status epilepticus, coma, fatal outcome or cognitive regression, cerebral edema, subsequent cerebral atrophy, changes in epilepsy after EA. Almost all cases they have mutation of SCN1A gene. Biological data (on blood and liquor) are not always specified. Antiepileptic treatments pre EA and treatment of SE are heterogeneous.

EA is a rare but dramatic complication of the SD. A multi-center study is necessary, in order to have more information on symptomatology, results of biological and neuroradiological examinations and treatment in different stages of evolution. We will try to better characterize this clinical entity and identify potential factors responsible for the onset of AE.

We propose to establish a protocol for the early management of the SE in DS that is prolonged despite appropriate treatment, to try to avoid the evolution towards the EA.

P30

GAIT DISTURBANCE OF DRAVET SYNDROME

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Dravet syndrome (DS) is a rare epilepsy syndrome mainly caused by SCN1A mutations. Ataxic gait and crouching gait are often reported in patients with DS. However, there is no report on the relationship between walking state, seizure frequency, EEG abnormality, and gene mutation in DS at various ages. We investigated the motor abnormalities in patients with genetically proven DS.

In nine patients with DS caused by SCN1A mutations (five patients with null mutations and four patients with missense mutations), we investigated seizure frequency, EEG abnormality and gait. Gait of the patients were analyzed using video recording. We evaluated patient's neurological symptoms using SARA (Scale for the assessment and rating of ataxia) and Berge balance scale.

We observed that the all patients with null mutation of SCN1A gene presented walking in a forward leaning posture without completely progressing the knee joint, not cerebellar ataxia walking. On the other hand, in the patients with missense mutations of SCN1A gene, obvious gait disturbance was not observed in young children, but in older children there was a tendency for a posture inclined forward. In all cases, SARA did not always show high scores. The association between seizure frequency and EEG abnormality and gait disturbance was not clear.

The patients of DS with SCN1A gene mutations were presented walking in a forward leaning posture. The gait disturbance was severe in the patients with null mutation. The motor dysfunction of DS may not be cerebellar ataxia.

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EPILEPTIC FEATURES IN 34 TEENAGERS WITH DRAVET SYNDROME

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To describe the natural history of epilepsy in a cohort of Dravet Syndrome (DS) patients aged 12-20 years, attempting a correlation between epilepsy severity during the course of the disease and cognitive functions and adaptive behavior at the outcome.

We report the epileptic outcome of 34 DS patients (20 F; mean 16 yrs 4 mths, median 16 yrs 2 mths) followed at the Neuropsychiatry Unit of Catholic University in Rome between 2000 and 2017. Patients underwent full clinical examinations -including seizure semeiology and frequency, neuropsychological (Wechsler Intelligence Scales for Children-revised (WISC-R) or Raven Cognitive Progressive Matrices (RCPM) and adaptive behaviour assessments (Vineland Adaptive Behaviour Scale) - longitudinal video-EEG recordings, neuroimaging and genetic tests. On the basis of seizure type and frequency, we determined three severity levels of epileptic outcome: mild (A), moderate (B), high (C).

Our series included 22 patients with complete form of DS, and 12 with the incomplete one. During early childhood (0-5 yrs) we observed only one patient in group A, 13 in group B, and 20 in the group C. During childhood (6-12 yrs) there were: 11 patients in group A, 14 in group B and 9 in group C. During adolescence there were: 14 patients in group A (mean age15 yrs3mths), among them 9 patients have been seizure-free during the last year, 11 patients in group B (mean age 15 yrs 3 mths) and 9 patients in group C (mean age 19 yrs). According to cognitive abilities, during adolescence 9/34 patients had a mild intellectual disability (ID); 14/34 had a moderate ID and 10/34 had a severe ID, only 1 patient did not present ID. The analysis of cognitive course from school-age to adolescence was possible in 24 children: we observed - a stability of cognitive level in 13 adolescents, among them 12 presenting a lowering of epilepsy severity, while a reduction of cognitive level was observed in 11 adolescents, among them 5 presenting a lowering epilepsy severity. Adaptive functions showed better performances in communication and socialization areas, independently of the group the patients belong to, and worse results in daily living and motor abilities.

Three different outcomes of epilepsy are identifiable in adolescence in this cohort. But the relationships between the respective outcomes of epilepsy and cognitive functions were heterogeneous. During adolescence we observed an improvement of epilepsy course in most of the patients (20/34), of these the majority (18/20) showed an improvement in the severity of epilepsy already in the second childhood. Nevertheless only 9 patients preserved a mild cognitive disability. The cognitive functions were more impaired in the group of patients with the most severe epilepsy. However the improvement of epilepsy during adolescence was not accompanied by an improvement of intellectual abilities, rather by a stability of cognitive level, even though it was correlated with an improvement of the adaptive functions and daily living skills.

Further multicentric studies on larger and prospective cohorts are needed to clarify the reciprocal role played by different co-factors such as genotype, epileptic features and treatments in determining the epileptic, cognitive/behavioral outcome of DS during adolescence.

P32

DE NOVO MISSENSE MUTATION OF X-LINKED SMC1A GENE CAUSES A SEVERE EARLY ONSET EPILEPSY AND INTELLECTUAL DISABILITY IN A FEMALE PATIENT

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The structural maintenance of chromosome 1A (SMC1A) gene, encoding part of the cohesion complex, is located on the X chromosome and is known to cause Cornelia de Lange Syndrome (CdLS) in both males and females. For a long time, missense mutations and in-frame coding deletions in SMC1A gene were considered incompatible with life, as such mutations had not been reported in neither male nor female patients. However, recently, literature reported such mutations in females with severe epilepsy and intellectual disability. Here we report a female patient, lacking the typical feature of CdLS, diagnosed with de novo SMC1A mutation presenting with a severe early onset epilepsy and profound intellectual disability.

This 5 years and 9-month-old girl exhibited the first seizure at the age of 5 months. The seizure pattern was characterized by upward gaze, generalized clonic seizures, and lip cyanosis. Since then, multiple seizure types, including epileptic spasms, atypical absence seizures, focal seizures with or without evolving to bilateral tonic-clonic seizures developed. Multiple anticonvulsants and ketogenic diet were tried, but the clinical efficacy on seizure control was limited. The patient also showed facial dysmorphism, hypotonia, absence of speech, and small hands and feet. A genetic testing was performed.

Whole genome sequencing showed SMC1A 3091 G>A mutation, which resulted in an amino acid substitution of Arginine to Histidine (R1066H).

SMC1A gene should be included in female patients with early infantile onset epilepsy and severe intellectual disability.

P33

COMPOUND HETEROZYGOTE OF NOVEL ALDH7A1 MUTATIONS

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To describe novel mutations of ALDH7A1 gene and the phenotype.

We report a newborn baby transferred to our hospital due to respiratory distress and infantile seizures. He was born at gestation 39 weeks with birth weight of 2865g with normal Apgar scores. He was a first baby of non-consanguineous couple with no family history of neurological and metabolic disorder. After admitted to neonatal intensive care unit (NICU), he got pulmonary hemorrhage and was intubated for two days. His respiratory state improved gradually and his seizures decreased with midazolam, levetiracetam and phenobarbital. On 41st day after birth, his attacks relapsed but intravenous pyridoxal phosphate hydrate abolished them immediately. His interictal electeroencephalogram was normal. His pipecolic acid level was markedly increased to 23.7μmol/L in serum (normal range(NR): 1□3.2) and 5.6μmol/L in spinal fluid (NR: <0.12). His α-aminoadipic semialdehyde (α-AASA) level was also increased to 7.4μmol/L in serum (NR: <0.1) and 11.0μmol/L (NR: <0.1). Genetic testing revealed a compound heterozygous mutation NM_001182.4:[c.1196G>T];[c.1200+1G>A] of ALDH7A1 gene. After given oral pyridoxal phosphate, he had no seizure without any antiepileptic drugs. His developmental milestones were head control at six months old and sitting alone at 13 months old.

We found novel mutations of ALDH7A1 gene. Although he has not have any seizures after administrating pyridoxal phosphate, he has developmental delay. We have to observe his intellectual development.

P34

SCN2A MUTATION IN AN INFANT PRESENTING WITH MIGRATING FOCAL SEIZURES AND INFANTILE SPASM RESPONSIVE TO A KETOGENIC DIET

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SCN2A mutations have been identified in various encephalopathy phenotypes, ranging from benign familial neonatal-infantile seizure (BFNIS) to more severe forms of epileptic encephalopathy such as Ohtahara syndrome or epilepsy of infancy with migrating focal seizure (EIMFS).

Thus far, no particularly effective treatment is available for severe epileptic encephalopathy caused by SCN2A mutations in children.

We present the case of a boy who developed seizures on the third day of life and received a diagnosis of EIMFS based on his clinical presentations and electroencephalography reports. Antiepileptic drugs, namely oxcarbazepine, phenytoin, valproate, levetiracetam, and clonazepam, as well as adrenocorticotropic hormone therapy failed to reduce the severity of the seizures.

Seizure pattern changed to infantile spasm with extensor thrust since 5 months of age. A ketogenic diet consisting of a medium-chain triglyceride recipe was introduced at 8 months of age and the seizures were resolved in the following 10 months.

A de novo mutation in SCN2A (c.573G>T; p.W191C) was proven through next-generation sequencing.

P35

ATYPICAL PYRIDOXINE-DEPENDENT EPILEPSY: A RARE CAUSE OF FAMILIAL EPILEPSY

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Pyridoxine-dependent epilepsy had been identified as a deficiency of the enzyme 1-α-aminoadipic semialdehyde dehydrogenase (ALDH7A1). The classical picture is characterized by severe, persistent neonatal seizures that are refractory to treatment with antiepileptic drugs but can be controlled by administration of pyridoxine. Here we report two siblings presenting with atypical clinical pictures of ALDH7A1 deficiency.

The elder sister and the younger brother exhibited the first afebrile seizure at the age of 19 days and 3 months, respectively. The seizure types could be described as generalized clonic seizures or focal tonic seizures with evolving to bilateral tonic-clonic seizures. The two siblings also showed cluster febrile seizures during the period of follow-up. The EEG and brain MRI revealed normal results. Both of them showed normal developmental milestones for their ages. Phenobarbital was prescribed but the symptoms persisted. A genetic testing was performed.

Whole genome sequencing showed compound heterogeneous ALDH7A1 gene mutations: one of the mutations was a 965 C>T mutation, which resulted in an amino acid substitution of alanine to valine (A322V); and the other was a 1547 A>G mutation, which resulted in an amino acid substitution of tyrosine to cysteine (Y516C). Vitamin B6 100mg QD was prescribed and phenobarbital was discontinued. The patients became seizure free even if they experienced febrile illness.

"Hidden" vitamin B6 deficiency might be rare but treatable causes of familial epilepsy expanding beyond the classical phenotypes.

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KCNQ2 MUTATIONS IN CHILDHOOD NON-LESIONAL EPILEPSY: VARIABLE PHENOTYPES AND NOVEL MUTATIONS IN A CASES SERIES

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Epilepsy caused by a KCNQ2 gene mutation usually manifests the phenotype of a neonatal seizure during the first week of life. KCNQ2 associated epilepsies continues to be reported on. However, the genotypes and phenotypes of the KCNQ2 mutations are still noteworthy.

The KCNQ2 sequencings were done selected from 131 nonconsanguineous pediatric epileptic patients (age range: 2 days to 18 years) with non-lesional epilepsy.

Eleven (8%) index patients had identified KCNQ2 mutations. The mutations were E515D□V543M□R432C□S247L □c.387+1 C>A (splicing), R581X and P285L. All mutation variants were predicted to be pathogenic by SIFT, PolyPhen and ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/) except V543M and R432C were variant of unknown significance. Two patients carrying S247L and P285T are novel and de novo had refractory neonatal seizures and suppression-burst EEG; however, seizures were remission after 6 and 2 months old respectively. The outcomes of KCNQ2 associated epilepsy varied from benign to severe consequences in our patients. Patients carrying c.387+1 C>A (splicing), R581X and V543M presented as benign familial neonatal convulsions. Five patients had E515D, but their seizure outcomes were favorable except one with moderate delay. Three patients (2 E515D and 1 R432C) presented with rolandic spikes in awakening and prominent spikes after sleeping, compatible with continuous spikes and waves during slow-wave sleep (CSWS). In addition to their relatives, 24 subjects were documented KCNQ2 mutations. Of them, neonatal seizures were 79% (19/24).

The KCNQ2 mutation accounts for 8% of pediatric non-lesional epilepsy. KCNQ2 mutations can cause variable phenotypes in children. S247L and P285T are novel mutations and can cause neonatal epileptic encephalopathy.

P37

THE SAFETY OF ACTH THERAPY FOR INFANTILE SPASMS ASSOCIATED WITH HYDROCEPHALUS

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The ideal treatment for infantile spasms is unclear. Intramuscular adrenocorticotropic hormone (ACTH) is most widely used for the treatment of infantile spasms; however, it is associated with severe side effects. We need to evaluate the risk of adverse effects when administering ACTH therapy. Hydrocephalus is a well-known cause of infantile spasms. There are no reports on the safety of ACTH therapy in the treatment of infantile spasms in patients with hydrocephalus. This report demonstrates the efficacy and safety of ACTH therapy in the treatment of infantile spasms in patients with hydrocephalus.

The patient was a 5-month-old girl with head enlargement, a bulging anterior fontanel, and psychomotor regression. Ventricular enlargement was observed on head CT. The patient was diagnosed with a communicating hydrocephalus, which was treated with a VP shunt. After a while, she experienced a series of epileptic spasms and hypsarrhythmia. She was diagnosed with hydrocephalus-associated infantile spasms. Antiepileptic drugs had no effect. Intramuscular ACTH was started and was continued for six days until the disappearance of her seizures. No serious adverse events, including VP shunt infection or cerebral hemorrhage, occurred during ACTH therapy.

In this case, because extreme thinning of the brain parenchyma was identified from images, the risk of cerebral haemorrhaging caused by ACTH treatment was believed increase by adding continuous drainage; however, we were able to safely carry out ACTH treatment in a short period of time by repeated head CT.

P38

SCALP HIGH-FREQUENCY OSCILLATIONS IN A SPECTRUM OF PEDIATRIC EPILEPSIES CHARACTERIZED WITH SLEEP-ACTIVATED SPIKES IN EEG

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Epileptic high-frequency oscillations (HFOs) in the ripple (80 – 200/250 Hz) band in electroencephalogram (EEG) data are recordable over the scalp and may reflect disease activity. We aimed to firstly compare the amount and characteristics of ripple oscillations among various types of pediatric epilepsies with the common characteristics of sleep-activated spikes in scalp EEG.

The subjects were a total of 102 children (59 boys, 43 girls) who were diagnosed with epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS) or related disorders, benign epilepsy with centrotemporal spikes (BECTS), Panayiotopoulos syndrome (PS), other types of focal epilepsies, febrile seizures, and EEG abnormalities without clinical seizures in 14, 23, 16, 19, 8, and 22 patients, respectively. In each individual sleep EEG record, we manually selected a 60 second-long-data section on a yearly basis, and detected ripples associated with spikes by a semi-automatic detection tool with subsequent visual confirmation. Then we analyzed the number of occurrence, frequency and duration of ripples in each EEG data.

Regarding ripples in the initial EEG records, the number of occurrence of ripples was significantly higher in CSWS than all the other diagnostic groups. Ripples tended to be more frequently observed during young age, particularly in CSWS, and to vanish in adolescence in all groups. There were no significant differences regarding frequency or duration of ripples among the groups.

Our study suggests that ripple oscillations associated with spikes in CSWS may be related to the pathophysiology of epileptic encephalopathy in childhood.

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OHTAHARA SYNDROME IN KCTN1-RELATED ENCEPHALOPATHY

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To describe the electroclinical features of an infant diagnosed with KCTN1-related encephalopathy.

We report the case of a 21 month-old child, with seizure onset at 3 months, high daily frequency (up to 200/day), 7-8s in duration, presenting in cluster during both wake and sleep, characterized by tonic elevation of the arms and sometimes left eye and mouth deviation. The interictal EEG pattern was characterized by slow-waves discharges intermixed with spikes alternated to low-voltage delta activity, with higher voltage on the posterior and right hemisphere; during sleep a burst-suppression like activity was observed. Ictal EEG was characterized by high amplitude slow wave followed by alpha-like activity of variable amplitude. VGB, ACTH, NZP, TPM and Pb were subsequently added with only temporary benefit on seizure severity. The neurologic examination has shown during the follow-up a spastic-dystonic posture and a severe cognitive impairment, with little benefit given from seizure reduction. Baclofen treatment was added with limited benefit on spasticity. MRI showed a marked cortical atrophy and delayed myelination with relative spare of basal ganglia and cerebellum at 12 months. After broad diagnostic work-up a de novo mutation c.1421G>A-p.(Arg474His) was found from a gene panel of epileptic encephalopathies.

KCNT1 has been associated to Ohtahara syndrome only in one case1 in which hemizigosity was demonstrated due to uniparental disomy. The exact mutation of our patient was reported in literature in 4 other patients reported to have a MMPSI or West-syndrome phenotype with earlier onset compared to our patient2,3. This case contributes to the definition of the electoclinical phenotype of KCTN1-related encephalopathy.

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P40

EARLY-ONSET GENETIC EPILEPSIES AND EPILEPTIC/DEVELOPMENTAL ENCEPHALOPATHIES: A SINGLE-CENTRE EXPERIENCE IN REGGIO EMILIA, ITALY

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We reviewed cases of early-onset genetic epilepsies and epileptic/developmental encephalopathies (DEE) diagnosed in Santa Maria Nuova Hospital, Reggio Emilia (Italy).

Inclusion criteria: epilepsy or DEE with onset ≤ 2 years of life and a genetic diagnosis made between 1/1/2013 and 31/12/2017, by means of array-CGH, single gene sequencing, targeted NGS or whole exome sequencing. We collected demographic and clinical data.

21 pathogenetic variants (PV) (n=4 PRRT2; n=3 PCDH19; n=2 1p36 microdeletion syndrome; n=2 KCNQ2 encephalopathy; and GABRA1, ATP1A2, KCNQ3, SCN2A, SCN1B, FOXG1, MECP2 duplication, MECP2 mutation, SCN1A, 1q44 microdeletion: 1 each) and 7 variants of uncertain clinical significance (VUS) (3 de novo; 3 A.D. inherited from an unaffected parent, 1 A.R. homozygous inherited from heterozygous carrier parents) were identified. Onset occurred in the neonatal period in 6 (PV: 4/21, 19%); between 1-12 months in 9 (PV: 7/21, 33%), between 13-24 months in 13 patients (PV: 10/21, 48%). Eight patients had a clinical diagnosis of focal-onset epilepsy (PV: 7/21, 33%), 6 of epilepsy with fever susceptibility (PV: 4/21, 19%), and 14 of DEE (PV: 10/21, 48% and VUS: 4/7, 57%). Seven PV (7/21, 33%) and 4 VUS (4/7, 57%) patients were pharmacoresistant in the long-term follow-up (number of antiepileptic drugs -mean, range - VUS: 4.14, 0-15; PV: 3.85, 1-9).

Our group of genetic epilepsies and DEE shows molecular and phenotypical heterogenity. A quarter of cases harbour a VUS. Approximately half of the cases are DEE (higher rate in the VUS group). Long-term pharmacoresistance is frequent.

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THE GENETIC LANDSCAPE OF EARLY ONSET EPILEPSY/EPILEPTIC ENCEPHALOPATHIES IN SAUDI ARABIA AND THE IMPACT ON THE TREATMENT

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The causes and the management of early onset epileptic encephalopathies represent a significant challenge. De-novo mutations are frequently identified; recessive disorders are rarely reported.

We sought to identify genetic causes of unexplained early onset epileptic encephalopathies in a highly consanguineous population, evaluate genotype-phenotype correlations and the impact on treatment.

We enrolled 300 patients with an unexplained early onset epileptic encephalopathy (without malformations of cortical development, hypoxic-ischemic insult or inherited metabolic cause). We performed detailed phenotypic assessment including seizure presentation, electroencephalography, and magnetic resonance imaging. Whole exome sequencing or epilepsy gene panel were performed in this cohort.

We identified disease-causing variants in 195 children (62 %), including mainly the following genes: SLC13A5 (n=10), FRRS1L (n=7), ADAT3 (n=7), WWOX (n=5), AFG3L2 (n=5), ARV1 (n=4), KCNA2 (n=3), KCNMA1 (n=2), SLC6A1 (n=2), PLCB1 (n=2), TRAK1 (n=2), etc. 165 variants were recessive, and only 30 variants were de novo. These genetic findings impact on treatment choices in 25% of patients.

We characterize the genetic landscape of unexplained epileptic encephalopathies in a highly consanguineous population, and demonstrate that recessive genes, in contrast to Western countries, are implicated in the majority of cases. Identification of the causative mutation is important for prognostic and genetic counseling, and may also carry treatment implications.

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EFFECTIVENESS OF VITAMIN B6 FOR WEST SYNDROME

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Some literature reports that Vitamin B6 is effective for West syndrome. However, correlation between the efficacy and etiology is still unclear. We report a girl with neonatal Herpes simplex viral infection who had West syndrome. She received a high-dose vitamin B6 treatment and showed good outcome.

The patient was a 8-month-old girl born at 37 weeks of gestational age with a birth weight of 2514g. She had diagnosed as systemic Herpes simplex virus (HSV) 2 infection due to apnea. Serum HSV was confirmed during neonatal period, but it has been negative at 7 month of age after acyclovir and foscarnet treatment. Her development was normal at that moment. She showed spasm attack at 8 month of age. Hypsarhythmia was observed in interictal EEG. Vitamin B6 was administered up to 50 mg/kg/day, the spasm attack was altered. No hypsarhythmia was seen in EEG after treatment.

We reviewed medical records with West syndrome patient who hospitalized Juntendo University Nerima Hospital during year 2006-2017. The efficacy of vitamin B6 was evaluated retrospectively.

13 patients were hospitalized. 4 cases were symptomatic West syndrome and 9 cases were cryptogenic one. Vitamin B6 was administered as initial treatment for 10 cases. 2 cases were effective and 1 case terminated the treatment due to drug-induced liver dysfunction. The effective cases were proposed case and a patient with tuberous sclerosis.

Vitamin B6 efficacy was 20% in our institution. Interestingly, both 2 cases were symptomatic West syndrome. Previous report suggested vitamin B6 was effective for symptomatic West syndrome. These results may suggest vitamin B6 modifies neurological-related metabolic pathway.

P43

PRELIMINARY RESULTS OF 1 AND 2 YEARS FOLLOW-UP STUDY IN THE PATIENTS WITH WEST SYNDROME IN GEORGIA

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This syndrome hasn't been thoroughly investigated in Georgia and our purpose is to assess clinical and etiological peculiarities of West syndrome. The evolution of West syndrome and its relation to patient characteristics. Neuropsychological outcome (after 1 and 2 years) and its early predictors.

We evaluated 31 patients (17 male, 14 female) with infantile spasms. Mean age of seizure onset 6.3 months. Inclusion criteria were newly diagnosed patients with infantile spasms from 2 to 18 months, abnormal EEG and written informed consent of parents/ caregivers. We collected birth, family and seizure detailed history. All patients were examined neurologically, investigated with prolonged sleep and awake video - EEG, brain MRI, developmental screening tests (ASQ) was done at admission.

One year follow-up assessments were provided in 22 (74%) cases. One patient died. Neuropsychological development was not changed in 12 (55%) individuals, in three cases some improvement was detected and in remaining six cases deterioration of development was identified. In all six cases of developmental deterioration seizures were started before seven months of age, this association was statistically significant (Pearson Chi-Square 6.3; df 1; p=0.019). Sixteen (52%) individuals were treated with ACTH only. In 12 (39%) cases ACTH and AED were used simultaneously and remaining two cases were treated with AED only.

In our study number of patients isn't much, though preliminary findings are consent to the other author's studies. This study is still in the process.

P44

IN VITRO CELL DIFFERENTIATION ANALYSIS OF INDUCED PLURIPOTENT STEM (IPS) CELLS FROM LEIGH-LIKE ENCEPHALOPATHY PATIENT WITH DNM1L MUTATION INTO NEURONAL AND MUSCULAR CELLS

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DNM1L, a member of dynamin superfamily, is a key protein involving in mitochondrial fission. Recent years, increasing number of patients with epileptic encephalopathy associated with DNM1L mutation have been reported. We encountered an infant with marked hypotonia and infantile spasms, and his electroencephalogram exhibited suppression-burst pattern. Although brain MRI didn't show typical abnormal images, brain pathology was compatible with Leigh encephalopathy. Whole exome sequence analysis revealed heterozygous DNM1L mutation (c.1217T>C, p.Leu406Ser). In order to clarify the mechanism of this disease, we performed cell differentiation analysis of iPS cells derived from the patient.

iPS cells were established from patient-derived fibroblasts, and they were differentiated into neuronal (dopaminergic neurons) and muscular cells. The differentiation efficiency was measured in iPS cells with DNM1L mutation and control. Because morphological abnormalities of mitochondria are common in fibroblasts with DNM1L mutation, mitochondrial shape were observed using Mito-Tracker GREEN FM and they were compared with control iPS cells.

The differentiation efficiency of patient's iPS cells into neuronal and muscular cells was impaired comparing with control iPS cells. Mitochondria in differentiated neuronal and muscular cells exhibited abnormally enlarged and prolonged shape. It is suggested that mitochondrial fission was disturbed in neuronal and muscular cells that seems to explain multi-organ failure observed in our patient.

P45

GOOD OUTCOME OF EARLY HEMISPHERECTOMY OR MODIFIED HEMISPHERECTOMY FOR REFRACTORY EPILEPSY DUE TO FOCAL ABUSIVE HEAD TRAUMA AND STROKE IN INFANCYS AND TODDLERS

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Hemispherectomy is an surgical procedure to treat intractable epilepsy effectively in adults with unilateral cortical disease secondary to acquired brain or congenital lesions. The topic will present a series of children with drug-resistant epilepsy related to unilateral lesion underwent hemispherectomy in our hospital.

From 1998 to 2018, totally 12 cases who received hemispherectomy/ modified hemispherectomy enrolled. 4 infants or toddlers who suffered from abusive head trauma or stroke were selected for analysis. Their clinical outcomes were accessed including seizure reduction frequency, cognitive function and development performance and adverse effects.

For the 4 selected cases, 3 underwent hemispherectomy and 1 underwent quadrispherectomy. The seizure reduction frequency showed 2 with free of disabling seizures and 2 had reduction frequency more than 90%. After operation, the 4 patients had follow-up from 6 months to 5 years with remarkable improvement of development including motor function and cognitive function.

Modified hemipsherectomy is important surgical method for infants or toddlers who suffered from abusive head trauma and strokes. The 4 cases in our series showed seizure free or almost seizure free for 6 months to 6 years might be indicative of early surgical intervention is important to achieve good surgical outcomes.

P46

INCREASED SUBCORTICAL OLIGODENDROGLIA-LIKE CELLS IN PHARMACO-RESISTANT FOCAL EPILEPSY IN CHILDREN CORRELATE WITH EPILEPTIC SPASMS

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Pediatric epilepsies often involve more extratemporal regions than adult epilepsies. Oligodendroglia-like cells (OLC) have been observed in surgical specimens in pharmaco-resistant epilepsy children. We hypothesize that OLC recruiting multiple lobe epileptogenic zones in pediatric pharmaco-resistant focal epilepsy, especially epileptic spasms (ESs).

We examined the surgical specimens from 30 children who underwent epilepsy surgery (mean age; 9.7years old). Immunohistochemical assay used Olig2 for a marker of OLC. We counted the OLC population in 3 sites; gray matter, junction of gray/white matter (Junction), white matter, and compare them to their clinical profiles.

The histopathological diagnosis was as follows; 14 (47%), focal cortical dysplasia (Type I;4, Type II;9, III;1); six (20%) oligodendrogliosis; six (20%) astrocytic gliosis; two (7%) protoplasmic astrocytopathy; two (7%) tuberous sclerosis. Nine children with ESs showed significantly increased OLC population at Junction (p=0.021) and white matter (p=0.025) compared to 21 children with other seizure types. The OLC population in the white matter was significantly increased in 15 multiple lobe resection (p=0.028) compared to that of 15 single lobe resection. There was a positive correlation between the number of resected electrodes and OLC population at white matter (correlation coefficient 0.581, p=0.001), between the number of resected electrodes and Junction (correlation coefficient, 0.426, p=0.027).

In pharmaco-resistant epilepsy children with the increased OLC, they presented ES and required the multiple lobe resection. The increased subcortical OLCs may contribute to the extensive epileptic network to provoke ESs.

P47

EFFICACY OF VIGABATRIN THERAPY FOR TUBEROUS SCLEROSIS: SEIZURE AND NEUROPSYCHIATRIC OUTCOMES

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To evaluate the efficacy of vigabatrin (VGB) for seizure control and neuropsychiatric outcomes in children with tuberous sclerosis (TS).

We examined a series of 17 children with TS visiting Tohoku University Hospital in Japan during 2010 and 2015. VGB was given to the patients for limited 6 months with titration from 30 mg/kg/day as an initial dose. After that, neuropsychiatric examination was performed by several psychological tests on 25 patients with tuberous sclerosis (14 VGB administrated and 11 non-administered) with the cooperation of four centers in Japan.

Main seizure types were classified into spasms (n =10) or tonic seizures (n = 7). Seizure reduction was positively associated with seizure type of infantile spasms. Seizure type of infantile spasm was an independent favorable predictor and also associated with long-term seizure reduction. No major adverse events of VGB treatment were observed. The neuropsychological prognosis was more favorable in the VGB treatment group, especially in patients with severe intellectual disability.

VGB is first-line treatment for TS children with infantile spasms. VGB administration could improve not only seizure control but also neuropsychiatric outcomes.

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